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Launched in 2013, *United European Gastroenterology Journal* is the official Journal of United European Gastroenterology (UEG), a professional non-profit organisation combining all the leading European societies concerned with digestive disease. UEG's member societies represent over 22,000 specialists working across medicine, surgery, paediatrics, GI oncology and endoscopy, which makes UEG a unique platform for collaboration and the exchange of knowledge.

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Letter of Thanks for UEG Week 2015 Reviewers

Dear Colleagues,

On behalf of the UEG Scientific Committee, I would like to take this opportunity to thank you most sincerely for your contribution as an abstract reviewer for the original programme of UEG Week Barcelona 2015.

The abstract reviewing process has been again very important this year with a number of innovations introduced to improve especially the poster abstract presentations.

I know just how much time and effort reviewing abstracts takes, but without your expertise we would not have the quality that I believe we have achieved in the free paper and poster sessions, and UEG Week would not be the top international digestive diseases meeting that it has become today. Thank you!

I am delighted to announce that we received a record number of 3758 abstracts in total for UEG Week Barcelona 2015. In total, 2304 abstracts were accepted, giving an acceptance rate of 66.34%. 441 abstracts will be delivered as oral presentations and 1863 as posters. I am even more pleased to tell you that standards have again reached a very high level and we can expect to be exposed to most interesting research and great presentations.

This high volume and high standard confirm that UEG Week is the most important forum at which to present your best research. Additionally, we have received 62 video cases which were formally evaluated by the Scientific Committee for presentation. As in previous years, late-breaking abstracts have been scored by the Scientific Committee for presentation in Barcelona.

The quality of reviewing this year was excellent, but if you have any further (positive or negative) comments, please do let us know!

Finally, but most importantly, thanks to all investigators both within and outside Europe who have submitted their research to the meeting, and who are clearly contributing to making UEG Week Barcelona 2015 such a great success!

Professor Magnus Simrén
Chair, UEG Scientific Committee, Barcelona 2015

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MONDAY, OCTOBER 26, 2015 08:00–10:30

OPENING PLENARY SESSION – HALL 6

OP001 COLONOSCOPIC PERFORATIONS IN THE ENGLISH NHS BOWEL CANCER SCREENING PROGRAMME (NHSBCSP) - BEWARE DIAGNOSTIC PERFORATIONS AND THE SIGMOID COLON

E. Derbyshire[1], A. Hungin[2], C. Nickerson[3], M. D. Rutter[1], on behalf of NHSBCSP Evaluation Group
[1]*North Tees & Hartlepool NHS Foundation Trust, Stockton-on-Tees,* [2]*Durham University, Durham,* [3]*NHS Cancer Screening Programmes, Sheffield, United Kingdom*

Contact E-mail Address: edderbyshire@hotmail.com
Introduction: Colonoscopies in the English National Health Service Bowel Cancer Screening Programme (NHSBCSP) are offered to 60-74 year olds with an abnormal Faecal Occult Blood Test and are performed at 61 Bowel Cancer Screening Centres (BCSCs) in England. There is a robust system for capturing details of adverse events, including perforation, following colonoscopy; patients are contacted at least twice post procedure and details are entered onto a national web based database.
Aims & Methods: This study aimed to (1) determine the overall rate of perforation in the NHSBCSP (2) describe perforation presentation, management and outcomes (3) determine post perforation surgery, stoma, morbidity and mortality rates and (4) identify factors associated with poorer patient outcomes.
We identified all reported colonoscopic perforations from the start of the NHSBCSP in 2006 up to 13/03/2014. The NHSBCSP defines perforation as: air, luminal contents or instrumentation outside the gastrointestinal tract. The database was interrogated to identify patient and procedure details. Bowel Cancer Screening Centres completed a detailed online questionnaire on patient presentation, management and outcome. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20. Fisher's exact test and Pearson's chi-square were used to assess explanatory and outcome variables. A p value < 0.05 was considered signifcant.
Results: From 263,129 endoscopic procedures, 147 perforations were identified, a rate of 0.06%. Complete data was received on 117 perforations. 69.2% of perforations were therapeutic. The endoscopist visualised the perforation in 12.8% of cases applying endoclips in 10.2%. Most diagnostic perforations occurred in the sigmoid colon ($n = 12$). Of 115 patients admitted to hospital, 54.8% had surgery. Diagnostic perforations were significantly associated with the need for surgery ($p = 0.001$) (RR:1.86, 95% CI 1.39-2.49). A stoma was formed in 26.1% of those having surgery, male sex ($p = 0.015$) (RR:2.07, 95% CI 1.05–4.07) and a colorectal location in the sigmoid colon when compared with all other colorectal locations ($p = 0.000$) (RR:2.56, 95% CI 1.50-4.38) were significantly associated with stoma formation. 19.7% had post perforation morbidity defined as an in-patient complication or new diagnosis following admission. Diagnostic perforations ($P = 0.009$) (RR:2.70, 95% CI 1.37-5.35) and surgery ($p = 0.000$) (RR:38.18, 95% CI 2.37-613.81) were significantly associated with post perforation morbidity. Median hospital stay was 9.5 days (range 0-51 days). 25.2% of patients were admitted to the Intensive Care Unit. The mortality rate was 0.87%.
Conclusion: (1) This is the largest cases series, to our knowledge, specifically reporting outcomes after colonoscopic perforation in Europe. (2) Over a half of perforations admitted are likely to require surgery and over a quarter are likely to leave hospital with a stoma (3) A post-perforation morbidity rate of 19.7% and mortality rate of 0.87% compares favourably with other series (4) Diagnostic Perforations carry a significant risk of poorer patient outcomes including surgery and post perforation morbidity (5) Perforations in the sigmoid colon carry a significant risk of stoma formation.
Disclosure of Interest: None declared

OP002 A PANCREATIC DIFFERENTIATION PLATFORM TO STUDY CYSTIC FIBROSIS IN A DISH

M. Hohwieler[1], S. Renz[1], T. Seufferlein[1], A. Illing[1], **A. Kleger**[1]
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Introduction: Current scientific efforts mainly focus on the pulmonary manifestation of cystic fibrosis (CF) but the pancreatic phenotype represents particularly in long-term survivors an increasingly important hurdle. Recently, it has been shown that different mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) determine different risks of pancreatitis. Present literature implicates CFTR-function already in the development of pancreatic progenitor cells. Induced pluripotent stem cells (iPSC) present a powerful tool to investigate embryonic development but also to model diseases.
Aims & Methods: The precise mechanism how CFTR-mutations lead to exocrine but also endocrine insufficiency and regulate development of the pancreas is poorly understood and relevant preclinical models are lacking. Herein, we applied a series of experimental tools to patient-specific induced pluripotent stem cells to bridge the gap between CFTR genotype and pancreatic phenotype.
Results: First, we report the generation of induced pluripotent stem cells from several cystic fibrosis patients and healthy control individuals from plucked human hair-keratinocytes. **Second**, we developed a step-wise differentiation protocol to recapitulate pancreatic exocrine and ductal commitment in the dish. Briefly, precise titrations of a complex cocktail of signalling clues mimicking pancreatic development allowed us to obtain virtually pure cultures of definitive endoderm but most importantly up to 60% of true pancreatic Nkx6.1/Pdx1-double positive progenitors. Subsequently, we developed these progenitors to form three-dimensional organoids, which can be passaged >6 passages *in vitro*. Detailed characterisation of these organoids including confocal laser microscopy and quantitative PCR techniques revealed mostly ductal but also exocrine pancreatic tissue. **Third**, we applied our CFTR-mutated and control iPSCs to this culture system and compared their step-wise pancreatic commitment capacity. Interestingly, there was no relevant difference between both genotypes reaching similar efficiencies of definitive endoderm, pancreatic endoderm and exocrine/ductal cells. **Finally**, we applied a series of assays to these cultures to phenotype the CFTR-genotype in the dish. While CFTR-mutated exocrine cultures appeared less robust but were still able to form pancreatic organoids, functional CFTR-activation revealed a dramatic difference: Forskolin, an established CFTR-activator, was applied to our organoid-cultures and lead to a pronounced and rapid swelling in wild-type cultures but to no relevant reaction in CFTR-mutant organoids.
Conclusion: Summarized, we provide a patient-specific platform to mimic and study pancreatic phenotypes of cystic fibrosis in a dish, a system never reported so far. Hereby, we ultimately erase a remaining hypothesis that CF-patients have defects in pancreatic development. Moreover, we reproduce the CF phenotype in our novel culture system to provide a patient- and pancreas- specific drug-screening platform.
Disclosure of Interest: None declared

OP003 TLR SIGNALLING IS DYSREGULATED IN OESOPHAGEAL ADENOCARCINOMA THROUGH SOMATIC MUTATIONS

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Introduction: Altered innate immune signalling may disrupt host-microbe homeostasis and promote an inflammatory microenvironment that favours tumourigenesis. The objective of this project was to assess whether somatic mutations in oesophageal adenocarcinoma (OAC) could interfere with Toll-like receptor (TLR) signalling, with a specific focus on TLR4.
Aims & Methods: We interrogated the mutational profiles of TLR genes in 170 OAC samples, which had undergone whole genome sequencing as part of the oesophageal ICGC study. We performed site-directed mutagenesis and created ten plasmids expressing mutant TLR4 with a CMV promoter (nine single nucleotide variants (SNVs), and one plasmid combined two SNVs). Luciferase reporter gene assays were performed in HEK293 cells stimulated with synthetic monophosphoryl lipid A (MPLA) to assess how the mutants altered TLR4 signalling and downstream activation of nuclear factor kappa B (NF-κB). Three of the TLR4 mutants were taken forward for transfection into the OAC cell lines OE33 and JH-EsoAd1, and ELISA was used to measure cytokine secretion after stimulation with MPLA and lipopolysaccharide (LPS).
Results: The TLR signalling pathway appeared to be recurrently mutated with missense mutations in 23/170 (13.5%) of tumour samples, including mutations in TLR1 (1.2%), TLR2 (0.6%), TLR4 (4.7%), TLR5 (0.6%), TLR7 (1.8%), TLR9 (1.2%), and MYD88 (1.5%). Based on our data and another recent study by Dulak *et al.*[1], TLR4 mutations were the most frequent (5.4% combined data). One tumour sample contained two TLR4 mutations, E439G and F703C. Interestingly, the mutation E439G was identified both in our dataset and in the study by Dulak *et al*. Furthermore, *in silico* modelling suggested that the E439G mutation is located proximal to the dimerization interface and may disrupt hydrogen bonds in the binding site of LPS and MD2. The use of NF-κB luciferase reporter assays demonstrated a significant decrease in ligand-dependent signalling for 7/9 of the TLR4 mutations tested in HEK293 cells. A double mutation of E439G with F703C revealed a further decrease in TLR4 signalling. Similarly, the concentration of IL-8 was significantly lower for TLR4 mutants R787H and E439G + F703C transfected into OE33 and JH-EsoAd1 cells stimulated with either MPLA or LPS, in comparison to wild-type TLR4. A similar trend was observed for IL-6. Interestingly, no significant decrease in TLR4 signalling was observed for mutant E439G stimulated with LPS in the OAC cell lines, suggesting that the strong agonist LPS is still able to bind the mutated ligand binding site, in contrast to the weak agonist MPLA.
Conclusion: TLR4 is recurrently mutated in OAC, and the majority of these mutations showed decreased TLR4 signalling in response to ligand stimulation in HEK293, OE33 and JH-EsoAd1 cells. The biological relevance of this in relation to host-microbe homeostasis and carcinogenesis is being explored.

Reference

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Disclosure of Interest: None declared

OP004 A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF OZANIMOD, AN ORAL S1P RECEPTOR MODULATOR, IN MODERATE TO SEVERE ULCERATIVE COLITIS: RESULTS OF THE MAINTENANCE PERIOD OF THE TOUCHSTONE STUDY

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Introduction: Ozanimod (RPC1063) is an oral, selective sphingosine 1-phosphate (S1P) 1 and 5 receptor modulator in clinical development for the treatment of ulcerative colitis (UC) and relapsing multiple sclerosis. The objective of the maintenance period of TOUCHSTONE was to evaluate the longer-term efficacy and safety of 0.5 mg (low dose, LD) and 1.0 mg (high dose, HD) ozanimod in comparison to placebo (PBO), in patients with moderate to severe UC.

Aims & Methods: This randomized, double-blind, placebo-controlled trial assessed the efficacy, safety and tolerability of two orally administered doses of ozanimod vs placebo in patients with moderate to severe UC. A total of 197 patients were randomized (1:1:1) and treated once daily with PBO (n = 65), LD (n = 65) or HD (n = 67). As previously reported[1], a significantly greater proportion of patients receiving HD were in clinical remission, clinical response, and had mucosal improvement than LD or placebo patients at week 8, the primary endpoint for induction. The patients who achieved clinical response at week 8 continued into the maintenance period (MP) with their original treatment for an additional 24 weeks.

Results: Of 197 patients in the induction period, 103 (52.3%), continued in the MP, and 91 (88.3%) completed. At Week 32, clinical remission occurred in 20.9%, HD ($p = 0.0108$ vs. PBO), 26.2%, LD ($p = 0.0021$), and 6.2%, PBO. Clinical response occurred in 50.7%, HD ($p = 0.0002$), 35.4%, LD ($p = 0.0571$), and 20.0%, PBO. Mucosal improvement (Mayo endo-subscore ≤ 1) occurred in 32.8% for HD ($p = 0.0046$), 33.8%, LD ($p = 0.0036$), and 12.3%, PBO. The improvement in total Mayo score at Week 32 from baseline was 3.4, HD ($p = 0.0026$), 2.5, LD ($p = 0.2073$), and 1.9, PBO.
During the MP, the frequency of TEAEs were generally similar among treatment groups: (HD, 11/42 [26.2%]; LD, 6/36 [16.7%]; PBO, 9/25 [36.0%]). The most common TEAEs were: worsening of UC (HD, 1 [2.4%]; LD, 0 [0%]; PBO, 3 [12.0%]) and UTI (HD, 0 [0%]; LD, 1 [2.8%]; PBO, 1 [4.0%]). No AEs of special interest (cardiac, pulmonary, ophthalmologic, hepatic, malignancy or serious infections) were reported during the MP.

Conclusion: Patients with moderate to severe UC who continued treatment with ozanimod were more likely to both achieve and maintain clinical remission, clinical response and mucosal improvement than those receiving placebo. These data support the longer-term efficacy and safety/tolerability profile of ozanimod in the treatment of moderate to severe UC.

Reference

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Disclosure of Interest: W. Sandborn Financial support for research: Receptos, Consultancy: Receptos, B. Feagan Consultancy: Receptos, D. Wolf Financial support for research: Receptos, Consultancy: Receptos, G. D'Haens Consultancy: Receptos, S. Vermeire Consultancy: Receptos, S. Hanauer Consultancy: Receptos, S. Ghosh Consultancy: Receptos, H. Smith Shareholder: Receptos, M. Cravets Shareholder: Receptos, P. Frohna Shareholder: Receptos, Directorship(s): Receptos, R. Aranda Shareholder: Receptos, Directorship(s): Receptos, S. Gujrathi Shareholder: Receptos, Directorship(s): Receptos, A. Olson Shareholder: Receptos

MONDAY, OCTOBER 26, 2015 11:00–12:30
MANAGEMENT OF CROHN'S DISEASE BEFORE AND AFTER SURGERY – ROOM F2

OP005 EARLY SURGERY OR IMMUNOSUPPRESSION IN CROHN'S DISEASE - EASY STUDY

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Introduction: Studies addressing the timing of surgery or medical treatment are scarce in Crohn's disease (CD) patients.

Aims & Methods: We aimed to compare the outcomes of CD patients submitted to immunomodulators or surgery in the first 6 months after diagnosis. A national, multicentric restrospective study in CD patients diagnosed and followed for more than 3 years. Global disability was defined if: 1 surgery or hospital admission in the first 5 years after index episode occurred; >1 surgery or 2 hospital admissions; >2 courses of steroids/year, steroid dependence or refractoriness; need to switch immunomodulator or the appearance of new clinical events.

Results: 516 patients were included and followed for 9.0 years (IQR: 5.7-14.2). We identified 3 cohorts: A-surgery in the 1st 6 months after diagnosis without any immunosuppression ($n = 87$), B-surgery in the 1st 6 months after diagnosis and immunosuppressors started 6 months after surgery ($n = 187$), C-immunosuppression in the 1st 6 months after diagnosis and without any surgery in this period ($n = 242$). Group A was the one with the lowest proportion of global disability (18% vs. B: 78% vs. C: 69%, $p < 0.001$). Diagnosis with >40 years old (OR 4.250, $p = 0.024$) was risk factor for belonging to group C in univariate analysis and in multivariate analysis, localization (L2-OR 0.162, $p = 0.016$ or L3 - OR 0.513, $p = 0.010$) was an independent risk factor. For early immunosuppression, localization (L2 -OR = 4,917, $p = 0.001$; L3 - (OR = 1,744, $p = 0.010$); behavior (B2-OR = 0.162, $p = < 0.001$, B3- OR = 0.130, $p < 0.001$) and age at diagnosis (A2- OR = 0.344, $p = 0.036$) were independent risk factors. Surgery rate/patient/10 year of follow-up (with index surgery) was lower in group C (0.35 vs. A: 1.20 vs. B: 1.45, $p < 0.001$).

Conclusion: The early introduction of immunomodulators showed to be best strategy in bowel sparing, however surgery in the first 6 months was associated with lower global disability particularly in those with more than 40 years at diagnosis.

Disclosure of Interest: None declared

OP006 ASSOCIATION OF BODY MASS INDEX (BMI) ON RISK OF FIRST INTESTINAL RESECTION IN CROHN'S DISEASE: NATIONAL POPULATION-BASED COHORT STUDY

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Introduction: Obesity in patients with Crohn's disease (CD) is increasing but the clinical impact of a higher BMI on long-term outcomes in CD is unknown. Obesity is considered a pro-inflammatory state and could potentially have an adverse impact.

Aims & Methods: We aimed to evaluate the association between BMI as recorded at diagnosis and rates of first intestinal resection in CD patients.

Methods: We constructed a population based adult cohort of incident cases of CD diagnosed between 1989-2010 using data from The Clinical Practice Research Datalink. We assigned patients to 4 groups based on BMI recorded within 30 days of initial diagnosis of CD. Kaplan-Meier analysis was used to calculate cumulative probability of surgery stratified by WHO definition of weight status. We used Cox regression to compute hazard ratios for factors associated with surgery.

Results: We identified 6183 eligible patients with CD. The median age at diagnosis was 33 years (IQR 25-52) and did not vary between the BMI subgroups. 58% of the cohort was female. The prevalence of obesity increased ~3 fold from 5% in those diagnosed between 1989-93 to 14% in those diagnosed 2006-10 ($p < 0.05$ chi-squared test for trend). The 5 and 10 year cumulative risk of intestinal resection in underweight, normal, overweight and obese patients was 9, 7, 5, 4% and 17, 12, 8, 9% respectively ($p < 0.001$ chi-squared test for trend). Risk of intestinal resection was significantly lower in overweight (HR 0.75; 95% CI 0.54 – 0.94) patients compared to normal weight. We also used BMI as a continuous rather than a categorical variable and found that increasing BMI was associated with a lower risk of surgery (HR -0.003, 95% CI -0.005 to -0.002) per unit increase in BMI. The associated need for thiopurines but not corticosteroids also reduced with increasing BMI with an HR of -0.79 (95% CI -1.06 to -0.52) and -0.27 (95% CI -0.57 to 0.03) respectively per unit increase in BMI.

Conclusion: The risk of subsequent intestinal resection is 25% lower in overweight patients with CD compared with those who are normal or underweight at diagnosis. Higher BMI is associated with lower rates of intestinal resection and thiopurine use and predicts a more stable disease course. The effect of improving BMI and nutritional status on CD patients at diagnosis needs further research.

Disclosure of Interest: S. Chatu: None declared, S. Saxena Conflict with: SS is funded by a National Institute for Health Research Career Development Fellowship (NIHR CDF-2011-04-048). This article presents independent research commissioned by the National Institute for Health Research (NIHR). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health., R. Pollok: None declared, V. Chhaya: None declared, V. Curcin: None declared, A. Majeed: None declared, V. Subramanian: None declared

OP007 POST-OPERATIVE ENDOSCOPIC RECURRENCE IN CROHN'S DISEASE: A PROSPECTIVE STUDY OF THE REMIND GROUP

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Introduction: Operative resection in Crohn's disease is not curative. After ileocecal resection, endoscopic recurrence is frequently observed on the anastomosis and/or on the neo-terminal ileum.

Aims & Methods: The aim of this study is to identify predictors of post-operative endoscopic recurrence. This is a prospective study performed in 9 centers of the REMIND group, collecting data at time of surgery and at 6 months, with extensive bio-banking. Inclusion criteria were: age > 18 years old; ileal or ileocecal CD; indication of surgery. Post-operative treatment was given according to a pre-established algorithm. Clinical, biological and endoscopic parameters (elementary lesions, Rutgeerts score) were collected at month 6. Factors associated with endoscopic recurrence were searched by univariate and multivariate regression analysis.

Results: 235 patients were included (109 male (47%) , 29 years old (IQR 26-39); disease duration 6 years (0-35)). At time of surgery, 77 patients (33%) were active smoker, 42 (18%) had a previous resection, and 51 patients (22%) had perianal lesions. Indication for surgery was stricturing disease (148), penetrating disease (91), and failure of medical therapy (29). At time of surgery, 139 patients (59%) had received anti-TNF therapy; most of them (78%) within the last 3 months. Also, 150 patients (64%) had been exposed to thiopurines. Endoscopy at month 6 was performed in 152 patients at time of analysis. After surgery, 25 patients received thiopurines alone, and 48 received anti-TNF therapy, combined with immunosuppressant in only 6 patients. An endoscopic recurrence (Rutgeerts score > 1) was observed in 70 patients (46%). In multivariate analysis, factors associated with post-operative recurrence (Rutgeerts score > 1) were: male gender (OR 3.2; IC95% 1.5-7.2), anti-TNF post-operative therapy (OR 0.41; IC95% 0.2-0.9), surgical indication for failure of medical therapy (OR 12; IC95% 2-27) or stricturing disease (OR 0.41; IC95% 0.2-0.9), active smoking (OR 7.6; IC95% 2.9-20), joint manifestations (OR 4.3; IC95% 1.4-13). Total absence of lesions (Rutgeerts score = 0) was observed in 51 patients (33%). The factors associated with a Rutgeerts score > 0 were: smoking (OR 3.2; IC95% 1.2-8.4), anti-TNF post-operative therapy (OR 0.44; IC95% 0.2-0.9) and presence of granuloma (OR 2.7; IC95% 1.04-6.9).

Conclusion: Despite a pre-established algorithm for prevention, almost half of patients had a significant endoscopic recurrence at month 6 with a Rutgeerts score of more than 1, and only one third of patients had no lesions. Several factors were associated with post-operative recurrence, including smoking behavior and anti-TNF therapy.

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Disclosure of Interest: M. Allez Lecture fee(s): Abbvie, MSD, Ferring, Consultancy: Novo Nordisk, Genentech, Pfizer, UCB, Janssen, C. Stefanescu: None declared, S. Nancey: None declared, A. Buisson: None declared, P. Desreumaux: None declared, P. Marteau: None declared, M. Fumery: None declared, J.-M. Gornet: None declared, N. Barnich: None declared, H. Sokol: None declared, P. Hofman: None declared, X. Treton: None declared, M.-C. Perier: None declared, X. Jouven: None declared, P. Seksik: None declared

OP008 APPRECIA: ADALIMUMAB VS AZATHIOPRINE IN THE PREVENTION OF CROHN'S DISEASE RECURRENCE AFTER SURGICAL RESECTION. A GETECCU MULTICENTER RANDOMIZED TRIAL

A. Lopez-Sanroman[1], on behalf of GETECCU, I. Vera-Mendoza[2], E. Domènech[3], C. Taxonera[4], V. Vega[5], I. Marín-Jiménez[6], J. Guardiola[7], L. Castro[8], M. Esteve[9], V. García[10], D. Ceballos[11], P. Martínez-Montiel[12], J. P. Gisbert[13], M. Mínguez[14], A. Echarri[15], X. Calvet[16], J. Barrio[17], J. Hinojosa[18], M. D. Martín-Arranz[19], M. Andreu[20], F. Bermejo[21], J. Rimola[22], V. Pons[23], P. Nos[23], on behalf of GETECCU, Grupo Español de Trabajo en Enfermedad de Crohn
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Introduction: Postoperative recurrence of Crohn's disease (CD) is almost constant if no preventive therapy is adopted. Adalimumab (ADA) is effective in CD, but data in this setting are scarce.

Aims & Methods: To evaluate the efficacy of ADA compared to azathioprine (AZA) in preventing CD recurrence, we conducted a phase-3, 52-week, multicentric, randomized, evaluator-blind, superiority study (ClinicalTrials.gov NCT015564823). 22 Spanish centres included patients with ileocolic resection, randomized to ADA 160-80-40 mg SC or AZA 2.5 mg·kg·d PO (metronidazole in both arms). Ileocolonoscopy was performed at 1 yr, with central blinded reading. Primary endpoint was endoscopic recurrence* (Rutgeerts' 2b, 3, 4). MRI was performed at end of the study. Patient losses were considered non-responders (Non Responder Imputation).

Results: 91 patients were recruited, 84 randomized and treated, fulfilling the predefined sample size for a binary outcome superiority trial. Mean age was 36.9 ys, 50% females, disease duration 7.7 ys, 23.8% smokers, 7.1% previous resections, no differences between groups. Treatment was prematurely discontinued in 12/39 (30.8%) in AZA group and 4/45 (8.9%) in ADA group, due to adverse events in 11 cases (13.1%), significantly less in ADA group (4.4%) than in AZA group (23.1%) (p = 0.01).

ITT analysis (84 patients). Therapy failure was observed in 23/39 in AZA group (59.0%) versus 19/45 in ADA group (42.2%) (p = 0.12).

Per Protocol analysis (61 patients with centrally evaluable images). Endoscopic recurrence appeared in 8/24 in AZA group (33.3%), versus 11/37 in ADA group (29.7%) (p = 0.77).

MR recurrence (Sailer's MR2 and MR3 degrees) was present in 33.3% in AZA group and 28.1% in ADA group (p 0.68).

No differences were found in markers of activity (CRP, calprotectin), surgeries, admissions or quality of life indexes between both treatment groups.

Conclusion: It was not possible to demonstrate superiority of ADA over AZA as prophylaxis of CD after ileocolic resection. Adverse events and treatment discontinuations were less frequent in ADA group. As a general rule, ADA should not replace AZA in the prophylaxis of POR, but its tolerance is significantly better.

Reference

1. *Domènech *Inflamm Bowel Dis* 2008.

Disclosure of Interest: A. Lopez-Sanroman Lecture fee(s): ABBVIE, MSD, FERRING, TILLOTTS, SHIRE, Consultancy: ABBVIE, MSD, FERRING, TILLOTTS, TAKEDA, I. Vera-Mendoza: None declared, E. Domènech: None declared, C. Taxonera: None declared, V. Vega: None declared, I. Marín-Jiménez: None declared, J. Guardiola: None declared, L. Castro: None declared, M. Esteve: None declared, V. García: None declared, D. Ceballos: None declared, P. Martínez-Montiel: None declared, J. Gisbert: None declared, M. Mínguez: None declared, A. Echarri: None declared, X. Calvet: None declared, J. Barrio: None declared, J. Hinojosa: None declared, M. D. Martín-Arranz: None declared, M. Andreu: None declared, F. Bermejo: None declared, J. Rimola Lecture fee(s): ABBVIE, MSD, Consultancy: ABBVIE, MSD, TAKEDA, ROBARTS, V. Pons: None declared, P. Nos Lecture fee(s): ABBVIE, MSD, FERRING, TILLOTTS, SHIRE, Consultancy: ABBVIE, MSD, FERRING, TILLOTTS, TAKEDA

OP009 RATE OF POSTOPERATIVE CLINICAL RECURRENCE IN CROHN'S DISEASE PATIENTS CLASSIFIED I2 ON RUTGEERTS SCORE WITH LESIONS CONFINED TO THE ILEOCOLONIC ANASTOMOSIS IS NOT DIFFERENT COMPARED TO PATIENTS WITH MODERATE LESIONS ON THE TERMINAL ILEUM

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Introduction: The Rutgeerts score, that have 5 grades of severity (i0-i4), is a suitable endoscopic model to predict clinical recurrence after small bowel resection in Crohn's disease (CD). i2 score is a heterogeneous group defined by moderate lesions on the terminal ileum (i2A) or lesions confined to the ileocolonic anastomosis (i2B). It has been suggested that patients classified i2B had less severe outcome compared to patients classified i2A. The aim of the present study was to evaluate rate of clinical recurrence in patients with i2A or i2B score.

Aims & Methods: We conducted a multicenter retrospective study, including all CD patients who underwent curative ileocolonic resection and who were classified i2 according to the Rutgeerts score at the first ileo-colonoscopy after surgery. Median (IQR) delay between surgery and first endoscopic evaluation was 7.3 months (6-12). Primary outcome was to evaluate the rate of clinical recurrence (CR) in patients classified i2A and i2B; secondary outcome was to evaluate the

rate of global recidive (GR) in both group; GR was defined as clinical recurrence and/or radiological recurrence and/or worsening of endoscopic lesions and/or by the optimization of the medical treatment and/or new intestinal resection.
Results: Fifty patients were included, in whom 27 were classified i2A and 23 classified i2B according to the first ileo-colonoscopy after surgery. Demographic and clinical characteristics (including surgical indication, previous treatment before surgery, treatment introduced or modified after surgery, treatment introduced or modified after first colonoscopy, and smoking status) were not different between the two groups. Probability of CR in the whole population was 21%, 48% and 55% at 1, 3 and 5 years respectively. There was no significant difference concerning probability of CR between patients classified i2A and i2B (19%, 40%, 52% and 24%, 52%, 58% at 1, 3 and 5 years respectively, p = 0.64). Median (IQR) time to CR after ileo-colonoscopy was not different between i2A and i2B (1007 (321-1215) and 460 (131-839) days respectively, p = 0.33). Probability of GR in the whole population was 21%, 51% and 65% at 1, 3 and 5 years respectively, with no significant difference between patients classified i2A and i2B, (p = 0.19).
Conclusion: Among patients with CD classified i2 on Rutgeerts score, rate of postoperative recurrence is not different in patients with lesions confined to the ileocolonic anastomosis compared to patients with moderate lesions on the terminal ileum. These results suggest that same therapeutic strategy should be applied in patients in classified i2 on Rutgeerts score with ileal lesions or with confined anastomotic lesions.

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Disclosure of Interest: None declared

OP010 POSTOPERATIVE COMPLICATIONS AFTER ILEO-CAECAL RESECTION FOR CROHN'S DISEASE: A PROSPECTIVE MULTICENTRE STUDY

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Introduction: Most of the data investigating postoperative complications after ileocaecal resection for Crohn's Disease (CD) come from retrospective studies or monocentric cohort. We aimed to determine the frequency and risk factors for early post-operative complication after ileocaecal resection in a well-characterized mutlicentric prospective cohort of CD.
Aims & Methods: The REMIND group conducted a nationwide study in 9 French academic centres. Patients undergoing ileocaecal resection between 1st September 2010 and 31th September 2014 were included in a prospective cohort. Clinical, biological, surgical data and medical therapies within the 3 months before surgery were prospectively collected. Early postoperative complication was defined by a medical or surgical event within 30 days after surgery. Factors associated with early post-operative complication were searched by univariate and multivariate regression analysis.
Results: 211 patients were included. 50% were male with a median age at surgery of 29 years (IQR 25-39). Indications for ileocecal resection were stricturing disease (n = 110, 52%), penetrating disease (n = 66, 31%), both stricturing and penetrating disease (n = 21.10%), and inflammatory disease with failure of medical therapy (n = 14, 7%). Seventy-two (34%) patients were exposed to corticosteroids within 3 months before surgery. Ninety-five (45%) and 41 (19%) patients were treated with anti-TNF within 3 and 1 months before surgery. Median duration between the last anti-TNF administration and surgery was 18 days (14-50). Laparoscopy was performed in 117 (73%) patients; 16 (13%) of them needed conversion to laparotomy. Initial stoma was performed in 35 (16%) patients. There was no postoperative death. Forty-three (21%) patients had a total of 56 early post-operative complications after a median time of 5 days (4-12): wound abscess (n = 17), intra-abdominal collection (n = 16), anastomotic leakage (n = 10), extra-intestinal infections (n = 9), and haemorrhage (n = 5). Reoperation was necessary in 16 patients and stoma in 7. Median duration of temporary stoma was 3.7 months (2.9-4.5). Multivariate analysis found that corticosteroids therapy within 3 months before surgery was the only factor associated to postoperative complications (p = 0.04, HR 2.0, IC95%[1.01-4.0]).
Conclusion: In this large multicentre prospective cohort, early postoperative complications after ileocecal resection were observed in 21% of patients. Corticosteroids therapy was the only factor associated to postoperative complications. The impact of nutritional status and through levels of ant-TNF at surgery on the risk of postoperative complications is being analysed.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 11:00–12:30
BENIGN OESOPHAGEAL STRICTURES – ROOM A1

OP011 POLYGLYCOLIC ACID SHEETS WITH FIBRIN GLUE FOR THE PREVENTION OF POSTOPERATIVE STRICTURE AFTER ESOPHAGEAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Postoperative stricture after endoscopic submucosal dissection (ESD) for wide-spreading superficial esophageal neoplasms is a very common yet severe complication, with an occurrence rate of 66-90% in cases with resection of over 3/4 the circumference of the esophagus. Although the use of steroids after ESD is known to decrease the incidence of postoperative stricture, this method is accompanied with a risk of severe adverse effects, and there is a clinical need for a safer method of prevention. The use of polyglycolic acid (PGA) sheets, a surgical suture material, adhered with fibrin glue, has been reported to safely minimize scar contracture in other medical fields. The aim of this study was to evaluate the efficacy of applying PGA sheets with fibrin glue to the post-ESD defect for the prevention of postoperative stricture after esophageal ESD.
Aims & Methods: After ethics committee approval and trial registry in July 2013, we enrolled subjects with a diagnosis of superficial esophageal squamous cell carcinoma covering over half the circumference of the esophagus in the study group. Immediately after the enrolled subjects underwent esophageal ESD, a PGA sheet was adhered to the post-ESD defect with fibrin glue. Following protocol treatment, all subjects underwent outpatient follow-up for a minimum of three months. As a historical control group, we listed all subjects at our institute who had undergone ESD for superficial esophageal squamous cell carcinoma covering over half the circumference of the esophagus during 2004 to April 2013. Statistical analysis of the incidence of postoperative stricture and required endoscopic balloon dilation (EBD) sessions was performed. In order to accurately access the efficacy of PGA sheets and fibrin glue, subjects with steroid use after ESD were excluded from analysis.
Results: Between September 2013 and July 2014, 13 subjects were enrolled in the study group. For the historical control group, there were a total of 36 consecutive subjects who met our inclusion criteria, with a follow-up period of over 3 months. After exclusion of subjects with steroid use, 12 subjects in the study group and 35 subjects in the historical control group were analyzed. There were no statistical differences in the background factors between the groups. The incidence of stricture was significantly lower in the study group (25.0% vs. 62.9%, $p = 0.02$). The number of required EBD sessions was also significantly lower in the study group (0.9 ± 2.1 vs. 6.8 ± 8.6, $p = 0.01$). There were no other adverse events in either group.
Conclusion: The application of PGA sheets with fibrin glue seems to be an effective and safe method for the prevention of postoperative stricture after esophageal ESD. Although further improvements of this method and prospective studies for confirmation of efficacy are required, this method is a promising novel technique.
Disclosure of Interest: Y. Sakaguchi: None declared, Y. Tsuji Lecture fee(s): Olympus Medical Systems, HOYA Pentax, Eisai, GUNZE, CSL Behring, Y. Kataoka: None declared, I. Saito: None declared, S. Shichijo: None declared, D. Yamaguchi: None declared, K. Niimi: None declared, S. Ono: None declared, S. Kodashima: None declared, M. Fujishiro Financial support for research: Astellas Pharmaceutical, Takeda Pharmaceutical, Zeria Pharmaceutical, Otsuka Pharmaceutical, Astrazeneca Pharmaceutical, Dainihon-Sumitomo Pharmaceutical, Taiho Pharmaceutical, Ajinomoto Pharmaceutical, and Eisai for his department outside the submitted work, Lecture fee(s): Olympus Medical Systems, HOYA Pentax, Eisai, MSD, Daiichi-Sankyo Pharmaceutical, Astrazeneca Pharmaceutical, Aska Pharmaceutical, Taisho-Toyama Pharmaceutical, Otsuka Pharmaceutical, Zeria Pharmaceutical, Takeda Pharmaceutical, Astellas Pharmaceutical, Seikagaku Corp., Johnson & Johnson, Ajinomoto Pharmaceutical, Amco, Novartis Pharmaceutical, Boston Scientific, and, Boehringer-Ingelheim outside the submitted work, Conflict with: non-financial support from HOYA Pentax, Olympus Medical Systems, and, Fujifilm for his department outside the submitted work, K. Koike: None declared

OP012 DOUBLE CELL SHEET TRANSPLANTATION FOR ESOPHAGEAL STRICTURE PREVENTION AFTER LARGE ENDOSCOPIC SUBMUCOSAL DISSECTION IN A PORCINE MODEL

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Introduction: Extended esophageal endoscopic submucosal dissection (ESD) is highly responsible for esophageal stricture. We conducted a comparative study in a porcine model to evaluate the effectiveness of adipose tissue-derived stromal cell (ADSC) double cell sheet transplantation.
Aims & Methods: Twelve female pigs were treated with 5 cm long hemi-circumferential ESD and randomized in two groups. ADSC group (n = 6) received 4 double cell sheets of allogenic ADSC on a paper support membrane and control group (n = 6) received 4 paper support membranes. ADSC were labelled

with PKH-67 fluorophore to allow probe-based confocal laser endomicroscopie (pCLE) monitoring. After 28 days follow-up, animals were sacrificed. At days 3, 14 and 28, endoscopic evaluation with pCLE and esophagography were performed.
Results: One animal from the control group was excluded (anesthetic complication). Animals from ADSC group showed less frequent alimentary trouble (17% vs 80%; $P=0.08$) and higher gain weight on day 28. pCLE demonstrated a compatible cell signal in 4 animals of the ADSC group at day 3. In ADSC group, endoscopy showed that 1 out of 6(17%) animals developed a severe esophageal stricture comparatively to 100% (5/5) in the control group; $P=0.015$. Esophagography demonstrated a decreased degree of stricture in the ADSC group on day 14 (44% vs 81%; $P=0.017$) and day 28 (46% vs 90%; $P=0.035$). Histological analysis showed a decreased fibrosis development in the ADSC group, in terms of surface (9.7 vs 26.1 mm^2; $P=0.017$) and maximal depth (1.6 vs 3.2 mm; $P=0.052$).
Conclusion: In this model, transplantation of allogenic ADSC organized in double cell sheets after extended esophegeal ESD is strongly associated with a lower esophageal stricture's rate.

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Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 11:00–12:30
UPDATE ON COELIAC DISEASE – ROOM A3

OP013 DETECTION OF GLUTEN PEPTIDES IN URINE OF CELIAC PATIENTS: CORRELATE WITH MUCOSAL DAMAGE

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Introduction: Ingestion of gluten found in wheat, barley, rye and in some circumstances, oats, leads to autoimmunity and small intestinal mucosal injury in patients with celiac disease (CD). To date, the mainstay of the management of CD is a strict life-long adherence to gluten-free diet (GFD). However, strict GFD is difficult because it is one of the most frequent ingredients in processed foods.
Aims & Methods: We have developed a novel method to determine gluten intake and to assess adherence to the GFD in celiac patients by detection of gluten immunogenic peptides (GIP) in urine. Urine samples of 76 healthy subjects and 58 celiac patients were collected. Urine GIP content was estimated by solid phase extraction and a quantitative lateral flow test with the highly sensitive and specific anti-α-gliadin monoclonal antibody G12.
Results: We detected the presence of GIP in concentrated urine samples from healthy individuals subjected to different dietary conditions as early as 4-6 h after gluten intake. GIP were detectable in healthy individuals' urine for 1-2 days after a GFD followed by a single gluten intake. The sensitivity of the assay was high, with detection of consumption of as little as 50 mg of gluten. The assay also appeared to detect GFD infringement or gluten contamination in CD patients, as over 50% of the patients studied presented detectable GIP in urine. Importantly, there was a correlation between urinary gluten and mucosal atrophy in CD patients. Retrospective analysis of duodenal biopsies, available in 27 CD patients, showed that 90% of CD patients with no villus atrophy had no detectable GIP in urine.
Conclusion: GIP could be sensitively detected in human urine. This sensitive, quantitative, specific and simple technique could be useful to monitor GFD compliance of CD patients as well as for therapeutic research applications. This trial was registered in ClincialTrials.gov as NCT02344758.
Disclosure of Interest: M. D. L. Moreno Amador: None declared, Á. Cebolla Ramírez Conflict with: own stock in Biomedal S.L., A. Muñoz Suano: None declared, C. Carrillo Carrión: None declared, I. Comino Montilla: None declared, Á. Pizarro Moreno: None declared, F. León Conflict with: own stock in Biomedal S.L., A. Rodríguez Herrera: None declared, C. Sousa Martín: None declared

OP014 ASSESSMENT OF BREAST MILK MYCOTOXIN CONTENT IN MOTHERS WITH COELIAC DISEASE: A PRELIMINARY OUTLINE

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Introduction: Gluten-free diet (GFD) is characterized by a higher consumption of corn that may undergo some xenobiotic contamination. Mycotoxins are secondary metabolites produced by several microscopic fungi genera such as Aspergillus, Fusarium and Penicillium. The aim of our study was to assess the risk of mycotoxin exposure (aflatoxin M1, ochratoxin A and zearalenone) in woman with coeliac disease (CD) and healthy control breastfeeding mothers (as well as in their offsprings) by quantifying these contaminants in breast milk.
Aims & Methods: From January 2011 to December 2013, 33 women with CD and 22 healthy brestfeeding controls completed the study. Human milk was collected throughout three days, during a complete 24h period, as following: one milk sample after overnight fasting, one 4 hours after lunch, and one 2 hours after dinner. Mycotoxin content in breast milk was investigated by a high-performance liquid chromatography (HPLC) method with fluorimetric detection. Dietary history on cereal consumption was recorded during the three days of breast milk collection.
Results: Aflatoxin M1 (AFM1) was detected in 37% (n = 96) of samples belonging to women with CD [mean ± SD = 0.012 ± 0.011 ng/mL; range = 0.0035 ÷0.340 ng/mL]. The slightly higher concentration in those samples collected during fasting [0.017 ± 0.028 ng/mL] resulted statistically significant when compared to those collected 4 hours after lunch and 2 hours after dinner [0.011 ± 0.010 ng/mL and 0.009 ± 0.006 ng/mL respectively] (ANOVA, p-value < 0.001, significance level 0.05). When comparing to mothers with CD, the control group showed lower AFM1 concentration level in 22% of samples [mean 0.008 ± 0.007 ng/mL; range = 0.0035 ÷0.0370 ng/mL] resulting statistically significant with a p-value 0.004 (significance level 0.05).Estimating a daily average milk consumption of 530g for a hypothetical body weight of 3.4 kg, the exposure of newborns from mother with CD and from healthy control mothers resulted 1.87 and 1.24 ng/kg bw/d, respectively. No statististical significant difference was found as regards breast milk zearalenone (ZEA) content in both groups. Ochratoxin A was not significantly present in the investigated human milk samples of both groups.
Conclusion: The presence of AFM1 in breast milk is a marker both for infant and mother exposure. In our assessment, the AFM1 breast milk content was higher among mother with CD than among healthy breastfeeding controls. However, the maximum tolerable level set by the EU Regulation 1881/2006 (0.11 ng/kg bw/d) was exceeded in both groups and this warrants further investigations.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 11:00–12:30
HOT TOPICS FROM LATIN AMERICA – ROOM 7.1

OP015 PREDICTION OF HISTOLOGY BY CONFOCAL LASER ENDOMICROSCOPY IN LUGOL-UNSTAINED ESOPHAGEAL SUPERFICIAL LESIONS OF PATIENTS WITH HEAD AND NECK CANCER

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Introduction: Surveillance programs of patients with head and neck cancer (HNC) detect synchronous or metachronous esophageal squamous cell carcinoma (ESCC) in up to 15% of the patients. The detection of ESCC in patients with HNC at early stage is desirable since it affects prognosis. Endoscopic surveillance of the esophagus with narrow band imaging (NBI) or Lugol chromoendoscopy presents high sensitivity but low specificity for the detection of early ESCC. Esophagitis may also present as Lugol-unstained areas. A non-invasive probe-based confocal laser endomicroscopy (pCLE) technique may improve the diagnosis allowing acquisition of high-resolution in vivo images at the cellular and microvascular levels.
Aims & Methods
Aim: To evaluate the accuracy of pCLE for the diagnostic differentiation of non-neoplastic and neoplastic Lugol-unstained esophageal lesions in patients with HNC.
Methods: Twenty-one patients with HNC who presented one or more Lugol-unstained esophageal lesions at surveillance endoscopy were prospectively included for pCLE. All patients repeated conventional white-light endoscopic examination with NBI and pCLE. After intravenous injection of fluorescein, a 1.8 mm GastroFlex probe (Cellvizio) was inserted into the esophagus. Diagnostic pCLE were followed by subsequent biopsies or endoscopic resection of suspected lesions. A senior pathologist was masked to the pCLE results.
Results: Patients mean age was 58.4 years (SD = 8.8), and 76.2% were men. All patients were smokers, and 16 patients (76.2%) had a history of alcohol abuse. The locations of HNC were larynx (n = 10), oral cavity (n = 7), and pharynx (n = 4). Twenty-four lesions from 19 patients were studied. The final diagnosis of the 24 suspicious lesions were: ESCC in 11 and benign lesions in 13. Two other patients with 8 mm and 10 mm lesions were referred directly to endoscopic resection, since NBI and pCLE results were suspicious for ESCC. The size of Lugol-unstained lesions varied from 6 mm to 80 mm (mean = 17.7 mm, SD =

17.1). The mean size of malignant lesions was larger than the size of inflammatory ones (30.6 mm versus 9.3 mm, p = 0.001). However, there were three cases of ESCC smaller than 15 mm. pCLE made the correct diagnosis in 95.8% of the lesions (23/24 lesions). pCLE misdiagnosed one lesion in one patient who had two ESCC. All 13 benign lesions were correctly diagnosed by pCLE. Sensitivity, Specificity and Accuracy of pCLE for the histologic diagnosis of ESCC in patients with HNC were: 90.9%, 100% and 95.8%, respectively.
Conclusion: 1. pCLE is highly accurate for real time histology of Lugol-unstained esophageal lesions in patients with HNC. 2. pCLE has the potential to change the management of patients under surveillance for ESCC, guiding biopsies and endoscopic resection, avoiding further diagnostic workup or therapy of benign lesions.

Reference

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Disclosure of Interest: None declared

OP016 EVOLUTION OF THE HUMAN GENOME AND HELICOBACTER PYLORI AND ITS IMPLICATIONS FOR THE RISK OF GASTRIC CANCER IN THE ANDES OF COLOMBIA

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Introduction: *Helicobacter pylori* is the principal cause of gastric cancer (GC), the second leading cause of cancer mortality worldwide. However, *H. pylori* prevalence generally does not predict cancer incidence.
Aims & Methods
Aims: To determine if the coevolution between host and pathogen influences the risk of GC in two Colombian populations: Tumaco, a coastal population with low risk of GC, and Tuquerres, a Andes mountain population with high risk of GC. Our hypothesis postulates an association between the severity of gastric lesions and the patterns of genomic variation in matched human and *H. pylori* samples.
Methods: 292 patients were recruited from the two populations. Histological diagnostics were based on the Sydney classification. 252 strains of *H. pylori* were included for MLST analysis. Human DNA was genotyped using the Immunochip to characterize the human ancestry. The Admixture model of STRUCTURE assigns proportions of ancestry to each individual sample across *K*-inferred ancestral clusters.
Results: All *H. pylori* isolates contained the genetic signatures of multiples ancestries. *H. pylori* isolates with an ancestral African cluster predominating in a low-risk (coastal population), and a European cluster in a high-risk (Andes mountain population). The human ancestries of the biopsied individuals also varied with geography, with mostly African ancestry in the coastal region (58%), and mostly Amerindian ancestry in the mountain region (67%).
Conclusion: The interaction between the host and pathogen ancestries completely accounted for the difference in the severity of gastric lesions in the two regions of Colombia. In particular, African *H. pylori* ancestry was relatively benign in humans of African ancestry but was deleterious in individuals with substantial Amerindian ancestry. Thus, coevolution probably shapes disease risk of the disease , and the disruption of coevolved human and *H. pylori* genomes can explain the high incidence of gastric disease in mountain population.

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Disclosure of Interest: None declared

OP017 NON-INVASIVE EVALUATION OF PANCREATIC FIBROSIS USING SHEAR WAVE ELASTOGRAPHY

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Introduction: It is difficult to collect pathological pancreatic parenchyma surgically for diagnosis of pancreatic fibrosis[1)]. Shear wave elastography using transabdominal ultrasonography (SW) is a potential technology for diagnosing stage of chronic pancreatitis, because SW can calculate the tissue elasticity as correlation value of Young's modulus[2)].
Aims & Methods: The aim of this study was to evaluate the accuracy of diagnosing pancreatic parenchymal fibrosis using SW. From September 2012 to May 2014, 155 patients who underwent SW estimating pancreatic parenchymal fibrosis were enrolled in this study. All patients were assessed for elastic modulus using SW with iU22 (Philips Healthcare, Bothell, WA, USA). We performed SW measurements more than five times at the same area. Elastic modulus was expressed as kPa and presented as mean value of 5 or more measurements. We checked measurement success rate (number of success measurement / number of all measurement * 100), and the patients whose success rate was less than 60% were excluded from this study. 120 patients (normal pancreas: NP group) underwent SW (head: 32, body: 70, tail: 18). 35 patients had pancreas tumors and underwent pancreatectomy (resected pancreas: RP group). RP group patients underwent SW at pancreatic parenchyma on the cranial or caudal side of the tumor preoperatively, and their elastic modulus were compared with degree of pancreatic fibrosis (DPF) postopereatively. DPF was classified to the 13 score (DPFS) using the scoring system reported previously[3)]. Evaluated points were as follows: 1) Diagnosis accuracy of SW in NP group.2) Correlation elastic modulus with degree of pancreatic fibrosis in RP group. This study was approved by the IRB of our hospital and registered in UMIN-CTR (000016497).
Results: 1) In NP group, 16 patients failed in SW measurement and excluded from this study. 104 patients (86.7%) were included in this study. The mean value of elastic modulus and success rate were 3.73 ± 1.84kPa and 79.4%, respectively, and these values in each pancreas lesion were head:3.74kPa/84.1%, body: 3.67kPa/78.1% and tail: 3.98kPa/77.1%, respectively, no significant difference (elastic modulus; $P = 0.93$, success rate; $P = 0.17$) .2) In RP group, the mean value of DPFS and elastic modulus were 4.26 ± 4.43 and 7.18 ± 5.50kPa. DPFS was significantly correlated with elastic modulus ($r = 0.724$, $P < 0.001$). In ROC analysis, the AUCs of elastic modulus for the diagnosis of mild grade fibrosis (DPFS > 3), moderate grade fibrosis (DPFS > 6), and severe grade fibrosis (DPFS > 10) were 0.920, 0.843 and 0.817, respectively.
Conclusion: Shear wave elastography using transabdominal ultrasonography was highly accurate and non-invasive in the diagnosis of pancreatic fibrosis.

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Disclosure of Interest: None declared

OP018 GENOTYPE-PHENOTYPE CORRELATIONS IN CYSTIC FIBROSIS PATIENTS WITH PANCREATITIS HIGHLIGHTS AN INCREASED LIKELIHOOD OF PANCREATIC INSUFFICIENCY AND IDENTIFIES UNIQUE MUTATION PAIRS THAT POTENTIALLY PREDISPOSE TO AND PROTECT FROM PANCREATITIS

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Introduction: 1-2% of cystic fibrosis (CF) patients develop symptomatic pancreatitis. Studies have shown these patients present later in life, are pancreatic sufficient (PS) & have a less severe CF phenotype. This study aimed to evaluate the genotype:phenotype relationship of CF patients with pancreatitis in a tertiary referral centre for CF.
Aims & Methods: CF patients with a history of pancreatitis were identified from 1216 patients in The Royal Brompton Hospital CF database. Each case was age & sex matched with controls. Clinical information on age, sex, PS status, age

when CF diagnosed, CF genotype & mortality were collected. To compare pancreatitis patients with controls, a two tailed t-test (age of CF diagnosis, R117H mutation rate) & Kaplan-Meir survival curves (rate of PI and mortality rates) were utilised.
Results: 37 patients (51% females) with pancreatitis were matched to 135 controls (3:1/4:1). Mean age of CF diagnosis was significantly higher in the pancreatitis group (19yrs) than controls (10.6yrs; p = 0.046). Median time between CF diagnosis and pancreatitis was 17 yrs (range 8-36 yrs). 65% (n = 24) of pancreatitis sufferers were PS at presentation to adult services; of these 63% (n = 15) remained PS until their most recent review or death. Furthermore, 67% (n = 16) suffered with recurrent or chronic pancreatitis. Using Log-rank (Mantal-Cox), there was no difference in survival between pancreatitis patients and controls (p = 0.97). However, pancreatitis patients were significantly more likely to develop PI (p = 0.012). The ˆF508:R117H mutation pair was noted more frequently in pancreatitis patients (18.9%;n = 7) than controls (3.8%;n = 5) but not significancantly so (p = 0.56). Interestingly in 43% (n = 16) of the remaining pancreatitis patients, 15 mutation pairs unique to this group were identified. Similarly in controls, 50% (n = 65) had mutation pairs unique to this group.
Conclusion: CF patients who suffer with pancreatitis are significantly more likely to develop PI than those who do not. They present with CF at an older age but this does not affect their survival. The R117H mutation is seen more frequently in the pancreatitis group but not significantly so for this phenotype. We have identified a number of mutation pairs that seem to either predispose or protect CF patients from pancreatitis.
Disclosure of Interest: None declared

OP019 STUDY OF THE GUT MICROBIOME IN CHRONIC PANCREATITIS: ASSOCIATION WITH PANCREATOGENIC DIABETES (TYPE 3C) AND EXOCRINE INSUFFICIENCY

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Introduction: Chronic pancreatitis (CP) is characterised by progressive fibrosis, pain, pancreatic exocrine (PEI) and endocrine insufficiency (Type3c diabetes mellitus [DM]). Studies have shown gut dysbiosis in Type 1 and Type 2 diabetes.
Aims & Methods: We aim to evaluate the gut microbiota in CP and its association with Type3c DM and PEI. 40 participants [16 CP without Type3c DM, 14 CP with Type3c DM and 10 healthy controls] were enrolled after informed consent. Clinical characteristics (history, biochemical and imaging parameters) and nutritional characteristics (anthropometry, Transferrin, Vitamin D, Vitamin B_{12}, Prealbumin and serum calcium) were recorded. Individuals having diarrhoea/constipation & who had antibiotics in past 3 months were excluded. Type3c DM was confirmed by serum C-peptide; PEI was measured using fecal elastase test. Bacterial 16S rRNA was sequenced using Illumina MiSeq 2000 platform. Metagenome data was uploaded in MG-RAST server and analyzed. Spearman's correlation was evaluated between disease characteristics, bacterial abundance and altered functional pathways. Pathway analyses was performed using KEGG and Biocyc platforms.
Results: Mean total sequence reads in the three groups were 1,999,561,23; 1,778,651,39; and 1,320,277,85 bp's respectively. Alpha diversities were 7309.5, 6699.71, and 7401.6 respectively in the three groups. Firmicutes: Bacteroidetes among CP patients with Type3c DM was higher compared to those without Type3c DM (2.04 vs 1.54). *Fecalibacterium* (butyrate producing bacteria) was found to be lower in CP with Type3c DM compared to those without Type3c DM. In CP with Type3c DM and PEI, *Bifidobacterium* was significantly lower than those with Type3c DM without PEI (7.25% vs 51.53%; $p < 0.05$). We observed positive correlation between *Fecalibacterium* and *Ruminococcus* with the glycemic status, whereas a negative correlation between *Fecalibacterium*, *Ruminococcus* and *Bifidobacterium* with malnutrition in CP with Type3c DM and PEI. *Clostridium*, *Eubacterium* and *Bacillus* also showed negative correlation with malnutrition. Species within these genus were found to have metabolic pathways related to disease characteristics. Enterotyping was done for CP with and without Type3c DM. Enterotype 1 (*Bacteroidetes* predominant) was higher in CP without Type3c DM whereas Enterotype 2 (*Prevotella* predominant) was higher in CP with Type3c DM. Fermentation pathways, one- carbon metabolisms and central carbon metabolisms were found to be abundant in all the 3 groups, whereas, pterine and folate metabolisms were found to be abundant in enterotype 2. Cell-wall biosynthesis, fatty acid biosynthesis and sugar alcohol metabolism were found to be least abundant in the 3 groups.
Conclusion: We report for the first time that PEI could be a contributing factor for dysbiosis in CP with Type3c DM.
Disclosure of Interest: None declared

OP020 ANTIOXIDANT COCKTAIL AND PREGABALIN COMBINATION AMELIORATES PAIN IN CHRONIC PANCREATITIS AFTER DUCTAL CLEARANCE: RESULTS OF A RANDOMIZED, DOUBLE BLINDED, PLACEBO-CONTROLLED TRIAL

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Introduction: Chronic pancreatitis is a complex disorder. A single modality for pain is unlikely to be effective. A substantial proportion of patients with CP has pain recurrence after ductal decompression.
Aims & Methods: To evaluate the effect of antioxidant cocktail and pregabalin in patients with CP who develops pain after ductal clearance.
CP patients with pain recurrence following endotherapy/LPJ were randomized to receive either methionine containing antioxidant cocktail and pregabalin combination, or matching placebo. Daily dosages were: Methionine 2g; Selenium 600mg; Beta-carotene 54mg; Alpha-tocopherol 280mg; Ascorbic acid 540mg; and pregabalin 150mg twice daily for one week followed by 300mg twice daily. Compliance, daily pain records and adverse events were captured during weekly telephone interview and end of study hospital visit. Study duration was 2mths. Primary outcome was pain score reduction; secondary outcomes were: change in neuropathic pain score, complete pain resolution, quality of life (QOL), adverse events, and depression score. Following tools were used: Visual analog scale (VAS) and Izbicki score for overall pain; painDETECT for neuropathic pain; Beck's inventory for depression; EORTC-QLQ30 with Pan28 questionnaire for QOL. Effect size was expressed as risk ratio (RR) (95%CI) and number needed-to-treat (NNT). Analysis was intention-to-treat
Results: After sample size calculation (80% power; 0.05 alpha; adjusted for 10% drop-out), we randomized 42 and 45 patients in the treatment and placebo arms respectively. Three patients in the treatment arm while one in the placebo lost to follow-up. Both arms matched for age, gender, duration between endotherapy/LPJ and enrolment, exocrine and endocrine insufficiency, type of ductal decompression, pain scores. At 2mths, there was significantly higher reduction in VAS (-45.5(±28.5) v/s -24.0(±32.6); p = 0.002) and painDETECT score was lower (2.6[±4.1] v/s 6.03[±4.9] p = 0.001) in the treatment group. 46.5% patients in the treatment arm had complete pain resolution compared to 26.7% in placebo (p = 0.04) (RR 1.87 [95%CI 1.0-3.2]); and NNT was 5.1 for complete pain resolution. Mean(SD) number of painful days was lower in treated patients [14.7(15.2) v/s 21.8(17.4)days; p = 0.05]. No improvement was observed in depression score and QOL. 23.8% and 38.1% of treatment arm patients experienced nausea/vomiting and drowsiness respectively.

	Antioxidant + Pregabalin (n = 42)	Placebo (n = 45)	p value
VAS (mean; SD)	29.7 (23.4)	62.1 (22.5)	< 0.0001
Izbicki score (Mean; SD)	14.8 (14.7)	30.5 ((23.01)	< 0.0001
PainDETECT score (Mean; SD)	2.6 (4.1)	6.02 (4.9)	0.001
Pc reduction in pain (Mean; SD)	-60.5 (34.4)	-28.3 (44.1)	< 0.0001
Patients with complete pain relief (n; %)	20 (46.5)	12 (26.7)	0.04
Patients with pain reduction (n; %)	36 (83.7)	32 (71.1)	0.22
Need for analgesics (n; %)	13 (30.9)	22 (48.9)	0.24

Conclusion: Combination of antioxidants with pregabalin results in significant relief in CP pain recurrence after endotherapy and/or LPJ.

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Disclosure of Interest: None declared

OP021 LACTATED RINGER'S SOLUTION VERSUS NORMAL SALINE FOR FLUID RESUSCITATION IN ACUTE PANCREATITIS, A RANDOMIZED CONTROLLED TRIAL

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Introduction: Basic research as well as an open label randomized controlled trial (RCT) (1) suggest that fluid resuscitation with Lactated Ringer's solution (LR) may be associated to reduced inflammation in patients with acute pancreatitis (AP) compared to normal saline (NS).
Aims & Methods: Our aim was to investigate the effect of LR and NS on inflammation and outcome of AP.
We performed a double blind RCT. Adult patients with a first episode of AP were randomized to receive LR or NS as fluid resuscitation during the first 3 days after hospital admission. The fluids were repacked in blinded bags and fluid rate

was determined by the study protocol. Complications were defined according to the Revised Atlanta Classification.
Results: Forty patients were included, 19 (47.5%) received LR and 21 (52.5%) NS. There were no statistically significant differences between both groups regarding basal characteristics (age, sex, etiology, body mass index, hematocrit, BUN, BISAP score and number of SRIS criteria).
Median (p25-p75) C-reactive protein (CRP) plasma levels at 48h were 2.8 (0.2-13.4) and 17.4 (8.1-29.2) for LR and NS respectively ($p < 0.05$); at 72h CRP levels were 2.5 (0.3-16.9) and 21.7 (5.9-32.3) mg/dl ($p < 0.05$). Median (p25-p75) number of SIRS criteria at 72h were 0 (0-1) and 1 (1-2) for LR and NS respectively ($p < 0.05$). LR was associated with 4 (21.2%) necrotizing AP versus 10 (47.6%) for NS, $p = 0.08$. Organ failure, hospital stay, ICU admission, need for nutritional support and mortality were not significantly different.
Conclusion: Lactated Ringer, when compared to normal saline, is associated to a decreased inflammatory response in patients with acute pancreatitis.

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Disclosure of Interest: None declared

OP022 ROLE OF AMMONIA PET-CT IN ASSESSING THE PANCREATIC NECROSIS IN PATIENTS WITH ACUTE PANCREATITIS

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Introduction: Contrast enhanced CT scan (CECT) is imaging modality of choice to evaluate necrosis and severity of acute pancreatitis. Ammonia (^{13}NH3) PET can also be alternative especially in setting of acute renal failure, however the comparative studies between these two is still lacking.
Aims & Methods: To evaluate whether Ammonia (^{13}NH3) PET reflects the perfusion status of pancreas in patients of acute pancreatitis(AP) to detect pancreatic necrosis and compare it with necrosis detected on contrast enhanced CT scan(CECT).
35 patients with AP were enrolled in the study. NH3 PET was done in all the patients while CECT was done in 32 patients and 3 patients with renal failure had only PET done for imaging. CECT images were interpreted and the percentage of necrosis, presence and absence of collection were recorded and CTSI (CT severity index) and MCTSI (modified CT severity index) were calculated. Ammonia PET images were separately analyzed and PET CTSI & MPET CTSI were calculated along with the amount of necrosis and collection both observers blinded to each other. Data was recorded in excel sheet and statistical analysis was done using SPSS v17.0.
Results: The mean age of our study population was 40.65 ± 15.1 years. Of these 24 (68.6%) patients were males and 11 (31.4%) were females. 25 patients had organ failure at presentation, with 3 (9%) having acute kidney injury and 22 (63%) patients having ARDS. A comparative analysis of CTSI with PET CTSI showed significant correlation between the two scores (P- 0.000). The scores showed a good agreement (kappa-0.451, P-0.000), suggesting that the two imaging identify patients with pancreatitis with a comparable severity estimation. Necrosis on both CECT and PET was compared separately, however no significant agreement was found (kappa-0.170, P-0.25). Ammonia PET identified 9 patients as having minimal necrosis while CECT showed no necrosis in them, probably suggesting that PET is either more sensitive in identifying necrosis than CECT or may be overestimating it in few patients with only mild pancreatitis. The agreement between two imaging in estimating collections was also analyzed. It showed a good agreement between the two (kappa-0.668 P-0.000). In 22 both CECT and PET diagnosed collection and in 6 they both denied evidence of any collection. Among the remaining 4 patients PET alone identified collection in 3 while CECT alone showed collection in 1 patient. For further confirmation in support of our study we also calculated the modified PET CTSI and the MCTSI scores and they were also correlated. They also showed a significant correlation (P-0.000).
Conclusion: Ammonia PET could be an alternative imaging modality for diagnosis of acute pancreatitis and assessing the severity of acute pancreatitis.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 11:00–12:30

NEW FRONTIERS IN MOLECULAR DIAGNOSIS AND MONITORING OF GI CANCER – ROOM E4

OP023 ROLE OF SQUALENE EPOXIDASE (SQLE) IN PROMOTING FATTY LIVER DISEASE-ASSOCIATED LIVER CANCER

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Introduction: Non-alcohol steatoheptitis (NASH) is a major risk factor for the development of hepatocellular carcinoma (HCC). Using whole transcriptome sequencing (RNA-seq), we have identified squalene epoxidase (*SQLE*) as a novel gene up-regulated in human NASH-associated HCC. *SQLE* is located at human chromosome 8q24.1, a frequently amplified region in HCC, and encodes a rate -limiting enzyme in the cholesterol biosynthetic pathway. The role of SQLE in human cancer remains unclear.
Aims & Methods: We aimed to investigate the biological function, molecular mechanism and clinical implication of SQLE in NASH-HCC. SQLE expression was validated in NASH-HCC patients and genetic obese *Foz/Foz* mice model. The biological functions of SQLE were determined in cell lines in vitro and xenografts in nude mice. The molecular mechanism of SQLE was identified by PCR array and Human Methylation 450K array analyses. Clinical application of serum SQLE levels in diagnosis of NASH was assessed in 220 NAFLD/NASH patients serum.
Results: *SQLE* was overexpressed in 17 out of 27 (63%) human NASH-HCC tumor samples compared with their adjacent non-tumor liver tissues. *SQLE* was also overexpressed in *Foz/Foz* mice fed a high-fat, high-cholesterol diet compared to a high-fat diet alone, indicating that cholesterol can induce *Sqle* expression. SQLE possessed an oncogenic function in NASH-HCC, as its overexpression in liver cell lines (LO2 and Huh7) significantly promoted cell proliferation, cell cycle progression and tumorigenicity in nude mice. Conversely, the silencing of SQLE in BEL-7404 cells and HepG2 cells had an opposite effect.
We investigated the role of cholesterol in regulating the expression of SQLE. *In vitro* treatment with cholesterol induced the expression of *SQLE* in LO2 and Huh7 cells through increasing the intracellular accumulation of acetyl-CoA. To identify the downstream molecules that mediate the oncogenic effect of SQLE, we performed PCR array analysis in SQLE overexpressing cells and revealed that SQLE induced alterations of genes involved in fatty acid metabolism and epigenetic programming. SQLE overexpression increased intracellular cholesterol and triglyceride levels. The accumulation of intracellular cholesterol activated ROS, ER stress and consequently inducing the AP1 and NF-kB pro-inflammatory pathways that contribute to NASH and NASH associated-HCC. Moreover, SQLE triggered a major epigenetic reprogramming via the up-regulation of DNMT3A, a de novo DNA methyltransferase. Consequently, SQLE expression induced promoter methylation of key tumor suppressor genes including PTEN and histone deacetylase 9 (HDAC9). HDAC9 silencing, in turn, promoted histone phosphorylation level (H3S10) and activated WNT pathway that contributes to tumorigenesis.
Finally, we assessed clinical significance of SQLE overexpression in NASH, and we demonstrated that serum SQLE levels exhibited a high overall accuracy in discriminating NASH subjects from control subjects with the area under the receiver operating characteristic curve (AUROC) of 0.773 (95% CI: 0.709–0.839), indicating that SQLE is a promising biomarker for NASH.
Conclusion: SQLE is a novel tumor-promoting gene which can be induced by cholesterol. SQLE links abnormal cholesterol metabolism to the malignant progression of NASH and NASH-associated HCC. SQLE is a potential biomarker for the clinical diagnosis of NAFLD and NASH patients.
Disclosure of Interest: None declared

OP024 INCREASED CELL-FREE DNA INFLUENCES CANCER GROWTH IN A MOUSE MODEL

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Introduction: Circulating free DNA (cfDNA) level is increased in tumorous deseases and regular physical activity. The positive effect of sport in cancer prevention is well-known. Activation of DNA-binding receptors may induce signal transduction pathways connected to cell circle or immune cell activation.
Aims & Methods: Our aim was to study the effect of increased cfDNA level on tumor progression using an animal model. Efficacy of sport was also evaluated as physiologically increased cell-free DNA condition. We studied fifteen C57BL/6 mice in four groups. C38 non-necrotic colorectal adenocarcinoma tissue was implanted subcutaneously in each mouse at the same time. Group I was treated with high concentration subcutaneously injected healthy C57BL/6 spleen-derived DNA (sdDNA), Group II with C38 tumor tissue-derived DNA (tdDNA). Both treatment started at the time of tumor implantation and was continued until the end of the study, three times per week. DNA was isolated from C38 tumor tissue and healthy spleen by our standard method using Zymo DNA columns (DNA Clean & Concentrator^{TM}-500, Zymo Research). Group III was strained by five hours long physical activity five times per week in a rodent wheel. Group IV was used as a control group injected with PBS. Tumor sizes were measured twice a week. Mice were slaughtered on the 22nd day and peripheral blood, fresh frozen and paraffin embedded tumor tissue and colon samples were collected. Hematoxylin-eosin stained sections were prepared. Cytokeratin, Ki-67, CD3 immunohistochemistry stainings were performed to analyse cell proliferation, necrosis and T-cell invasion. We verified our results on HT29 human colorectal carcinoma cell line. We created three groups using human healthy DNA, HT29 derived DNA treatment and PBS, as controls. Cell cycle analysis was performed by flow cytometry following propidium iodide staining.
Results: The size of tumor in group I (sdDNA) was 48%, in group III (sport) was 51% compared to control group. In Group II (tdDNA) 34% of animals died during the experiment, 20% of tumors were exulcerated due to increased growth, and all mice were cachectic. Histological investigation of implanted tumor tissues showed increased cell proliferation and dedifferentiated tumor tissue in tdDNA treated group. Number of living tumor cells showed significant differences in Group I and III: 44% and 34% respectively, in comparison to 78% in Group II. CD3 expression was lower in group II (4%) and showed

Abstract number: OP025

Indicators /Type of lesions	Sensitivity (95%CI)	Specificity (95%CI)	Positive predictive value(95%CI)	Negative predictive value(95%CI)	Kappa value(95%CI)
Non-metaplasic non-neoplastic	0.928 (0.926–0.93)	0.982 (0.98–0.983)	0.97 (0.968–0.972)	0.955 (0.954–0.957)	0.917 (0.913-0.92)
Metaplastic	0.928 (0.925-0.93)	0.945 (0.944-0.947)	0.90 (0.898-0.903)	0.961 (0.96-0.962)	0.867 (0.863-0.871)
Neoplastic	0.893 (0.89-0.897)	0.954 (0.953-0.955)	0.872 (0.868-0.875)	0.962 (0.961-0.964)	0.84 (0.835-0.845)

strong positivity in group I and II (19% and 17%) compared to the control group (7%). In group II the number of lymphoid tissue plaques decreased and the mucosa layer of colon samples was destructed. On DNA histogram of HT29 cells increased proliferation was observed following HT29 DNA treatment and increased apoptosis following normal DNA treatment, in correlation with observations of our animal experiments.

Conclusion: Physical activity and normal DNA treatment may have similar cancer preventive effect by increased amount of lymphoid tissue and inhibited proliferation of tumor cells. The present findings may emphasize the importance of physical activity in cancer prevention. The positive autocrin effect of tumor derived cfDNA on tumor cells is a new and important factor and a unique observation.

Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 11:00–12:30

ADVANCES IN ENDOSCOPIC IMAGING OF THE UPPER GI TRACT – ROOM E3

OP025 COMPUTER-AIDED DIAGNOSTIC SYSTEM FOR THE REAL-TIME PATHOLOGY PREDICTION AND CLINICAL DECISION SUPPORT DURING NARROW BAND IMAGING MAGNIFICATION ENDOSCOPY IN STOMACH

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Introduction: Narrow-band imaging endoscopy with magnification (NBI-M) is recommended to be utilized for clinical decision-making during screening or follow-up of individuals at high risk for gastric cancer [1]. Nevertheless, its application in clinical practice has some challenges due to the presence of various histological and endoscopic pattern changes of gastric mucosa. Nowadays computer-aided decision support systems in endoscopy are being designed to assist a medical expert in mastering advanced techniques that require a high level of expertise.

Aims & Methods: The aim of this study was to design a computer-aided diagnosis hardware-software complex for real time clinical decision support during NBI-M in stomach. This complex was incorporated into endoscopic documentation system for real-time pathology prediction based on the automated assessment of mucosal patterns of saved images. Image processing techniques were applied for extracting of geometrical and topological features. For creating a multi-class classifier a naive Bayesian approach was used to combine results of several binary Adaboost classifiers. We selected and analyzed 91 endoscopy NBI-M images of gastric lesions from 52 patients (Olympus Exera GIF Q160Z, Lucera GIF Q260Z). All images were independently assessed by an expert and computer-aided system according to validated simplified NBI-classification [2]: type A (circular), B (tubulo-villous), C (irregular). Histology was used as the ground truth information. Training and testing were performed for every image by a bootstrap method.

Results: Among 91 images 25 had type A pattern (16 normal mucosa, 9 chronic gastritis), 31 had type B pattern (22 intestinal metaplasia, 9 pseudopyloric metaplasia), and irregular 35 has type C pattern (9 high-grade dysplasia, 26 adenocarcinoma). The average percentage of correctly recognized areas was $91.8 \pm 4.4\%$ (92% in type A, 92% in B, 89% in C). The results of computer-aided classification are summarized in the table.

Conclusion: The newly designed endoscopic computer-aided diagnostic hardware-software system could provide effective recognition of three main types of gastric mucosal patterns and thus may lead to real-time pathology prediction and support for clinical decision-making.

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Disclosure of Interest: None declared

OP026 PROSPECTIVE CONTROLLED TRIAL OF NARROW BAND IMAGING FOR DETECTION OF GASTRIC CANCER PRECURSORS

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Introduction: Gastric intestinal metaplasia (GIM) is a precursor lesion of gastric cancer. Narrow band imaging (NBI) enhances the mucosal and vascular pattern of the gastric surface. Recently a simplified NBI approach for evaluation of gastric cancer precursors was introduced.[1]

Aims & Methods: AIM was to compare in a prospective tandem manner whether NBI improves detection of GIM compared to white light exam and random biopsy protocols in a population with high (67%) prevalence of *H. pylori.*

Methods: Patients with symptoms of dyspepsia, epigastric pain, and iron deficiency anemia but not active bleeding or known gastric metaplasia/neoplasia were evaluated by upper endoscopy. Each patient underwent white light exam by one endoscopist, followed by NBI exam by a second endoscopist blinded to the white light findings. Targeted biopsies were performed of abnormal areas detected by white light and NBI. All patients then underwent a random biopsy protocol comprised of 2 biopsies from the lesser curvature (body and antrum), 2 biopsies from the greater curvature (body and antrum), and one from the incisura. Biopsies directed by 3 methods (white light, NBI, and random biopsy protocol) were coded and read by a pathologist blinded to the modality which guided the biopsies. PRIMARY OUTCOME was the proportion of patients with GIM, according to NBI, white light, and random biopsy. The yield of the 3 modalities to detect GIM on a per lesion (abnormal region) basis was a secondary outcome.

Results: 70 patients were included in this interim analysis (32% of the proposed sample of 220); and all had at least 3 sites biopsied (total sites = 294). Indications for upper endoscopy were dyspepsia in 25, epigastric pain in 27, and iron deficiency in 18. Overall, 24 (34%) of patients were confirmed on biopsy to have gastric intestinal metaplasia; it was localized to the antrum in 13 but multifocal in 7. The overall accuracy rate for patients was 77% for white light, 90% for NBI, and 90% for random biopsy. While white light identified 8/24 (33%) of individuals with metaplasia, NBI and random biopsy identified 17 (71%) (McNemar's $p = 0.02$)(Table 1). Among the 24 patients, intestinal metaplasia was detected only by NBI in 6 patients, only by random biopsy in 6, and a combination of methods in the remainder. NBI required less biopsies, a mean of 10 to detect each patient with GIM compared to 18 for the random biopsy protocol.

Table 1

		Correct identification of metaplasia		
	Prevalence of Metaplasia N (%)	White Light	Narrow Band Imaging	Random Biopsy Protocol
Patients with GIM (per patient analysis) N = 70	24 (34%)	8 (33%)	17 (71%)	17 (71%)
Individual sites (per site analysis) N = 294	39 (13%)	11 (28%)	20 (51%)	23 (59%)
Biopsies targeted by each modality		89	171	300

Conclusion: Gastric intestinal metaplasia is frequently missed by white light endoscopy. In this preliminary analysis, NBI and random biopsies appear to improve detection, with NBI requiring less biopsies.

Reference

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Disclosure of Interest: None declared

OP027 MORPHOLOGICAL CLASSIFICATION AND CLINICAL SIGNIFICANCE OF WHITE OPAQUE SUBSTANCE WITHIN GASTRIC NEOPLASIA VISUALIZED BY MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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Introduction: White opaque substance (WOS) within gastric neoplasia is a unique finding of magnifying endoscopy with narrow-band imaging (ME-NBI) and indicates intramucosal accumulation of lipid droplets. We presented the morphological classification of WOS within gastric neoplasia at UEGW in 2014. However, the morphological classification of WOS within gastric neoplasia and the accuracy of this classification has not been thoroughly investigated by studies with large sample sizes.

Aims & Methods: The aim of the current study was to establish a morphological classification system for WOS and investigate whether this system can be used to discriminate between adenoma and early carcinoma. This study retrospectively investigated 308 patients with 343 gastric neoplasias (40 adenomas and 303 early carcinomas) who underwent ME-NBI before endoscopic resection at our hospital between January 2010 and February 2015. We studied the frequency of WOS in these gastric neoplasias and identified the following morphological patterns: 1) dotted pattern, scattered and distributed as dots; 2) linear pattern, shaped like a line composed of aggregated dots; 3) reticular pattern, shaped like a honeycomb composed of connected lines; 4) speckled pattern, mottled and composed of aggregated dots; and 5) diffuse pattern, diffusely distributed with dense WOS in the intervening part. We also investigated the irregularity of WOS within adenomas and early carcinomas. We defined irregular WOS as a disorganized and asymmetrical distribution of WOS on any pattern.

Results: WOS was more frequently observed in adenomas (17/40: 42.5%) than in early carcinomas (98/303: 32.3%). The sensitivity, specificity, and accuracy of dotted WOS for discriminating carcinoma from adenoma were 53.1%, 76.5%, and 56.5%, respectively. The sensitivity, specificity, and accuracy of reticular WOS for discriminating adenoma from carcinoma were 47.1%, 87.8%, and 80.0%, respectively. The sensitivity, specificity, and accuracy of irregular WOS for discriminating carcinoma from adenoma were 98.0%, 58.8%, and 92.2%, respectively. WOS within adenomas showed a symmetrical distribution with a regular reticular pattern. WOS within carcinomas showed an asymmetrical distribution with an irregularly dotted pattern.

	Adenoma (17)	Carcinoma (98)	*P value*
Dotted pattern	4/17 (23.5%)	52/98 (53.1%)	<0.05
Linear pattern	7/17 (41.2%)	23/98 (23.5%)	0.217
Reticular pattern	8/17 (47.1%)	12/98 (12.2%)	<0.01
Speckled pattern	6/17 (35.3%)	48/98 (49.0%)	0.435
Diffuse pattern	2/17 (11.8%)	8/98 (8.2%)	0.98
Irregular WOS	7/17 (41.2%)	96/98 (98.0%)	<0.01

Conclusion: In gastric neoplasias, the findings of WOS with reticular, dotted, and irregular patterns are useful for discriminating between adenoma and early carcinoma. This study focuses on the utility and effectiveness of the morphological classification of WOS when examining WOS within gastric neoplasias using ME-NBI.

Disclosure of Interest: None declared

OP028 ATLAS OF HIGH-QUALITY HISTOLOGICAL CORRELATIONS OF VOLUMETRIC LASER ENDOMICROSCOPY IMAGES OF BARRETT'S ESOPHAGUS FOR IDENTIFICATION OF EARLY NEOPLASIA

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Introduction: Early neoplastic lesions in Barrett's esophagus (BE) are difficult to detect with white-light endoscopy. Volumetric Laser Endomicroscopy (VLE) is a novel balloon-based OCT imaging technique that provides a 6-cm long circumferential volumetric scan of the esophageal wall layers to a depth of 3 mm with a resolution comparable to low-power microscopy. Correlation of VLE to histology is essential to be able to identify VLE features of early BE neoplasia.

Aims & Methods: The aim was to compose high-quality one-to-one correlated histology-VLE images for identification of VLE features of early BE neoplasia. An ex-vivo VLE scan of endoscopic resection (ER) specimens including reference markers from BE patients with and without neoplasia was performed. Tissue blocks were carefully sectioned from the ER specimens alongside the reference markers. Histology slides were sectioned from each tissue block and when necessary extensive sectioning of tissue blocks was performed in order to visualize all markers. All histology slides were evaluated by an expert BE pathologist and annotated using a custom-made program for epithelium type, grade of dysplasia and (sub)mucosal structures. All VLE scans and corresponding histology slides were evaluated by 2 observers and considered a match when on both modalities ≥ 2 reference markers were visible and mucosal patterns matched. In each match areas of interest (AoIs) were identified based on the histological diagnosis and division of the match by the reference markers. In an unblinded learning phase all AoIs were evaluated for potential VLE features predictive of neoplasia.

Results: In total 52 ER specimens were obtained in 29 BE patients ((66 yrs, 19 male, overall histological diagnosis 16 early adenocarcinoma (EAC), 5 high-grade dysplasia (HGD), 2 low-grade dysplasia (LGD) , 6 non-dysplastic (ND)BE)). 86 histology-VLE matches were constructed including 185 AoIs (31 squamous epithelium, 43 gastric epithelium, 41 NDBE, 22 LGD, 20 HGD, 27 EAC. In a first evaluation the following VLE features were identified as potentially predictive for dysplasia: lack of layering, homogeneity ,surface maturation and irregular glands.

Conclusion: This study presents the first atlas of high-quality histology-VLE correlations of BE and neoplasia, allowing further research on development of VLE features to distinguish early neoplasia in BE. The learning phase identified several potential VLE features for early BE neoplasia, which is the first step towards validation of VLE for detection of early BE neoplasia.

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OP029 FLUORESCENCE DETECTION OF HEAD AND NECK SQUAMOUS CELL CARCINOMA BY TOPICALLY SPRAYING A GAMMA-GLUTAMYLTRANSPEPTIDASE-ACTIVATED PROBE

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Introduction: Although early detection of head and neck squamous cell carcinoma (HNSCC) is imperative for better outcome, it is difficult to detect early HNSCC endoscopically, because there are few morphological changes. Lugol chromoendoscopy has been widely accepted for the detection of early esophageal squamous cell carcinoma; however, it can not be applied to the head and neck lesion due to severe mucosal irritation. Therefore, a valuable method to detect early HNSCC is required.

γ-glutamyl transpeptidase (GGT), a cell surface enzyme, is overexpressed in several cancers, and it has been reported that an enzymatically activatable fluorescent probe, γ-glutamyl hydroxymethyl rhodamine green (gGlu-HMRG), which becomes fluorescent after cleavage of a GGT-specific sequence, can be activated within a few minutes after spraying in a cancer-bearing animal model (Sci Transl Med 3:110ra119, 2011).

Aims & Methods: To evaluate whether early HNSCC can be detected by spraying gGlu-HMRG, using fresh clinical samples obtained by endoscopic submucosal dissection (ESD) or surgical resection.

gGlu-HMRG was applied to four HNSCC cell lines (HSC2, HSC3, HSC4, SCC25), and fluorescence was observed by fluorescent microscopy and flow cytometry. Immunohistological examination was performed to the past three ESD cases to investigate the expression of GGT. Fluorescent imaging with gGlu-HMRG for five cases resected by ESD or surgery was performed. Fluorescent intensity of region of interest (ROI) of tumor and normal mucosa was measured.

Results: All four cell lines applied gGlu-HMRG emitted green fluorescence. Immunohistological examination demonstrated that GGT was highly expressed in HNSCC but barely expressed in normal component. Fluorescent imaging showed that lugol-voiding lesion became fluorescent within a few minutes after spraying gGlu-HMRG in all five resected cases. Fluorescent intensity of ROI in tumor region was significantly higher than in normal mucosa in five minutes after spraying gGlu-HMRG ($p < 0.05$).

Conclusion: Fluorescent imaging with gGlu-HMRG is useful for early detection of HNSCC.

Disclosure of Interest: None declared

OP030 A NOVEL ENDOSCOPIC DIAGNOSIS OF CANCER FUNCTION USING HYPOXIA IMAGING ENDOSCOPY EQUIPPED WITH LASER LIGHT SOURCE

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Introduction: Recent endoscopy has evolved into image-enhanced endoscopy (IEE), such as Narrow Band Imaging and Blue Laser Imaging. IEE focused on increasing abnormal microvessels in the surface of early cancers. In contrast, hypoxia is one of the functional characteristics in cancer, with strong

association to the biological features. The investigation of cancer hypoxia was started in the 1960s, and there have been many reports. Therefore, hypoxia imaging was innovated to visualize directly the biological and functional changes in cancer.
Aims & Methods: The aim of this prospective study is to evaluate the visualization of human cancers using hypoxia imaging endoscopy in the first in human clinical trials. In endoscopic equipment, we utilized a difference of absorption between oxy- and deoxy-hemoglobin in visible light wavelength. The signals converted from laser light were calculated in oxygen saturation (StO_2) by processor. Hypoxia imaging was obtained in real-time, displaying two types of StO_2 images. One was a pseudocolor image showing StO_2 levels as different hues, and the other was an overlay image that overlapped low StO_2 levels in blue on a white light illumination image of background mucosa. In the initial trial, patients who had been confirmed to have pharyngeal, esophageal, gastric, or colorectal neoplasia by previous endoscopy were enrolled. To compare histologic findings to hypoxia imaging, all patients received endoscopic resection immediately after conventional and hypoxia imaging endoscopy. We determined the corresponding areas of neoplasia and non-neoplasia in the endoscopic images and obtained StO_2 levels from the StO_2 map. In the second clinical trial, we investigated the changes of hypoxia imaging before and after chemotherapy, and efficacy of chemotherapy in advanced cancers of the esophagus, stomach, and colorectum.
Results: Forty patients with early-sided lesions in the pharynx, esophagus, stomach and colorectum were analysed. The hypoxic area was completely corresponded to the portion of early cancer. Furthermore, 8 colorectal low-grade adenomas were also detected as hypoxia, ranging from 3 to 10 mm in diameter. All esophageal cancers including 2 Barrett's cancers were detected in hypoxia images. Median StO_2 differences between neoplastic and non-neoplastic areas in the pharynx, esophagus, stomach and colorectum were -15.4%, -14.5%, -5.1% and -21.5%, respectively. Significant differences of StO_2 levels were seen in the esophagus ($p = 0.0078$, $n = 8$) and colorectum ($p = 0.0001$, $n = 14$), but not in the stomach ($p = 0.9341$, $n = 15$) or pharynx ($p = 0.2500$, $n = 3$). In the advanced cancers, hypoxia imaging before chemotherapy could be partly related to efficacy of chemotherapy.
Conclusion: Hypoxia imaging with the laser endoscope enables us to visualize spatial and temporal information of hypoxic conditions in adenoma, early and advanced cancers. Hypoxia imaging illustrates a novel aspect of cancer biology as a potential biomarker and can be widely utilized in cancer diagnosis.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 11:00–12:30
LIVER: FROM INFLAMMATION TO FIBROSIS – ROOM E5

OP031 THE PERFORMANCE OF POINT SHEAR WAVE ELASTOGRAPHY USING ARFI TECHNIQUE -ELASTPQ IN CHRONIC HEPATOPATHIES

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Introduction: In the last decade , different types of ultrasound based elastographic methods that noninvasively quantify liver fibrosis, have been developed.
Aims & Methods: The aim of this study was to compare the performance of point shear wave elastography using ARFI technique- ElastPQ, in patients with different liver diseases, using Transient Elastography (TE) as the reference method, since it is a validated method for liver fibrosis assessment.
The study included 121 consecutive subjects with chronic hepatopathies (33.9% HBV, 23.9% HCV, 5.8% NASH, 1.7% ASH, 4.1% colestatic liver disease) and 30.6% with liver cirrhosis by means of TE. Liver stiffness (LS) was evaluated in the same session by means of 2 elastographic **Methods:** TE (Fibroscan, Echosens) and ElastPQ (Philips, Affinity) technique.
Reliable LS measurements were defined as follows: for TE – the median value of 10 LS measurements with a success rate $\geq 60\%$ and an interquartile range $< 30\%$, for ElastPQ- the median value of 10 LS measurements in the liver parenchyma avoiding large vessels. For TE M and XL probes are used. LS was expressed in kPa for both TE and ElastPQ. For differentiating between stages of liver fibrosis we used the following cut-off values: for TE - significant fibrosis ($F \geq 2$) - 7.2 kPa and for liver cirrhosis (F4) -14.5kPa (Tsochatzis, 2011); for ElastPQ $F \geq 2$ -5.9 kPa, $F4 = 12$ kPa (Ferraioli, 2013). Reliable liver stiffness evaluation were obtained in 74.4% by means of TE and 99.3% with ElastPQ.
Results: In the final analysis were included 90 subjects (90/121 - 74.4%) with reliable LS measurements by means of TE. By using ElastPQ with the proposed cut-offs, as evaluation method, the frequency of no or mild fibrosis ($F < 2$), significant fibrosis ($F \geq 2$) and cirrhosis ($F = 4$) in our cohort was: 62.2% ($F < 2$), 17.8% ($F \geq 2$) and 20% ($F = 4$). Considering TE as the reference method, the sensitivity (Se) and specificity (Sp) for the diagnose of absence or mild fibrosis by means of ElastPQ were: 87.7% and 91.2%.
For significant fibrosis ($F \geq 2$) we obtained a sensitivity (Se) of 57.9% and specificity (Sp) of 91.2%, while for cirrhosis, the Se was 83.3% and the Sp 95.8%. ElastPQ was significantly better for diagnosing cirrhosis than significant fibrosis: accuracy 93.3% vs. 82% ($p = 0.03$), while for absence or mild fibrosis vs. significant fibrosis the accuracies were similar: 87.7% vs. 82% ($p = 0.39$).
Conclusion: ElastPQ is a promising non-invasive elastographic method that can accurately diagnose liver cirrhosis.

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Disclosure of Interest: None declared

OP032 SIGNIFICANCE OF INTEGRIN ALPHA 11 IN PHENOTYPIC REGULATION OF HEPATIC STELLATE CELLS IN LIVER FIBROSIS

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Introduction: Liver fibrosis, characterized by excessive accumulation of ECM produced by proliferative and differentiated hepatic stellate cells (myofibroblasts), is the growing cause of mortality worldwide. Thus, understanding of the factors that induce myofibroblasts differentiation is paramount to prevent the fibrotic process. Previous studies have shown that mechanical stress derived from the integrin-mediated interaction between extracellular matrix and the cytoskeleton promotes myofibroblasts differentiation.
Aims & Methods: Integrin alpha 11 (ITGA11) is collagen receptor expressed on fibroblasts and in this study we aimed to explore the significance of this receptor in hepatic stellate cells during liver fibrosis. Liver fibrosis was induced in mice by intraperitoneal administrations of CCl_4 for 4 weeks (intermediate) and 8 weeks (advanced). Protein and mRNA expression levels of various fibrotic parameters and ITGA11 were examined using QPCR and immunostaining. We also analyzed ITGA11 expression in human cirrhotic liver tissues and in TGFβ-activated human hepatic stellate cells (LX2). To elucidate the possible role of ITGA11, we knocked-down its expression in LX2 cells using ITGA11-shRNA plasmid. Morphological changes and fibrotic parameters in control and ITGA11 knock-down cells were studied with and without TGFβ activation, using immunostainings, quantitative PCR and RT^2 profiler human fibrosis array. Furthermore, to assess its functional role in fibrosis-related processes, we performed collagen I adhesion assay, 3D-collagen gel contraction assay, wound closure/migration assays and indirect effect on angiogenesis (tube formation assay).
Results: *In vivo* in liver fibrosis mouse models, we found an increase of the ITGA11 expression with increasing degree of fibrosis as well as it was highly expressed in human cirrhotic livers. The ITGA11 expression was found to be co-localized with α-SMA positive myofibroblasts in both mice and human cirrhotic livers. *In vitro*, ITGA11 expression levels (mRNA and protein) were highly up-regulated in TGFβ-activated human hepatic stellate cells while remained undetected in hepatocytes and monocytes. Following stable ITGA11 knock-down, we observed 80% reduction in ITGA11 which resulted in decreased mRNA expression levels of a-SMA, IGF2, vimentin, TIMP1 and paxillin. We further found drastic reduction in TGFβ-induced collagen I, a-SMA and vimentin protein expression in ITGA11 knock-down versus control cells. Strikingly, in RT^2 profiler human fibrosis array, ITGA11 knock-down cells showed a significant reduction in 19 fibrosis-related genes, as compared to control cells. Interestingly, ITGA11 knock-down cells displayed decreased proliferation and diminished filopodia and lamellipodia extensions signifying ITGA11 importance in maintaining the HSCs phenotype. In the functional assays, ITGA11 knock-down resulted in attenuated would healing, reduced adhesion to collagen-I matrix, impaired collagen contractility and inhibited HSC-induced endothelial cell tube formation (angiogenesis).
Conclusion: These findings suggest that ITGA11 is a promising target in myofibroblasts during liver fibrosis which regulates proliferation, differentiation and fibrosis-related functions of myofibroblasts.
Disclosure of Interest: None declared

OP033 ROLE OF THE PROTEASE-INHIBITOR SERPINB3 IN THE REGULATION OF WNT FAMILY MEMBERS IN MONONUCLEAR CELLS

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Introduction: Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related death world-wide. HCC nearly always develops in the setting of liver cirrhosis and hepatitis B and C viral infection. Recent publications revealed that Notch/WNT pathway orchestrates liver stem cell activation and differentiation and that deregulation of this pathway is associated with HCC development. Our recent data demonstrate that SerpinB3, a member of the ovalbumin-serin protease inhibitor family, plays a primary role in hepatocellular carcinoma development. In addition, its detection in the liver progenitor cells niche, suggests an involvement in staminal cell activation. Furthermore, SerpinB3 induces EMT and modulates miR122 which is involved in WNT-1 production. The aim of this study was to evaluate the role of SerpinB3 in the modulation of Notch-WNT signalling in macrophages, principal players in the modulation of liver staminal niche through WNT paracrine signalling
Aims & Methods
Methods: Primary human mononuclear cells were isolated from healthy donors and treated with or without recombinant SerpinB3 (200 ng/ml) or medium as

control up to 168 hours. WNT-family mRNA expression was evaluated by Q-PCR, while cell viability was measured daily up to 7 days.
Monocyte-derived THP-1 cell line was also transfected with a plasmid vector containing SerpinB3 or a empty vector as control, and characterised after 48 h. To evaluate the effect of SerpinB3 in inflammatory cells, mononuclear cells were pre-treated with recombinant SerpinB3, stimulated with 1 μM LPS and analyzed up to 24 hours.
Results: In human monocytes the addition of SerpinB3 induced a 30% cell viability increase at day 7. In monocytes stimulated with SerpinB3 a significant up-regulation of WNT-1, but not of WNT-3a, WNT-5a and WNT-7a, compared to controls, was detected. In mononuclear cells stimulated with LPS, to mimic inflammation, WNT-1 was weakly expressed, but pre-treatment with SerpinB3 determined a remarkable up-regulation of this molecule. In monocyte-derived THP-1 cells transfected with SerpinB3, WNT-1 was slightly increased and its expression was further enhanced after exposure to LPS. In this latter experimental condition a significant increase of WNT-5a was also observed.
Conclusion: SerpinB3 prevents natural cell death of primary human monocytes in vitro. The modulation of WNT-family members is differently influenced by SerpinB3 in relation to inflammatory conditions, suggesting that this serpin may affect the liver staminal niche behaviour by modulating the WNT-family member profile.
Disclosure of Interest: None declared

OP034 IL-10-PRODUCING REGULATORY B CELLS ENHANCED REGULATORY T CELLS FUNCTION: A NEW IMMUNOSUPPRESSIVE MECHANISM DURING HBV-RELATED LIVER FIBROSIS

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Introduction: Chronic hepatitis B (CHB) infection is a leading cause of liver fibrosis, cirrhosis and even hepatocellular carcinoma. Although hepatitis B virus (HBV) itself is non-cytopathic, both HBV-related liver damage and viral control are immune-mediated. There were abundant evidences to believe that regulatory T (Treg) cells play pivotal roles in the immunopathogenesis of HBV and its related liver diseases, especially in immune tolerance phase and persistent virus infection. Nowadays, a new subset of IL-10-producing B cells, also known as regulatory B (Breg) cells has been shown to play vital roles in modulating autoimmune diseases. However, its relationship with infectious disease has rarely been studied.
Aims & Methods
Aims: Here, we evaluated the role of Breg cells in the pathogenesis of HBV-related liver fibrosis (HBV-LF) and assess their impact on the proliferation of CD4 + T cells and further investigated the immunoregulatory effects on Treg cells.
Methods: A total of 67 treatment-naïve patients who were diagnosed as chronic hepatitis B (CHB) patients underwent liver biopsies and 25 healthy donors took part in the study. Firstly, peripheral blood mononuclear cells (PBMC) were isolated for the study of Breg subset markers (CD19, CD24, CD27, CD38, CD25, CD40, IgM, IgD, IL-10). And then, we determined the changes in number and function of Breg cells in CHB patients compared with that of healthy controls. For the *in-vitro* experiments, human Breg, CD4 + T and Treg cells were purified using flowcytometry. Purified anti-CD3 antibody stimulated CD4 + T cells were cultured alone or with autologous Breg cells and their proliferation response was determined by the thymidine method. Simultaneously, to elucidate the exact effects of Bregs on Tregs and the potential methanism during HBV-LF, human Breg and Treg cells were co-cultured in the stimulation with HBcAg, anti-IL-10 and anti-TGF-β antibody.
Results: B cells and Breg cells were both enriched in patients, and among which, Breg cells frequencies had a close relationship with viral load, liver inflammation and degree of fibrosis. Stimultaneously, we demonstrated the phenotype of these Breg cells: memory B cells ($CD24^{hi}CD27^{+}$B cell) and transitional B cells ($CD24^{hi}CD38^{hi}$B cell), and the phenotype was pridominantly characterized as $CD19^{+}CD24^{hi}CD38^{hi}$B cell subset. In the co-culture of Breg cells from CHB patients with autologous CD4 + T cells, the proliferation capacity of CD4 + T cells was significantly reduced in a dose-dependent manner compared with controls. In addition, Breg cells from patients with CHB were found to have further enhanced effect on the proliferation of Treg cells as well as the release of IL-10 and TGF-β cytokines than such cells from healthy donors. Furthermore, blockage of IL-10 and CTLA-4 but not TGF-β decreased the inhibitory effect of Breg cells on Treg cells. The regulatory function of Breg cells on Treg cells was mainly dependent on direct cell-cell contact as well as IL-10 but not TGF-β-dependent manner.
Conclusion: Our data revealed that elevated Breg cells, which can inhibit the proliferation of CD4 + T cells and regulate Treg cells immunity, maybe an indicator for the development of HBV-related liver fibrosis.
Disclosure of Interest: None declared

OP035 TARGETING NOTCH SIGNALING PATHWAY BY SMALL MOLECULE Γ-SECRETASE INHIBITOR BMS-708163 ATTENUATES EARLY LIVER FIBROGENESIS IN VIVO

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Introduction: Hepatic fibrosis, mainly caused by viral infections, alcohol abuse or metabolic syndrome leading to liver dysfunction, is the growing cause of mortality worldwide. Currently, there is no clinically-approved therapy available for the treatment of this disease. Hepatic stellate cells (HSCs) known as "master producers" and macrophages (inflammatory cells) as "master regulators" of fibrosis, are the key cell types that strongly contribute to the initiation and progression of liver fibrosis. Therefore, therapeutic inactivation of these key cell types may lead to reversal of fibrosis.
Aims & Methods: Since aberrant activation of the notch signaling cascade occurs in patients with liver fibrosis, we hypothesized to target this pathway for intervention in liver fibrosis using BMS-708163, a small molecule that specifically inhibits γ-secretase. Activation of Notch signaling pathway was examined *in vitro* in activated HSCs (LX2), M1- and M2-differentiated RAW macrophages and *in vivo* in liver fibrosis mouse models. Effects of Notch signaling inhibitor BMS-708163 on fibrotic parameters and contractility were evaluated in TGFβ-activated LX2. In addition, effect of the BMS-708163 were examined in M1 (inflammatory) and M2 (restorative) differentiated macrophages. Effect on cell viability was examined in both cell types at increasing concentrations of BMS-708163 using alamar blue assay. Finally, BMS-708163 was evaluated for anti-fibrotic effects in CCl_4-induced acute liver injury mouse model.
Results: Notch signaling pathway components were significantly up-regulated in TGFβ-activated HSCs (Notch3, JAG1 and Hes1), M1-differentiated macrophages (Notch1,2,3, Jag1, Dll1,4 and Hes1) and *in vivo* in in acute liver injury and advanced fibrosis mouse models (Notch1,3, Jag1, Dll1,4 and Hes1). *In vitro*, in TGFβ-activated human LX2 cells, BMS-708163 significantly inhibited protein and gene expression of major fibrotic parameters (Collagen I, α-SMA and Vimentin) and 3D-collagen I gel contractility. Furthermore, in M1- and M2-differentiated murine macrophages, BMS-708163 significantly suppressed M1 markers (IL-1β, IL-6, iNOS and nitric oxide release) while no effect on M2 markers (Arginase I and MRC1) were observed. No significant effects on cell viability was observed with increasing concentrations of BMS-708163. *In vivo* in CCl_4-induced acute liver injury mouse model, post-disease administration of BMS-708163 (10 mg/kg) significantly attenuated collagen accumulation, HSC activation and proliferation. Interestingly, BMS-708163 significantly inhibited inflammatory M1 macrophages and up-regulated M2 macrophages.
Conclusion: Because no effective treatment for liver fibrosis exists, selective inhibition of notch signaling pathway suggests a potential unique therapeutic approach targeting key pathogenic cell types (both hepatic stellate cells and macrophages) in liver fibrosis.
Disclosure of Interest: None declared

OP036 ASSESSMENT OF LIVER FIBROSIS WITH SHEAR WAVE ELASTOGRAPHY IN CHRONIC HEPATITIS B VIRUS INFECTION

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Introduction: Real-time shear wave elastography (SWE), as the latest generation of hepatic elastography technique, is promising in noninvasive liver fibrosis measurement but with limited data in Chronic Hepatitis B (CHB).
Aims & Methods
Aims: The purpose of this study is to investigate the diagnostic performance and influence factors of SWE with CHB.
Methods: Patients with CHB from the First Affiliated Hospital of Sun Yat-sen University from July 2013 to February 2015. All had undergone SWE, anthropometry measurement, blood cell count and liver function while 37 patients received liver biopsy. Liver fibrosis was staged from F0 to F4 by METAVIR score. Simple noninvasive fibrosis screening scores APRI and FIB-4 [1]were also calculated with published formulas. Following items were evaluated: Diagnostic accuracy was compared between SWE, APRI and FIB-4 respectively and cooperatively with Receiver operating characteristic curve (ROC) using liver hepatic pathology and decompensated cirrhosis as gold standards. The cut-off value of SWE for liver fibrosis due to HCV was applied to differentiated liver fibrosis stage in these patients[2]. A multiple linear regression model was performed to estimate the correlation between anthropometry, liver function and SWE.
Results: 248 patients with CHB (30 decompensated cirrhosis) were included. 170 (68.5%) patients were males and the average age was 37.4(18∼52) years. Distribution of liver fibrosis stage in 67 patients (37 obtained liver biopsy, 30 decompensated cirrhosis) were as follow: F0:3, F1:21, F2:12, F3:4, F4:30. The Area Under ROC (AUC) for liver stiffness measurement with SWE were 0.891, 0.921 and 0.947 for the diagnosis of significant fibrosis ($\geq$ F2), advanced fibrosis ($\geq$ F3) and cirrhosis (F4), respectively, which is superior to the AUC of APRI [0.798 ($p = 0.094$), 0.823 ($p = 0.046$), 0.806 ($p = 0.038$)] and FIB4 [0.669($p = 0.002$), 0.796($p = 0.016$), 0.838 ($p = 0.048$)]. A multifactor logistic regression combined model of SWE, APRI and FIB4 was build, the AUC of which is 0.902 ($p = 0.97$), 0.942 ($p = 0.620$), 0.933 ($p = 0.796$), respectively, showing no significant differences in SWE alone. When predicting the liver fibrosis stage with cut-off values of SWE from HCV patients[2], misdiagnostic rate of significant fibrosis was 13.1%, omission diagnostic rate was 23.8%. Body Mass Index (BMI) ($\beta = 11.59$, $p = 0.026$), GGT ($\beta = 0.113$, $p = 0.000$) and total bilirubin ($\beta = 0.19$, $p = 0.000$) represent a significant positive correlation with SWE.
Conclusion: SWE have a good value for the noninvasive liver fibrosis assessment, but combination with APRI and FIB4 do not improved diagnostic accuracy. The cut-off values of SWE from HCV patients are not suitable to CHB. SWE may be influenced by BMI, GGT and total bilirubin.

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Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 11:00–12:30
THE INFLAMED STOMACH – ROOM E6

OP037 TARGETED COMPARATIVE PROTEOMICS OF HELICOBACTER PYLORI ISOLATED FROM GASTRIC DISEASES

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Introduction: The infection with the bacterial pathogen *Helicobacter pylori* (HP) is among the risk factors for the occurrence of several gastric diseases, including Gastric Cancer (GC), Duodenal Ulcer (DU), and Atrophic Autoimmune Gastritis (AAG). The characterization of HP differential proteomes in gastric diseases may undoubtedly improve the knowledge of the molecular events associated to the pathological scenario.

Aims & Methods: Therefore, in this work we analysed the differentially expressed proteins of HP in patients affected by DU or GC or AAG by 2D-DIGE, to identify potential HP molecular sentinels to be specifically associated with gastric diseases.

After image analyses with Decyder, a total of 30 proteins were totally found as differentially expressed in a first comparative analysis 'DU *versus* GC', while 36 differentially expressed spots were revealed a second comparative analysis 'AAG *versus* either DU or GC'. Proteins were identified after MALDI-TOF and peptide mass fingerprinting.

Results: Most proteins of HP up-regulated in DU *vs*. GC were oxidoreductases and were involved in various biosynthetic/metabolic processes. The HP proteins overexpressed in GC *vs*. DU were related to protein synthesis and DNA replication/transcription translation. While a higher antioxidant activity was found in AAG-associated HP strains, which were hypothesized to be less motile/virulent and able to neutralize the high local hydrogen concentration as well as to accomplish protein biosynthesis, in comparison with DU- or GC-associated HP.

The overall found differential proteins were then characterized in terms of network connections, biological processes and molecular functions.

Conclusion: The differential protein panels we obtained in HP strains specifically associated with the different pathologies may represent candidate disease markers to be further validated and offer a tool for further analyses aimed to get better insight the pathogenic physiology of some HP strains.

Disclosure of Interest: None declared

OP038 DIFFERENCE OF MICOROMUCOSAL PATTERNS OF THE GASTRIC CORPUS MUCOSA BETWEEN HELICOBACTER PYLORI-ASSOCIATED AND AUTOIMMUNE GASTRITIS PATIENTS

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Introduction: *Helicobacter pylori* (*H. pylori*)-associated and autoimmune gastritis are two major entities of chronic atrophic gastritis. However, characteristics of micromucosal structure observed by magnifying endoscopy of these diseases has not been fully investigated.

Aims & Methods: Aim of this study is to compare magnifying endoscopic appearance between *H. pylori*-associated and autoimmune gastritis. Seven *H. pylori* naïve, 21 *H. pylori*-associated gastritis and 7 autoimmune gastritis patients gave written informed consent to enroll in this study. A videoendoscope: EVIS GIF-FQ260Z that can be used in high-resolution white light, autofluorescence (AFI) and magnifying narrow band imaging (NBI) modes was used. Extent of mucosal atrophy in the corpus was determined as extent of greenish mucosa in AFI image. A 2×2 cm area at the lesser curvature of the corpus about 4 cm proximal to the angulus was set as a region of interest for evaluation of micromucosal patterns. The micromucosal patterns were classified into Foveola and Groove type according to magnifying chromoendoscopic and NBI images. The Foveola type mucosa was characterized as mucosa with round, oval, or short linear foveolae (gastric pits) on magnifying chromoendoscopy, and, on NBI, had dark brown subepithelial capillary that surround light brown epithelium. The Groove type mucosa was characterized by mucosal crests or papillae that were divided by continuous grooves on magnifying chromoendoscopy, and had ridged or papillary light brown epithelium that encase dark brown subepithelial capillary. Proportion of the micromucosal patterns were categorized as, Foveola 80%<; Foveola 50-80%; Groove 50-80%; and Groove 80%<. Biopsy sample was taken from the region of interest.

Results: The corpus mucosa of all of *H. pylori*-naïve patients was purple in the AFI image. 15 of 21 (71%) *H. pylori*-associated gastritis patients had medium to large greenish atrophic mucosa at the corpus lesser curvature and all autoimmune gastritis patients had large area of greenish mucosa in the entire corpus ($p < 0.0001$). The micromucosal pattern of all *H. pylori*-naïve patients was Foveola type. 19 of 21 (90%) patients with *H. pylori*-associated gastritis had various proportion of Groove type mucosa in the region of interest, whereas 5 of 7 (71%) autoimmune gastritis patients showed Foveola type mucosa that is similar to those of *H. pylori*-naïve patients ($p = 0.001$). *H. pylori*-associated gastritis showed higher grade of intestinal metaplasia than autoimmune gastritis in the biopsy specimen.

Conclusion: Micromucosal pattern of the corpus mucosa in patients with *H. pylori*-associated gastritis is likely to show Groove type that mimic the antral or intestinal mucosa, while that of autoimmune gastritis was Foveola type suggesting different pathogenesis of these diseases.

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Disclosure of Interest: None declared

OP039 CO-INFECTION WITH HELICOBACTER PYLORI AND EPSTEIN-BARR VIRUS IN BENIGN UPPER DIGESTIVE DISORDERS. A PROSPECTIVE ENDOSCOPIC-SEROLOGIC PILOT STUDY

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Introduction: About 10-30% of gastric carcinomas are associated with Epstein-Barr virus.[1] The prevalence of *Helicobacter pylori* + Epstein-Barr virus co-infection in benign upper digestive disorders is less known.

Aims & Methods: 104 patients were included in a prospective endoscopic-serologic study. *Helicobacter pylori* IgG was determined by chemiluminescence, Epstein-Barr virus IgG, IgM and viral capsid antigen titers were assayed by ELISA test. *Helicobacter pylori* was determined from 2 antrum and 2 corpus biopsies by the modified Giemsa stain. The prevalence of bacterial and viral infection and that of any co-infection with both agents was calculated in the whole group, as well as in peptic ulcer, functional dyspepsia and reflux patients. Significance between the groups was calculated by the chi-square test.

Results: The overall prevalence of *Helicobacter pylori* was 56.7%. Duodenal ulcer patients were infected in 72.5% of the cases, the prevalence being 33.3% in functional dyspesia ($p = 0.0008$) and 25.8% reflux patients ($p = 0.0001$). Epstein-Barr virus IgG was detected in 73 sera of the whole group (70.1%) and was found in 75% peptic ulcer patients, 51.2% in functional dyspepsia ($p = 0.04$) and 51.6% in reflux disease cases ($p = 0.04$). Co-infection with *Helicobacter pylori* + Epstein-Barr virus was detected in 60% of peptic ulcer patients, 18.1% in functional dyspepsia ($p = 0.00014$) and 12.9 in reflux disease ($p = 0.00012$) Anti-viral IgG titer was of 30.87 ± 2.98 cut-off index in *H. pylori* positive cases and 20.30 ± 2.56 in those negative ($p = 0.01$) The IgG titer was of 31.7 ± 3.0 cut-off index in peptic ulcer, 20.5 ± 3.5 in functional dyspepsia ($p = 0.01$) and 21.4 ± 3.6 in reflux cases ($p = 0.03$). Viral capsid antigen was found in 75% of the peptic ulcer cases, 60.6% ($p = 0.12$) of dyspeptic patients and 51.3% ($p = 0.02$) in reflux cases; its level, however, was not siginificantly different in *H. pylori*-positive and negative patients.

Conclusion: Both *Helicobacter pylori,* Epstein-Barr virus and co-infection with these agents were significantly more prevalent in duodenal ulcer patients than in dyspeptic or reflux cases. Anti-viral IgG titer was also higher in *H. pylori*-positive patients than in those negative. In gastric cancer cases, the virus was found in association with the tumor and non-atrophic gastritis, supporting its role in early precursor lesions.[2] The viral DNA load is higher in *Helicobacter pylori*-positive patients.[3] Co-infection with *H. pylori* and Epstein-Barr virus is associated with more severe gastritis in children.[4] The significance of this viral infection in duodenal ulcer must be further studied.

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Disclosure of Interest: None declared

OP040 THE EFFECT OF HUMEN HERPESVIRUSES PERSISTENCE IN THE GASTRIC MUCOSA ON THE INFLAMMATION IN CHILDREN WITH CHRONIC GASTRITIS

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Introduction: The role of herpesviruses did not study enough in children with chronic gastritis.
Aims & Methods: The evaluation of the role of some Herpesviridae representatives in formation of chronic inflammation in the gastric mucosa in children.
The study involved 320 children aged 7 to 17 years with chronic gastritis (CG). All the patients underwent esophagogastroduodenoscopy and morphological examination of the gastric mucosa (GM) with an establishment of the persistence of human herpes viruses 4, 6 and 8 using the polymerase chain reaction.
Results: No case of the persistence of humen herpes simplex virus type 8 in GM is reported. Humen herpesvirus 6 (HHV-6) and 4 (Epstein-Barr - EBV) were observed in 63.4% and 49.2% of patients respectively. Detection of HHV-6 was comparable in subgroups of patients with various degrees of inflammation. Comparative clinical-endoscopic and morphological examination of patients did not found any effect of virus persistence on the nature of the chronic inflammatory process. At the same time, pathogenic role of EBV in GM with its chronic inflammation in children was established. It is manifested with a sharp increase in the number of EBV-positive patients with the progression of the process: from 11.1% with its absence up to 66.7% in case of severe inflammation ($p < 0.01$). *Helicobacter pylori* (Hp) in the EBV-positive patients was detected in 78% of cases, while in the EBV-negative group it was only 55% ($p < 0.01$). Alternatively, in the presence of Hp Epstein-Barr virus was detected in 52% of children and only in 27% when there was no Hp ($p < 0.005$). Thus, these infections are conjugated. It was established that the presence of a mixed infection (Hp + EBV) in comparison with Hp-associated variant of CG without concomitant EBV persistence is accompanied by generalizing of inflammation in GM up to pangastritis (52%). EBV contributed to the process enhancement both in the fundus and in the antrum, which was reflected by the change in the macroscopic picture. In the majority of cases (76%) the process was hyperplastic, whereas without EBV persistence a superficial inflammation predominated (55%). According to the data of morphological examination, signs of GM atrophy, mainly in the antrum, were significantly more often detected in this group of patients; in 16% of cases GM atrophy was moderate. Severe inflammation was manifested as a quite frequent detection of focal hyperplasia, microerosions and lymphoid follicles in GM. The persistence of EBV was almost double as often associated with colonization of GM with highly pathogenic strains of Hp (35.9% vs. 20.2%, $p < 0.05$)
Conclusion: In children with chronic gastritis high rates of persistence of human herpesvirus type 6 have been found, which had no effect on inflammation in the gastric mucosa. Almost half of the patients revealed the presence of Epstein-Barr virus. The combination of Hp and EBV contributes to the formation of severe and generalized inflammation. In a significant part of patients it was associated with the colonization of the gastric mucosa with highly pathogenic strains of Hp.
Disclosure of Interest: None declared

OP041 PREVALENCE OF, AND RISK FACTORS FOR, ATROPHIC GASTRITIS WITH OR WITHOUT INTESTINAL METAPLASIA IN THE ITALIAN GENERAL POPULATION: AN HISTOPATHOLOGICAL STUDY

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Introduction: Epidemiology of atrophic gastritis and intestinal metaplasia in the general population is still unclear.
Aims & Methods: We aimed to evaluate the prevalence of, and the risk factors for, atrophic gastritis with or without intestinal metaplasia in a representative sample of the Italian general population. A total of 1533 inhabitants of two villages were invited to undergo gastroscopy with multiple gastric biopsies and ^{13}C-urea breath test. Gastric biopsy specimens were available in 1003 subjects. Biopsy specimens were classified and graded using the visual analogue scales according to the Updated Sydney System. Data on demographic and lifestyle characteristics were also collected for each subject. Potential risk factors were evaluated using a multivariable logistic regression analysis.
Results: Of the 1003 subjects, 323 (32.2%) had atrophic gastritis: 247 (24.6% of the study sample) had atrophic gastritis with intestinal metaplasia and 76 (7.6% of the study sample) without intestinal metaplasia. Of the 323 subjects, 252 (78%) had antrum-restricted atrophic gastritis and 11 (3.4%) corpus-restricted atrophic gastritis, whereas 60 (18.6%) had atrophic gastritis in both the antrum and corpus. The prevalence of antrum-restricted, corpus-restricted and both antrum and corpus atrophic gastritis in the study sample was 25.1%, 1.1% and 6%, respectively. Atrophic gastritis was classified as mild in 212 subjects (21.1% of the study sample), moderate in 61 subjects (6.1% of the study sample) and severe in 50 subjects (5% of the study sample). Moderate-severe atrophic gastritis was significantly more frequent in subjects with both antrum and corpus atrophic gastritis (Odds Ratio (OR): 4.67, 95% confidence interval (CI), 2.58-8.47). *H. pylori* infection, age over 51 years, cigarette smoking and positive first degree family history of gastric cancer were independently associated with presence of atrophic gastritis. A negative association was found between obesity and atrophic gastritis.
Conclusion: Atrophic gastritis with or without intestinal metaplasia seems to be present in about one third of the Italian general population. Most subjects have antrum-restricted atrophic gastritis, whereas only 1% of the general population has a corpus-restricted atrophic gastritis. Subjects with both antrum and corpus atrophic gastritis are more likely to carry a more severe atrophy. *H. pylori*, age > 51 years, smoking and a positive family history of gastric cancer are positively and independently associated with atrophic gastritis, while obesity seems to be negatively associated.
Disclosure of Interest: None declared

OP042 PEPSINOGEN AND INCIDENT CHRONIC ATROPHIC GASTRITIS AND INTESTINAL METAPLASIA: A LONGITUDINAL STUDY

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Introduction: Pepsinogen (PG) I and II are the two main precursors of pepsin, and are both produced by chief cells and mucous neck cells of the stomach.[1, 2] PG II is also produced by pyloric gland cells. When atrophic mucosal change develops, the chief cells are replaced by pyloric glands, leading to a decrease in PGI. However, PG II decreases in very small amount.[2] Thus, low serum PG I level and low PG I/II ratio are well known to be serological markers of gastric atrophy.
Aims & Methods: This study was performed to investigate association between serum pepsinogen (PG) level and incidence of chronic atrophic gastritis (CAG) and intestinal metaplasia (IM).
This is a retrospective cohort study. Our data were composed of 3,927 participants (over 30 years of age) who underwent upper endoscopy and serum PG test between March 2008 and December 2009 whose baseline endoscopy showed no evidence of CAG and IM. Of these, 2,166 participants underwent follow-up endoscopy after at least 1 year. Thus, the final study subjects consisted of 2,166 adults with follow-up data. Structured questionnaires were reviewed about purported risk factors for CAG and IM such as family history of gastric cancer, current smoking, and alcohol consumption. Serum PG I and PG II were measured by a latex-enhanced turbidimetric Immunoassay. Serum anti-*Helicobacter pylori* (*H. pylori*) IgG was detected by enzyme-linked immunosorbent assay. Follow-up endoscopy was performed either at 1-year or 2-year intervals by taking into account factors such as age, family history of gastric cancer, and patients' preference. CAG and IM were diagnosed endoscopically by experienced board-certified endoscopists.
Results: Median follow-up in the 2,166 participants was 1490.5 days (interquartile range, 772.8-1898.0). There were a total of 783 patients with CAG and 166 patients with IM during the follow-up. Subjects with a PG I/II ratio of ≤3.0 showed higher incidence of CAG and IM compared with those with a PG I/II ratio of >3.0 by using log-rank test ($p < 0.001$, both for CAG and IM). The results of Cox's regression analysis confirmed that the PG I/II ratio was significantly inversely associated with incident CAG (HR, 0.86; 95% CI, 0.82-0.90; $p < 0.001$) after full adjustment for risk factors. The PG I/II ratio was also significantly inversely associated with incident IM (HR, 0.76; 95% CI, 0.68-0.85; $p < 0.001$). To test diagnostic performance of the PG I/II ratio for incident CAG, we performed a receiver-operating curve analysis. The cutoff value that is farthest from the line of equality was PG ratio of 4.6, with modest sensitivity (54.5%; 95% CI, 51.0% > 58.1%) and specificity (66.1%; 95% CI, 63.5% > 68.6%).
Conclusion: The PG I/II ratio was found to be significantly inversely associated with development of CAG and IM in asymptomatic population without CAG and/or IM at baseline.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 11:00-12:30
BIOLOGY OF COLORECTAL CANCER - ROOM B3

OP043 DIAGNOSTIC COLORECTAL ADENOMA-CARCINOMA RELATED MIRNA SIGNATURES IN MATCHED TISSUE PLASMA SPECIMENS

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Introduction: Several microRNA has been found to play critical role in colorectal carcinoma developement. Recently, miRNA-specific high-throughput arrays became available to detect expression alterations of the whole miRnome in colorectal cancer (CRC). While miRNA expression markers are well characterized in CRC, less is known about miRNA expression profiles in colorectal adenoma.
Aims & Methods: The purpose of this study was to identify miRNA expression patterns through colorectal adenoma dysplasia sequence.Furthermore, our aim was to analyze the expression level of miRNA in matched plasma samples focusing on biomarker candidates.
Sixty fresh frozen colorectal biopsy tissue (normal [**N**] n = 20; tubular adenoma [$\mathbf{AD_T}$] n = 11; tubulovillous adenoma [$\mathbf{AD_{TV}}$] n = 9; colorectal cancer [**CRC**] n = 20) and 16 matched plasma samples (n = 4 N, n = 4 AD_T, n = 4 AD_{TV}, n = 4 CRC) were collected and total RNA including miRNA was isolated. MiRNA microarray experiments were conducted by GeneChip® miRNA 3.0

Array (Affymetrix). Then, a series of pools of RNA from the same groups of tissue samples was made to validate the data of microarray by RT-qPCR (microRNA Ready-to-use PCR Human Panel I + II V2.R; Exiqon). Plasma samples from the same patients set was selected to confirm the microarray results on the same array, RT-qPCR platform. Data were analyzed using Expression Console (Affymetrix).

Results: Out of the 1733, the detectable miRNAs, which could be found in each group was N = 442, AD = 460, CRC = 441 in tissue and N = 306, AD = 334, CRC = 321 in plasma. Interestingly, 12 miRNA were upregulated (e.g. miR-31 logFC = 3, $p < 0.001$) and 11 miRNA were downregulated only (e.g. miR-10b, logFC = -1.7 $p < 0.001$) in neoplastic lesions (AD + CRC) compared to N tissue samples. 11 miRNA showed altered expression between AD_T and AD_{TV} (e.g. miR-183 LogFC = 1.5 $p < 0.007$). Expression levels of 9 miRNA were found to be changed between $AD_{T,TV}$ and CRC groups based on tissue biopsy microarray data (e.g. miR-196a logFC = -1.8 $p < 0.001$). Three miRNA(-31;-4506;-452*) have been found to be differentially expressed in adenoma compared to normal in both matched tissue plasma samples analyzed by microarray. Significant positive overexpression was observed in tissue (logFC = 5 $p = 0.003$) and in plasma (logFC = 0.3 $p = 0.02$) in case of miR-31 in adenoma. Moreover, increased expressions were detected in CRC compared to healthy controls in tissue and plasma levels of miR-187;-675;-3591-3p ($p < 0.05$). MiRNA expression data could be confirmed by RT-PCR in both plasma and tissue samples.

Conclusion: 23 miRNA showed characteristic expression changes in CRC development in biopsy tissue. Our observations suggest that miRNA are also present in plasma fraction and positively correlate with matched tissue expression levels. The identified miRNA expression changes could be verified by other more simple RT-PCR methods eventually for routine application.

Disclosure of Interest: None declared

OP044 ORIGIN AND ALTERED SECRETION OF ALIX POSITIVE EXOSOMES IN COLORECTAL ADENOMA-CARCINOMA SEQUENCE

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Introduction: During carcinoma formation the exosomes as intercellular regulators play important role in convey of complex signals between epithelial/carcinoma cells and their abnormal microenvironment including α-SMA+ blast-like cells.

Aims & Methods: Our aim was to examine the alteration in exosome-based communication during colorectal adenoma-carcinoma sequence (ACS) by the determination the changes of epithelial/epithelial-origin carcinoma and stromal ALIX exosome marker expression in protein level. Our study was performed on healthy (n = 30), adenomas with low-grade (n = 15) and high-grade (n = 30) dysplasia as well as non-invasive (n = 12; Dukes A and B) and invasive (n = 26; Dukes C and D) colorectal carcinoma (CRC) samples. Immunohistochemistry was performed for ALIX exosome, cytokeratin epithelial, podoplanin (PDPN) lymphatic vessel, Ki-67 proliferative, α-SMA myofibroblast and Musashi-1 (MSI1) stem cell markers. We determined the intensity of ALIX expression with Q-score method and the percentage of cells with granular ALIX expression (PCGE) by counting 800-1300 cells both in epithelial and stromal cells in 5 representative core/ sample groups with Pannoramic Viewer digital microscope.

Results: We found strong/moderate diffuse cytoplasmic ALIX expression in normal epithelium which significantly ($p < 0.05$) decreased both in adenoma and CRC samples. In parallel with decreased ALIX intensity, we found altered expression pattern (i.e. diffuse to granular cytoplasmic) with significantly increased ($p < 0.05$) frequency of PCGEs both in epithelial/CRC and stromal compartment (including α-SMA+ blast-like cells) in all examined pre-neoplastic and neoplastic lesions. The granular ALIX expression was not limited to the Ki-67+ proliferative and MSI1+ stem/cancer stem cells, but it could be observed in budding, cytokeratin+ stromal cells, as well as in the lumen of lymphatic vessels in invasive CRCs.

Conclusion: The heterogenic ALIX expression pattern in pre-neoplastic lesions suggests that the abnormal exosome transport may play important role in adenoma to carcinoma transformation. Furthermore, the appearing of ALIX expression in budding tumor cells in the stroma and in the lumen of lymphatic vessels may help in the development of pre-metastatic microenvironments of invasive CRC patients.

Disclosure of Interest: None declared

OP045 PREVALENCE OF APC/MYH GERMLINE MUTATIONS DETECTED IN A POPULATION BASED COLORECTAL CANCER SCREENING PROGRAMME IN SPAIN

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Introduction: Adenomatous polyposis syndromes such as familial adenomatous polyposis (FAP) / MUTYH-associated polyposis (MAP)/ attenuated polyposis (AFAP) are inherited genetic conditions, being FAP and MAP in an autosomal-dominant manner and AFAP in an autosomal-recessive pattern. Such genetic conditions have an increased predisposition to multiple colorectal adenomatous polyps, and hence to colorectal cancer. Germline mutations in the base excision repair gene MUTYH have been associated with a recessively inherited form of the disease. Population-based CRC screening programmes with FOBT have demonstrated polypectomy during colonoscopy reduces incidence and mortality by CRC. Such screening programmes not only detect adenomatous lesions through colonoscopy but also may reduce mortality from CRC in patients with such hereditary related colorrectal polyposis. CRC is the most frequent cancer in Spain with 28.551 new cases in 2008 according to Globocan. In Murcia, a population-based CRC screening programme was initiated in 2006, since 2008 such programme was extended to our Hospital.

Aims & Methods: To evaluate the proportion of APC/MUTYH gene mutation in individuals included in the CRC screening programme, where colonoscopy performed after positive FOBT, detects 10 or more adenomatous polyps.

Since January 2010 to December 2014 participants between 50 and 69 years with no personal history of CRC, IBD, FAP or HNPCC, have been included in the CRC screening program. All participants with a positive FOBT, who underwent colonoscopy and had more than 10 adenomas resected were included in this study. After histopathology confirmed the presence of adenomatous polyps, patients were referred to Genetic counseling. Informed consent was obtained from each participant to investigate the presence of APC and MYH germline mutation. In serum DNA all exons and nearby regions to those genes were analysed through genome sequencing.

Results: A total of 32,034 participants underwent CRC screening with immunochemical FOBT (FIT). Of those, 4,388 had positive FIT and 3,909 participants had colonoscopy done. Amongh those who underwent colonoscopy 107 patients (2.7%) with ≥ 10 adenomas were identified, of them 9 had APC mutation, 4 of which corresponded to a variant of uncertain significance (VUS), 1 had a double mutation in MUTYH gene and 2 had one MUTYH mutation. The same APC germinal pathogenic mutation was identified in four of the 5 remaining APC mutation carrier patients, none of them related with each other. Such germline mutation was previously identified in Murcia in other no related families all of which showed a very atenuated polyposis syndrome.

Conclusion: Prevalence of a germinal mutation in APC or MUTYH gene in asympthomatic participants of a population based CRC screening program with ≥10 adenomas resected is 11.2%. It is important to diagnose such genetic condition since interval for surveillance colonoscopy is different from average risk participants of a CRC screening program.

Disclosure of Interest: None declared

OP046 LATERALLY SPREADING TUMORS ARE A RISK FACTOR FOR SYNCHRONOUS NEOPLASMS

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Introduction: Lateral spreading tumors (LST) are challenging to recognize and resect endoscopically. A subset may progress more rapidly to cancer, indicating such lesions contribute to the occurrence of postcolonoscopy colorectal cancers. A comprehensive characterization of the clinical phenotype associated with presence of LSTs is presently lacking. In this large population-based study, we explored the incidence, clinical features and risk profile of patients with LSTs.

Aims & Methods: We have previously trained the endoscopists (faculty and trainees) at our institution in recognition of flat, depressed neoplasms, and serrated polyps. We reviewed prospectively collected clinical, endoscopic and histopathology data from all patients who underwent an elective colonoscopy at our hospital from Feb 2008 to Feb 2012. Furthermore, we asked all participants to fill in a questionnaire regarding risk profiles (i.e. smoking, alcohol intake, BMI, and aspirin use). We defined a LST as a flat appearing neoplasm > 10 mm in size. We excluded patients with hereditary CRC syndromes, inflammatory bowel disease or a history of colon resection.

Results: In total, 8033 patients undergoing colonoscopy for symptoms (84.6%), screening (6.7%) or surveillance (8.7%) were included. Of them 61.8% filled in the questionnaire. Overall, 180 patients with 224 LSTs and 2746 patients with any neoplasm (without LSTs) were identified. Of the 224 LSTs, 78.1% were proximally located. Patients with LSTs were significantly older than those with any lesion (66.5 vs 63.9 yrs, $p = 0.005$), and were more likely under surveillance at time of inclusion (21.1% vs 14.4%, age and gender adjusted OR: 1.6, 95% CI 1.1-2.3). Logistic regression analysis, adjusted for age and gender, showed that patients with LSTs had significantly more often adenomas, advanced adenomas and sessile serrated adenomas/polyps (SSA/Ps), and also greater numbers of synchronous neoplasms than patients with any neoplasm (without LSTs) (**Table**). Gender, smoking, alcohol intake, BMI and aspirin use did not differ significantly between groups.

Of the 224 LSTs, 160 were of nongranular, 54 granular and 10 of unknown subtype. Histopathologic examination showed 34 hyperplastic polyps, 32 SSA/Ps, 140 adenomas, and 18 CRCs (8 TNM-stage I, 10 stage II-IV). Compared with polypoid neoplasms larger than 10 mm (n = 964), LSTs contained less often villous histology (28.6 vs 41.8%, $p < 0.001$) and more often serrated histology (14.2 vs 4.0%, $p < 0.001$).

Conclusion: Patients with LSTs have often synchronous advanced adenomas and sessile serrated adenomas/polyps. A second look clearing colonoscopy in patients with LST may safeguard the effectiveness of cancer prevention.

Disclosure of Interest: R. Bogie: None declared, C. le Clercq: None declared, M. Bouwens: None declared, B. Winkens: None declared, R. de Ridder: None declared, A. Masclee: None declared, S. Sanduleanu Consultancy: Pentax Medical Systems

Abstract number: OP046 Table: Clinical features of LSTs vs any neoplasm patients

Clinical features	Patients with ≥ 1 LST n = 180	Patients with any lesion (no LSTs) n = 2746	Unadjusted p-value	Adjusted OR (95% CI) **
Surveillance indication, n (%)	38 (21.1)	394 (14.4)	*<0.001*	*1.6 (1.1-2.3)*
Mean number of colonoscopies (SD)	1.9 (1.1)	1.2 (0.5)	*<0.001*	*3.1 (2.6-3.7)*
≥ 1 adenoma, n (%)	148 (82.2)	2055 (74.8)	*0.026*	*1.5 (1.0-2.2)*
≥ 1 advanced adenoma*, n (%)	88 (48.9)	723 (26.3)	*<0.001*	*2.6 (1.9-3.5)*
≥ 1 serrated polyp, n (%)	22 (12.2)	83 (3.0)	*<0.001*	*4.9 (2.9-8.0)*
≥ 1 sessile serrated adenoma, n (%)	17 (9.4)	66 (2.4)	*<0.001*	*4.1 (2.3-7.1)*

* Advanced adenoma: size excluded ** Adjusted for age and gender

OP047 COLORECTAL LARGE POLYPS MANAGEMENT: THE ROLE OF VEGF AS POSSIBLE MARKER OF MALIGNANCY

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Introduction: Endoscopical screening programs for colorectal cancer (CRC) have reduced the mortality rates by finding lesions at initial stages or by directly treating precancerous lesions. However, adenomatous polyps may not always be removable endoscopically and colonic resection may be still necessary. Nowadays, in these cases radical colonic resection with a full oncological lymphoadenectomy is still indicated due to the possible understimation of the invasiveness of large adenoma with focal bipsies negative for cancer. Vascular endothelial growth factor (VEGF) is a sub-family of growth factors that are signaling proteins involved in both vasculogenesis and angiogenesis.
Aims & Methods: The aim of the study was to evaluate the accuracy of VEGF expression as a marker of malignancy in colorectal adenoma.
We prospectively enrolled 92 healthy subjects and patients with colonic adenoma or adenocarcinoma who underwent screening colonoscopy or surgical colorectal resection. Real time RT-PCR for VEGF-A mRNA expression and immunohistochemistry for VEGF-A were performed. Immunoassay for VEGF-A, VEGF-C, VEGFR-1, VEGFR-2 and VEGFR-3 were also performed. Non parametric statistics, ROC curves analysis and logistic multiple regression analysis were used.
Results: VEGF-A mRNA expression was higher in patients with high-grade dysplasia or adenocarcinoma than in those with adenomas with low-grade dysplasia ($p = 0.01$). At IHC, VEGF-A expression was significantly higher in patients with adenocarcinoma than in those with adenomas ($p < 0.001$) and the accuracy of VEGF-A expression for prediction of the progression form adenoma to adenocarcinoma was 91.7 (95%CI = 78.7-97.9). VEGF-C protein expression was lower in CRC patients than in patients with simple adenomas ($p = 0.02$). VEGF-A levels were directly correlated to polyp size (rho = 0.73, $p = 0.0062$). Multivariate analysis demonstrated that malignancy and polyp size were independent predictors of VEGF-A mucosal levels.
Conclusion: This study demonstrated that VEGF-A levels can be a marker of malignancy of colorectal polypoid lesions with a high accuracy. The analysis of confounders showed that only the transformation from benign to malignant lesions and the dimensions of the lesion can influence VEGF-A levels.
Disclosure of Interest: None declared

OP048 MODULATION OF DNA MISMATCH REPAIR SYSTEM BY COLIBACTIN-PRODUCING ESCHERICHIA COLI IN SPORADIC COLORECTAL CANCER

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Introduction: Inactivation of DNA Mismatch Repair (MMR) genes as MLH1 is observed in 15% of sporadic colorectal cancer (CRC) exhibiting microsatellite instability phenotype (MSI). Colonic mucosa-associated *Escherichia coli (E. coli)* are more frequently identified in CRC patients. Some pathogenic *E. coli* strains acquired virulence factors, including colibactin toxin encoded by *pks* island, which interfere with eukaryotic cell cycle and induce DNA double-strand breaks, leading to genomic instability. Colibactin-producing *E. coli* are more frequently detected on gut of CRC patients. We evaluate, in CRC patients, colonic mucosa-associated and -internalized *E. coli* levels in relation to tumoral microsatellite stability status. Impact of colibactin-producing CRC-*E. coli* infection on MMR protein expression was then investigated.
Aims & Methods: MSI status was assessed by immunohistochemical staining of MMR nuclear proteins and by multiplex PCR in tumor sections from 90 CRC patients, and correlated to corresponding level of mucosal associated and internalized *E. coli*. Effect of infection by colibactin-producing *E. coli* strains on MLH1 expression in T-84 cells was studied by western blot analysis. Adhesion, internalization and persistence assays for colibactin-producing *E. coli* strains were performed in T-84 (MMR system-competent) and HCT-116 (MMR system-deficient) cells.
Results: MSI tumor phenotype was noted in 14.4% patients. There was significant increase in mucosa-associated ($p = 0.025$) and -internalized *E. coli* ($p = 0.028$) levels in patients with MSI tumor phenotype. We noted significant increase in normal mucosa-associated ($p = 0.018$) and internalized *E. coli* ($p = 0.031$) levels in patients with MLH1-negative tumors, suggesting *in vivo* interaction between *E. coli* and DNA MMR system in CRC. *In vitro*, higher proportion of *E. coli* was able to invade ($p = 0.009$) and persist ($p = 0.007$) in MMR-deficient cells, suggesting that gut *E. coli* colonization was favored in MMR-deficient patients. Immunoblots revealed marked reduction in MLH1 protein expression 3 hours after infection, compared to uninfected cells and cells infected with non-pathogenic K12-C600 *E. coli* strain. MLH1 inhibition was dependent on presence of *pks* island in CRC strains. Colibactin-producing *E.coli* isolated from CRC patients could thus inhibit a DNA repair system to induce genomic instability and to favor CRC.
Conclusion: Involvement of colibactin-producing *E. coli* in CRC is now well supported. We report the first clinical evidence of interaction between colibactin-producing *E. coli* and MMR deficiency.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 14:00–15:30
MANAGEMENT OF IBD AFTER ANTI-TNF FAILURE – ROOM B2

OP049 THE FRENCH REAL-LIFE EXPERIENCE OF VEDOLIZUMAB EFFICACY AND SAFETY IN CROHN'S DISEASE: A PROSPECTIVE OBSERVATIONAL MULTICENTER COHORT STUDY

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Introduction: Vedolizumab (VDZ) is a humanized monoclonal antibody that specifically antagonizes $\alpha 4\beta 7$ integrin by inhibiting its binding to the gut-specific intestinal mucosal address in MAdCAM1. Efficacy and safety of VDZ in Crohn's disease (CD) has been evaluated in two large phase 3 randomized controlled trials (GEMINI II and III), leading to the approval of the drug by both EMA and FDA. Herein, we assessed safety and efficacy of VDZ in a large real-life experience cohort of patients with CD.
Aims & Methods: All consecutive active CD patients treated with VDZ in France from Jun to Dec 2014 were assessed. From Jun to Sep, VDZ was available through a centralized pre-approval program piloted by the French regulatory agency (ANSM). After its approval by ANSM (reimbursement of the drug by social services is still pending), recruitment was extended until Dec 2014. Patients received VDZ at a dose of 300 mg at weeks 0, 2 and 6 as induction therapy and then every 8 weeks. Patients who did not respond to VDZ induction therapy at week 6 could receive VDZ 300 mg every 4 weeks. Patients were evaluated prospectively at W14. Remission was defined as a Harvey-Bradshaw index ≤ 4. Response was defined as a reduction in the Harvey-Bradshaw index of at least 3 points. C-reactive protein as well as safety were ascertained.
Results: One hundred and seventy patients (61 males, median age: 36.3 IQR [29.2-47.0] yrs) were included in 31 centres. Median disease duration was 10.7 [6.5-16.5] yrs; 165 (97%) patients have been previously treated with immunosuppressant, 168 (99%) with at least one anti-TNF and 83 (48.8%) underwent prior intestinal resection. VDZ was given for luminal disease in 91 (53.5M) patients and for luminal and perianal disease in 79 (46.5%). At baseline, mean Harvey-Bradshaw index was 10.3 ± 4.2 and mean CRP level was 30.5 ± 30.0 mg/L. At week 14, Response and remission rates were 59% and 38%, respectively; the steroid-free response and remission rates were 47% and 32%, respectively. The mean decrease of Harvey-Bradshaw index was 3.1 ± 4.9

($p < 0.001$). The mean CRP level decrease was 0.3 ± 40.1 ($p = 0.77$). Adverse events were reported in 34 (20%) patients and consisted in opportunistic infection (n = 18) including nasopharyngitis (n = 4), upper respiratory tract infection (n = 4), gastrointestinal infection (n = 4), intraabdominal abscess (n = 2), catheter-related bloodstream infection (n = 2), urinary tract infection (n = 1), herpes zoster ophthalmicus (n = 1), cutaneous reaction (n = 6), paresthesia (n = 6), infusion reaction (n = 1), headache (n = 2) and rectal adenocarcinoma (n = 1).
Conclusion: In this first real-life experience cohort of patients with refractory CD, VDZ induced clinical response in more than 50% of cases, with an acceptable safety profile.
Disclosure of Interest: None declared

OP050 RESPONDERS TO HAEMOPOIETIC STEM CELL TRANSPLANTATION FOR CROHN'S DISEASE

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Introduction: We recently reported that about one third of patients with Crohn's disease experience prolonged regression of ileocolonic disease following haemopoietic stem cell transplantation (HSCT). Here we compare the characteristics of responders and non-responders.
Aims & Methods: Patients with impaired quality-of-life from active Crohn's disease not amenable to surgery despite treatment with at least 3 immunosuppressive agents all underwent stem cell mobilisation before randomisation to immuno-ablation followed by unselected cyclophosphamide-based conditioning and HSCT after one month (Early HRCT) or one-year (Delayed HS CT). Patients in whom all endoscopic evidence of Crohn's disease disappeared (SES-CD score of zero) were classified as Responders. Supporting histology was available in 17 of them.
Results: Forty four patients with ileocolonic involvement underwent mobilisation before randomisation to Early or Delayed HSCT. Of 38 patients that could be classified 14 were Responders. Ten had SES-CD of zero after 1 year, (maintained in the second in 3 of 4 with available data) and 4 achieved responder status in year 2. Four of 6 followed to 4 years remain free of Crohn's disease vs 1 of 15 non-responders. Responders were significantly more likely to have histologically normal segments post HSCT

(Table)

% with normal histology	Site	Responder	Non Responder	p
Pre HSCT	Ileum	44%	40%	1.00
	Colon	59%	37%	0.045
Post HSCT	Ileum	91%	50%	0.069
	Colon	83%	52%	0.004

A Responder status tended to be more likely with no family history (39% vs 20%), in non-smokers (54% vs 30%), with early-onset of disease (Montreal A1, 46% vs 32%)) and with more than 10-year history (46% vs 17%); those with pure colonic involvement (L2) were less likely to respond than those with ileal involvement (L1, L3, 14% vs 43%) but these fell short of statistical significance on univariate analysis.
Conclusion: A group of patients can be identified who have a substantial and long lasting regression of Crohn's disease following HSCT. Endoscopic response following HSCT is associated with regression of histological evidence of Crohn's disease.
Disclosure of Interest: None declared

OP051 FAECAL DIVERSION FOR MANAGEMENT OF PERIANAL CROHN'S DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Temporary faecal diversion (FD) is sometimes used for management of refractory perianal Crohn's disease (CD) with variable success. Diversion of faecal stream from the severely inflamed segments has long been known to decrease CD-related inflammation.
Aims & Methods: We performed a systematic review with meta-analysis to evaluate effectiveness, long-term outcomes, and factors associated with success with temporary FD for refractory perianal CD.
The title and abstract of studies identified in the search were reviewed by two authors independently (SS, ND). From a systematic literature review using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines until February 2015, we identified 14 cohort studies (472 patients) reporting outcomes after temporary FD. We estimated pooled rates (with 95% confidence interval [CI]) of early clinical response, attempted and successful restoration of bowel continuity after temporary FD (without symptomatic relapse), and rates of re-diversion (in patients with attempted restoration) and proctectomy (with or without colectomy and end-ileostomy). We identified factors associated with successful restoration of bowel continuity.
Results: From a total of 671 unique studies identified using our search strategy, we identified 14 studies as meeting all inclusion criteria. On meta-analysis, 68.5% (95% CI, 60.1-75.9) patients had early clinical response after FD for refractory perianal CD. Restoration of bowel continuity was attempted in 34.4% (95% CI, 26.4-43.3) of patients, and was successful in only 15.0% (95% CI, 10.1-21.9). Most attempts at restoration of bowel continuity were made on average between 1-1.5 years after FD. Of those in whom restoration was attempted, 31.5% (95% CI, 16.8-51.1) required re-diversion because of severe relapse. Overall, 44.7% (95% CI, 36.4-53.4) patients required proctectomy after failure of temporary FD. On multivariate analysis, Gu et al [1] observed that rectal involvement was associated with 7.5 fold higher risk of failure to achieve restoration of bowel continuity. Similarly, on univariate analysis, in two studies, Harper et al [2] and Regimbeau et al [3] observed that restoration of bowel continuity was possible in 85.8-87.5% of patients without rectal involvement, compared with 11.1-53.3% patients with rectal involvement.
There was no difference in successful restoration of bowel continuity after temporary FD in pre-biologic or biologic era (13.7% vs. 8.6%, $p = 0.51$), in part due to selection bias.
Conclusion: Temporary FD may be used for amelioration of severe perianal CD refractory to medical therapy, with good early clinical response in over 2/3rd of patients. However, bowel restoration is successful in only 15% patients. While factors associated with successful restoration of bowel continuity after temporary FD are poorly understood, healing of rectal disease should be a minimum prerequisite before restoration of bowel continuity.

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Disclosure of Interest: None declared

OP052 EFFICACY OF VEDOLIZUMAB WITH AND WITHOUT CONTINUED IMMUNOSUPPRESSANT USE IN GEMINI 1 AND GEMINI 2

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Introduction: In GEMINI 1 and GEMINI 2, vedolizumab (VDZ) was safe and effective in patients (pts) with ulcerative colitis (UC) or Crohn's disease (CD), respectively, on stable doses of immunosuppressants (IS).[1,2] The effect of discontinuing IS in pts who responded to VDZ induction therapy in these studies has not been characterised.
Aims & Methods: Pts who responded to VDZ at week (wk) 6 were re-randomised to placebo (VDZ/PBO) or VDZ every 4 or 8 wks (VDZ/VDZ Q4W or Q8W) for 46 wks. At United States (US) sites, re-randomised pts discontinued IS use at wk 6. At non-US sites, pts could continue IS use. Efficacy, VDZ serum concentration, and immunogenicity (via an enzyme-linked immunosorbent assay) data were evaluated post hoc in pts with baseline IS use stratified by region.
Results: At wk 52, rates of clinical remission and response (**Table**), mucosal healing (UC), durable clinical remission, and corticosteroid-free remission were higher with VDZ, mostly irrespective of IS use. Mean trough concentrations were similar between US and non-US pts at wk 46 (**Table**). Higher percentages of US VDZ/PBO pts were positive for anti-VDZ antibodies compared with non-US pts
Conclusion: Discontinuing IS did not appear to substantially affect efficacy of VDZ maintenance therapy. Interpretation of these post hoc analyses is limited by potential IS discontinuation in non-US pts and the relatively small sample sizes.

Reference

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Disclosure of Interest: B. Feagan Consultancy: Abbott/AbbVie, ActoGenix, Amgen, Astra Zeneca, Avaxia Biologics, Axcan, Baxter Healthcare Corp, Boehringer-Ingelheim, Bristol-Myers Squibb, Celgene, Elan/Biogen, EnGene,

Abstract number: OP052 (Table). Table: Maintenance VDZ With and Without Continued IS Use

	UC		CD	
	US (Discontinued IS)	Non-US (Continued IS)	US (Discontinued IS)	Non-US (Continued IS)
	VDZ/PBO n = 10; VDZ/VDZ n = 18	VDZ/PBO n = 41; VDZ/VDZ n = 70	VDZ/PBO n = 5; VDZ/VDZ n = 9	VDZ/PBO n = 44; VDZ/VDZ n = 94
Efficacy endpoints	**% Difference from PBO (95% CI) at wk 52**			
Clinical remission[a]	28.9 (-10.5, 63.3)	25.2 (8.0, 42.4)	4.4 (-49.6, 54.7)	17.3 (0.4, 34.1)
Clinical response[b]	18.9 (-20.8, 54.7)	35.0 (17.1, 52.9)	15.6 (-39.9, 63.8)	17.7 (0.2, 35.3)
Immunogenicity	**No. of pts with ≥1 positive sample**			
VDZ/PBO	3	1	1	4
VDZ/VDZ	1	2	0	0
VDZ Concentration	**Mean trough concentration, μg/ml at wk 46**			
VDZ/VDZ Q8W	13.0 (n = 2)	10.7 (n = 27)	9.4 (n = 2)	11.8 (n = 27)
VDZ/VDZ Q4W	39.0 (n = 6)	44.1 (n = 26)	38.8 (n = 3)	31.7 (n = 28)

[a] UC: complete Mayo score of ≤2 and no individual subscore >1. CD: CD Activity Index (CDAI) score ≤150.[b] UC: durable clinical response is a reduction in complete Mayo score of ≥3 and ≥30% from wk 0 with a decrease in rectal bleeding subscore (RBS) of ≥1 or absolute RBS of ≤1 at wks 6 and 52. CD: enhanced clinical response is a ≥100-point reduction in CDAI score from wk 0.

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OP053 VEDOLIZUMAB FOR INFLAMMATORY BOWEL DISEASE IN CLINICAL PRACTICE – EXPERIENCE FROM A PROSPECTIVE GERMAN REGISTRY

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Introduction: Vedolizumab (VDZ), targeting $\alpha 4\beta 7$ integrin became available for prescription in Germany in July 2014. Here we report its efficacy and safety in a real world setting.

Aims & Methods: 17 private and 9 academic centers included 318 patients (ulcerative colitis (UC) n = 165), Crohn's disease (CD) (n = 174), median age 40 years, disease duration 106 months, male n = 153). Patients received 300 mg i.v. VDZ induction at 0, 2, 6 and maintenance q8 weeks and were followed for 14 weeks. In UC, disease activity was scored using clinical parameters of the Mayo index, and in CD by Harvey Bradshaw Index (HBI) at weeks 0, 6 and 14, respectively. Where available, endocopy (UCCIS, SES-CD), lab and QoL data were collected.

Results: Most had extensive mucosal involvement in UC (50% pancolitis) and CD (60% ileocolonic) and were exposed to multiple anti-TNFs. 22% had prior surgery for IBD and 26% were hospitalized within the previous 12 months. At baseline, patients had moderately active disease with significant clinical improvement at weeks 6 and 14. Clinical or endoscopic remission were rare events at week 14. QoL improved only on the EQ5D derived VAS, but not IBDQ.

UC	N*	Week 0	N*	Week 6	N*	Week 14
CRP	134	0.49 ± 1.15	66	0.52 ± 1.07	59	0.36 ± 0.88
Calprotectin	74	1512.5 ± 1665	32	893.5 ± 1415	32	273.4 ± 622
IBDQ	46	135 ± 49	8	159.5 ± 58	25	159 ± 36
EQ5D VAS	40	30 ± 10	29	70 ± 25	29	80 ± 21
Part. Mayo	158	7 ± 3	84	5 ± 3	66	3.5 ± 4
UCCIS	77	63.6 ± 39.5	9	38.1 ± 53.2	24	13.3 ± 15.2
CD						
CRP	149	0.9 ± 2.3	74	1.05 ± 2.46	60	0.63 ± 3.05
Calprotectin	81	800 ± 1775	39	860 ± 1801	28	362.3 ± 1037
IBDQ	43	131 ± 53	20	131 ± 61	27	123 ± 46
EQ5D VAS	40	30 ± 18	48	60 ± 20	40	65 ± 24
HBI	160	10 ± 6	89	7 ± 6	66	7 ± 4
SES-CD	70	12 ± 7	4	11.5 ± 7	19	9 ± 7

* complete records entered as of April 1, 2015.

Conclusion: Clinical response preceded laboratory improvement. Endoscopic data can't be fully interpreted yet due to ongoing recruitment and analysis. Full data set to be presented at UEG.

Disclosure of Interest: D. Baumgart Lecture fee(s): Takeda, Consultancy: Takeda, R. Atreya Consultancy: Takeda, O. Bachmann: None declared, M. Bläker: None declared, B. Bokemeyer Consultancy: Takeda, N. Börner: None declared, J. Büning: None declared, A. Dignass Lecture fee(s): Takeda, Consultancy: Takeda, A. Drabik: None declared, R. Ehehalt: None declared, A. Fischer: None declared, F. Hartmann Lecture fee(s): Takeda, Consultancy: Takeda, H. Hartmann: None declared, S. Howaldt: None declared, P. Jessen: None declared, T. Krummenerl: None declared, T. Kühbacher: None declared, A. Lügering: None declared, J. Maul: None declared, M. Mross: None declared, M. Neurath Lecture fee(s): Takeda, Consultancy: Takeda, S. Nikolaus: None declared, J. Preiss Lecture fee(s): Takeda, M. Reinshagen: None declared, R. Schmelz: None declared, C. Schmidt Lecture fee(s): Takeda, Consultancy: Takeda, S. Schreiber Lecture fee(s): Takeda, Consultancy: Takeda, B. Siegmund Lecture fee(s): Takeda, Consultancy: Takeda, A. Stallmach Lecture fee(s): Takeda, Consultancy: Takeda, N. Teich Lecture fee(s): Takeda, Consultancy: Takeda, U. von Arnim: None declared

OP054 THE FRENCH REAL-LIFE EXPERIENCE OF VEDOLIZUMAB EFFICACY AND SAFETY IN ULCERATIVE COLITIS: A PROSPECTIVE OBSERVATIONAL MULTICENTER COHORT STUDY

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Introduction: Vedolizumab (VDZ) is a humanized monoclonal antibody that specifically antagonizes $\alpha 4\beta 7$ integrin, by inhibiting its binding to the gut-specific intestinal mucosal address in MAdCAM1. Efficacy and safety of VDZ in ulcerative colitis (UC) has been evaluated in a large phase 3 randomized controlled trials (GEMINI I) leading to the approval of the drug by both EMA and FDA. Herein, we assessed safety and efficacy of VDZ in a large real-life experience cohort of patients with UC.

Aims & Methods: All consecutive active, non-operated UC patients treated with VDZ in France from June to December 2014 were assessed. From June to September 2014, VDZ was available through a centralized pre-approval program piloted by the French regulatory agency (ANSM). After its approval by ANSM (reimbursement of the drug by social services is still pending), recruitment was extended until December 2014. Patients received VDZ (at a dose of 300 mg) at weeks 0, 2 and 6 as induction therapy and then every 8 weeks. Patients who did not respond to VDZ induction therapy at week 6 could receive VDZ 300 mg every 4 weeks. Patients were evaluated prospectively at W14. Remission was defined as a partial Mayo score <2. Response was defined as a reduction in the partial Mayo score of at least 3 points and a decrease of at least 30% from baseline. C-reactive protein as well as safety were ascertained.

Results: One hundred and twenty-one patients (67 males, median age: 40.4 IQR [29.7-55.2] years) were included in 33 centres. Median disease duration was 6.5 [3.8-11.4] years; 115 (95%) patients have been previously treated with immunosuppressant and 116 (96%) with at least one anti-TNF. At baseline, mean total Mayo score was 8.3 ± 2.4 and mean CRP level was 19.4 ± 21.1 mg/L. Response and remission rates at W14 were 52% and 35%, respectively. The steroid free response and remission rates were 45% and 31%, respectively. At week 14, the mean decrease of partial Mayo score was 2.5 ± 2.8 ($p < 0.001$) and the mean decrease of CRP level was 3.8 ± 22.5 ($p = 0.02$). Adverse events were reported in 22 (18%) patients and consisted in opportunistic infection (n = 13) including nasopharyngitis (n = 6), upper respiratory tract infection (n = 4) and *Clostridium difficile* superinfection (n = 1), cholecystitis (n = 1) and tuberculosis (n = 1), cutaneous reaction (n = 5), paresthesia (n = 2), strokes (n = 1) and deep venous thrombosis (n = 1).

Conclusion: In this first real-life experience cohort of patients with refractory UC, vedolizumab induced clinical response in more than 50% of cases, with an acceptable safety profile.

Disclosure of Interest: A. Amiot Lecture fee(s): MSD, Consultancy: Abbvie, Takeda, Biocodex, L. Peyrin-Biroulet: None declared, C. Stefanescu: None declared, J.-C. Grimaud: None declared, J. Filippi: None declared, B. Pariente: None declared, X. Roblin: None declared, R. Altwegg: None declared, D. Laharie: None declared, P. Marteau: None declared, A. Buisson: None declared, C. Trang: None declared, S. Nancey: None declared, M. Allez: None declared, G. Savoye: None declared, S. Viennot: None declared, H. Brixi-benmansour: None declared, F. Carbonnel: None declared, Y. Bouhnik: None declared

MONDAY, OCTOBER 26, 2015 14:00–15:30

DIAGNOSIS AND TREATMENT OF CHRONIC CONSTIPATION – ROOM E1

OP055 CONSTIPATION SYMPTOMS IN THE U.S. GENERAL POPULATION: RESULTS FROM THE ROME NORMATIVE GASTROINTESTINAL SYMPTOMS SURVEY (RNGSS)

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Introduction: Rome III diagnostic criteria include 6 different symptoms of functional constipation (FC). Little is known about how frequently these symptoms occur in the U.S. general population and how they vary between demographic groups.

Aims & Methods: Data from the 2013 RNGSS were used to characterize these population constipation parameters. A national sample of 1,665 U.S. adults completed a secure Qualtrics internet survey including demographics, health history questions and the questions of the Rome III Diagnostic Questionnaire with the new validated response formats (*Gastroenterology* 2013;144(5),Suppl.1:S-916) planned for Rome IV. These new response scales assess frequency of the six Rome III functional constipation symptoms in the past 3 months in 10% increments from 0-100%, providing more detailed view of their frequency than previously available in Rome III. To minimize bias in the sample, survey invitations described the study as a physical symptoms survey rather than a survey of gastrointestinal symptoms. Stratified sampling was used to ensure equal gender proportions and minority representation close to census distribution. Responders providing inconsistent survey answers were excluded from analysis, leaving 1,277 response sets.

Results: The analysis sample was 648 females and 629 males, from all 50 U.S. states plus D.C. and Puerto Rico; 54.5% white race; mean age 46.4 years (range 18-94); 45.7% had a college degree. The majority of individuals (68.9%) reported 1 or more FC symptom at a frequency of 10% or higher of all BMs (or 10%+ of weeks in the case of infrequent stools). Average number of FC symptoms reported in the whole sample was 2.3. The 3 most common FC symptoms were straining, hard stools and feeling of incomplete BMs, each reported at 10% or higher frequency in about half of the entire sample (see Table). Digital facilitation of BM was the least common symptom, only reported by 20.5% of people. Compared to males, women had higher rates of presence of all 6 FC symptoms ($p < 0.0001$ for all), higher average number of symptoms in the past 3 months (2.7 vs. 2.1, $p < 0.0001$), and greater average frequency of the symptoms (14.3% vs. 9.3%, $p < 0.0001$). Individuals age 65+ reported slightly fewer constipation symptoms on average than subjects under 30 or those aged 30-64 (1.93 vs. 2.44 and 2.47 respectively; $p < 0.02$) and also had modestly lower mean frequency of constipation symptoms compared to the younger age groups (14.8% vs. 17.6% and 17.8%; $p < 0.008$).

Table: Frequency distribution of the six functional constipation symptoms among individuals in the sample

	Frequency of the symptom in the past 3 months					
	0%	10%	20%	30%	40%	50%+
Functional constipation symptom:						
Fewer than 3 BMs per week	73.2	9.7	3.2	3.3	1.1	6.1
Hard or lumpy stools	49.5	21.1	9.4	6	2.3	7.8
Straining during BM	46.0	24.2	8.1	7.2	2.9	8.6
Feeling of incomplete evacuation	50.4	19.1	10.2	5.2	3.1	3.4
Feeling of blocked passage	62.6	16	6.4	4.9	2.6	5.1
Digital faciltation of BM	79.5	8.8	3.4	2.3	1.1	3.2

Conclusion: Constipation symptoms are highly prevalent in the general population, with the majority experiencing at least 1 FC symptom (mean = 2.3) at 10% frequency or higher. Women have significantly greater number and frequency of constipation symptoms than men. Unlike some previous reports, we found a slight decrease in constipation symptoms in older individuals compared to younger subjects. [Supported by the Rome Foundation and R01 DK31369]

Disclosure of Interest: None declared

OP056 DIAGNOSIS OF DYSSYNERGIC DEFECATION BY QUESTIONNAIRE AND PHYSICAL EXAMINATION

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Introduction: It is important to distinguish dyssynergic defecation (DD) from other subtypes of constipation because DD has a distinct physiological mechanism and responds to different treatments. However, diagnosis currently depends on costly, invasive tests which are not widely available.

Aims & Methods

Aim: To evaluate the sensitivity and specificity of symptom questions and physical examination.

Methods: 307 Italian patients with refractory constipation were referred to author GC for management. Those who responded to a 30-day trial of fiber supplements or were non-adherent were excluded, leaving 238. Following a questionnaire and physical exam, they were evaluated by anorectal manometry, balloon evacuation test (BET), and defecography (selected patients only), and were assigned "gold standard" diagnoses as follows: Mechanical obstruction (MO) if rectal prolapse on physical exam or abnormal defecography plus BET >2 minutes; DD if paradoxical contraction or failure to relax pelvic floor muscles on anorectal manometry plus BET >2 minutes plus absence of MO; slow transit constipation (STC) if $>5/24$ Sitzmarks remained 5 days after ingestion plus BET <2 minutes; and normal transit constipation (NTC) in the absence of MO, DD, or STC. The predictor variables were the symptom questions and physical examination findings listed in Table 1. We randomly assigned the 238 patients to two groups of 119 each. We first tested the utility of each predictor variable for discriminating DD from other types of constipation in the Learning Sample and selected the best predictors for validation in the Validation Sample.

Results: Average age was 45.2 years, and 92% were females. Anorectal manometry, BET, and defecography identified 102 as having DD, 31 as STC, 37 as MO, and 63 as NTC. Five were not classifiable by these tests. Table 1 shows that the best predictor of DD status was a question on which muscles were used to defecate; a response of "anus" identified 91.1% of DD , and any other answer correctly identified 88.7% of those with other types of constipation. Test performance in the Validation Sample was similar (Table 1). The concordance between answers to this question on two occasions 30 days apart was 98.7%. The physical examination finding that the anal sphincter relaxes on straining correctly identified 97.8% of patients who did not have DD, and test performance was similar in

the Validation Sample. No symptoms or exam findings reliably identified other types of constipation.

Table 1: Sensitivity and Specificity of Minimally Invasive Tests

	Learning Sample		Validation Sample	
	Sensitivity	Specificity	Sensitivity	Specificity
Questionnaire:				
Incomplete evacuation	100	2.8	100	5.1
Anal blockage	55.6	58.3	63.2	54.2
Digital maneuvers	37.8	61.1	31.6	55.9
Squeeze anus to defecate	**91.1**	**88.7**	**82.1**	**86.2**
Physical Examination:				
Abd wall contracts to defecate	73.3	5.6	61.4	8.5
Anal sphincter relaxes to defecate	**76.4**	**97.8**	**72.9**	**94.7**

Conclusion: Asking patients which muscles they use to defecate has an overall accuracy of 87% for distinguishing patients with DD from those with other types of constipation. This question could be used in epidemiological studies to estimate the prevalence of DD, in primary care to guide treatment, and in pharmaceutical trials to select patients for inclusion. [Supported in part by grant R01 DK31369]
Disclosure of Interest: None declared

OP057 NALOXEGOL FOR OPIOID-INDUCED CONSTIPATION: MECHANISM OF ACTION AND CLINICAL IMPLICATIONS

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Introduction: Opioid-induced constipation (OIC) results from the binding of opioid agonists to mu-opioid receptors in the enteric nervous system.[1] Conventional therapies do not target all underlying mechanisms of OIC and have limited efficacy. Naloxegol (Movantik™, Moventig® in Europe), a peripherally acting mu-opioid receptor antagonist, was approved by the FDA and EMA in 2014.
Aims & Methods: To summarize the study results that characterized the mechanism of action and clinical effects of naloxegol. Assessments of naloxegol included in vitro determinations of its affinities for opioid receptor subtypes, functional antagonism at mu-opioid receptors, and properties as a P-glycoprotein (PGP) substrate using a Caco2 cell transport assay. Single (8–1000 mg) oral dose-ranging studies assessed pharmacodynamics of the antagonism of morphine-induced decreases in orocecal transit time (OCTT) and pupillary miosis, safety and tolerability, and pharmacokinetics (PK) in healthy men. The efficacy, safety, and tolerability of daily doses of naloxegol (12.5, 25 mg) were evaluated in phase 3 trials in patients with OIC and chronic noncancer pain.[2,3] Endpoints included response rate (sustained changes in spontaneous bowel movements), safety assessments, and changes in daily opioid dose, pain scores, and signs of opioid withdrawal.
Results: Naloxegol is a PEGylated derivative of naloxone and a potent ($K_i = 7.42$ nM), competitive antagonist of the human mu-opioid receptor. Naloxegol was a substrate for the PGP transporter, with low apparent permeability in the Caco2 transport assay, and penetrated the CNS 15 times slower than naloxone in a rat brain perfusion model. In healthy men, dose-ordered antagonism of the morphine-induced delay in OCTT was observed. The placebo:naloxegol OCTT ratio declined with increased naloxegol AUC, consistent with exposure-dependent antagonism of morphine-induced slowing of GI transit. Doses $\leq$125 mg produced negligible antagonism of morphine-induced miosis, indicating no antagonism of central mu-opioid receptors. In 2 identical randomized, double-blind, placebo-controlled 12-week phase 3 studies, response rates were significantly increased in patients treated with naloxegol 12.5 mg (KODIAC-04, $P = 0.02$ and 25 mg (KODIAC-04, $P = 0.001$; KODIAC-05, $P = 0.02$) vs placebo.[2] Patients treated with naloxegol for 12 or 52 (KODIAC-08, 25 mg) weeks exhibited good safety profiles. Most AEs were GI-related; discontinuations and AEs were higher with the 25-mg dose.[2,3] In the 12-week and 52-week studies, there were no significant changes in opioid dose and pain scores; signs of opioid withdrawal were infrequent.
Conclusion: Naloxegol exhibits PK properties important for selective action on mu receptors in the periphery, is efficacious, generally safe and well tolerated, and does not affect opioid-mediated analgesia at therapeutic doses in patients with OIC and chronic noncancer pain.

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OP058 EFFECTIVENESS OF LACTOBACILLUS REUTERI IN THE TREATMENT OF FUNCTIONAL CONSTIPATION IN CHILDREN: A RANDOMIZED, DOUBLE–BLIND, PLACEBO-CONTROLLED, MULTICENTER TRIAL

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Introduction: Functional constipation in childhood is treated with defecation training and macrogole/lactulose administration but a number of patients do not respond to the therapy or present with some complaints even if number of bowel movements increases. This is the reason to look for additional treatment methods on top of macrogole or lactulose. Several probiotic strains have been tested in a few trials but the results in children were negative- still most of the studies were performed in children responding very well to standard lactulose therapy. *Lactobacillus reuteri* has been proven to improve symptoms in functional gastrointestinal disorders including constipation.
Aims & Methods: The aim of the study was to assess the effectiveness of *Lactobacillus reuteri* as an adjunct to macrogole in the treatment of functional constipation in children.
A double-blind placebo randomized controlled trial was conducted in a group of 129 children (57 girls, 72 boys) aged 4.66 ± 1.33 years (mean $\pm$ SD), with functional constipation (average duration: 23 months) who were treated with a poor effect for at least two months prior to the study.
Patients were randomly assigned to one of the two groups: 1. *Lactobacillus reuteri* (1 tablet containing 10^8 CFU) and macrogole therapy or 2. macrogole and matching placebo for 8 weeks.
Results: 121 patients completed the study. The majority (119/121) of patients increased their bowel movements in both groups (59 vs 60, ns.) and there was no statistically significant difference in the number of bowel movements per week at week 8 between the study and the placebo group (7.5 ± 3.3 vs 6.9 ± 2.5, respectively).
Additionally, there were no significant differences between groups in the numbers of patients complaining of pain at defecation (13/47 vs 8/53), abdominal pain (19/41 vs 25/36), withholding stools (15/45 vs 13/48), passing hard stools (7/53 vs 3/58) or large stools (14/46 vs 12/49), fecal incontinence (17/43 vs 11/50). Patients in both groups required similar dose of macrogole per week (265g vs 300g, ns.)
Conclusion: *Lactobacillus reuteri* supplementation was not effective in the treatment of functional constipation in children aged 2-7 years.
Disclosure of Interest: None declared

OP059 HOW DOES PSYLLIUM REALLY WORK IN CONSTIPATION? A DOUBLE-BLIND CROSSOVER STUDY TO EVALUATE ITS IMPACT ON MAGNETIC RESONANCE IMAGING BIOMARKERS

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Introduction: Ispaghula/psyllium (PS) is a recognised treatment for constipation. Its effect is believed to be mediated by its ability to trap water in the lumen although exactly where in the gut this occurs is unclear. Magnetic Resonance Imaging (MRI) can assess whole gut transit(WGT)[1], small bowel free water content[2], colonic volume[3] and colonic chyme T_1 and T_2 - constants of a substance's physical structure that increase with greater fluidity.
Aims & Methods:
Aims: To assess these parameters in patients with functional constipation disorders, and test whether they were sensitive to the effect of PS. Hypotheses: PS would accelerate WGT, and increase luminal water content, T_1 and T_2.
Methods: A double-blind crossover study of adults with functional constipation or constipation-predominant irritable bowel syndrome by Rome III criteria. Intervention: Metamucil Original Coarse Fiber® (P&G, USA) 14g tds, (daily

PS dose 21g). Placebo comparator: Maltodextrin(MD) 14g tds. Treatment periods were preceded by 10 days of usual laxatives, then 8 days without therapy. At 0800 on day 5 of treatment subjects swallowed 5 MRI transit markers. On day 6 MRI scans were taken fasting and serially after a standard test meal for 7 hours, with a final fasting scan on day 7 of treatment. Primary endpoint: Weighted Average Position Score of transit markers 24 hours after ingestion (WAPS24). Score increases with longer WGT. Secondary endpoints: free water content of the small bowel (SBWC) and ascending colon (ACWC); T_1 and T_2 values of the chyme in the ascending colon (AC) and descending colon (DC). Colonic volume (CV) was also measured.

Results: 16 subjects completed both treatment periods. All reported analyses by paired t-test. PS accelerated WGT such that WAPS24 decreased by mean 0.8 ($\pm$1.8, $p = 0.05$, 1-tailed), or 24%. Postprandial SBWC rose markedly with PS: mean SBWC 32.9mL $\pm$16.7 on MD vs. 81.5mL $\pm$41.2 on PS ($p < 0.001$). This was followed by a smaller increase in ACWC ($p < 0.05$). Fasting T_1 values were lower than previously reported in healthy volunteers(HVs) but on PS rose in both the AC ($p < 0.001$) and DC ($p < 0.01$) to values within the normal range. CV increased by 332mL (95%CI 214-451, $p < 0.001$), or 48%. Table 1 shows the distribution of key parameters in previous studies[1,3,4] of HVs alongside data in constipation on MD and on PS.

Mean (SD) orMedian (Q25-Q75)	Healthy Volunteers	Constipation subjects on MD	Constipation subjects on PS
WAPS24	0.8 (0-1.6)	3.4 (1.6-4.8)	2.2 (1.5-3.0)
Colonic Volume (mL)	561 (239)	690 (218)	1022 (240)
T_1 AC (secs)	0.77 (0.64-0.92)	0.55 (0.49-061)	0.82 (0.44-1.14)
T_1 DC (secs)	0.55 (0.39-0.85)	0.23 (0.19-0.55)	0.57 (0.32-0.78)

Conclusion: Psyllium decreased WGT while both CV and fluidity of the colonic chyme (T_1) increased. All these measures on placebo were different to prior data in healthy volunteers and showed a significant response to therapy. The sequences used are readily translatable to any MRI scanner in clinical use and show great promise as non-invasive biomarkers for the assessment of constipation and the effect of gut modulators.

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Disclosure of Interest: K. Murray: None declared, G. Major: None declared, C. Hoad: None declared, A. Nowak: None declared, L. Marciani: None declared, A. Silos-Santiago: None declared, C. Kurtz: None declared, J. Johnston: None declared, P. Gowland: None declared, R. Spiller Financial support for research: a collaborative study funded by Ironwood Pharmaceuticals Inc.

OP060 SACRAL NERVE STIMULATION FOR REFRACTORY CONSTIPATION: PRELIMINARY RESULTS OF A MULTICENTER RANDOMIZED CROSS-OVER DOUBLE BLIND STUDY

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Introduction: Uncontrolled studies have reported conflicting results on the benefit of sacral nerve stimulation (SNS) in patients suffering from refractory constipation. We assessed the efficacy of SNS in a multicenter randomized cross-over double blind study.

Aims & Methods: Patients with severe constipation refractory to conservative therapy were included if they had at least 2 criteria among: i) Less than 3 bowel movements (BM) per week, ii) straining to evacuate on >25% of attempts, iii) sensation of incomplete evacuation on >25% of occasions. Response to therapy was defined by a number of BM $\geq$3/wk and/or > 50% improvement in symptoms. Responders to a 3-week temporary stimulation were offered permanent neurostimulator implantation. After a 2-week wash-out period, patients were randomly assigned in a cross-over design with 2 periods of 8-week of active (ON) or sham (OFF) stimulation. The 2 periods were separated by a 2-week wash out period. Patients and investigators were blinded to the stimulation sequence. At the end of the 2 trial periods, all patients were offered to receive active stimulation until the last evaluation at 1 year. Symptoms (Wexner score, Visual Analogic Scale), Quality of Life scale, and tolerability/side effects were assessed before and at the end of each period. Colonic transit time and anorectal manometry were performed at inclusion and at the end of follow-up.

Results: From July 2012 to November 2013, 36 patients (mean (SD) age: 45 years (14), 33 female) underwent a temporary stimulation, the majority of whom (n = 28, 77.8%) had predominant dyschesia. A total of 21 patients (58.3%) were responders, and 20 received permanent stimulation (mean (Standard Deviation) age: 44 years (15), 19 female) (1 patient refused the implantation). Response was obtained in 60% and 55% after ON and OFF stimulation periods, respectively (ITT analysis, missing = failure). During the study period, 3 patients had the stimulator explanted, 2 for infection of the stimulator site, 1 for consent withdrawal (lack of efficacy), and 1 was excluded for non compliance to study protocol. After a 1-year follow-up, 55% of implanted patients (n = 11) remained responders. Median Wexner scores were 20 at inclusion (min-max: 13-28), 15 after the temporary stimulation (min-max: 2-29), and 13.5 at one year (min-max: 3-24, n = 18).

Conclusion: In patients with refractory constipation who responded to temporary SNS, this randomized double-blind study could not demonstrate any significant effect of active stimulation (ON) compared to absence of stimulation (OFF). SNS may be a therapeutic option in a small subgroup of patients: indeed, a positive response 1 year after permanent implantation of the stimulator remained in 30% of the patients initially tested.

Disclosure of Interest: F. Zerbib Financial support for research: Medtronic, L. Siproudhis: None declared, P.-A. Lehur Conflict with: Medtronic, C. Germain: None declared, F. Mion: None declared, A.-M. Leroi Conflict with: Medtronic, B. Coffin: None declared, A. Le Sidaner: None declared, V. Vitton: None declared, C. Bouyssou-Cellier: None declared, G. Chene: None declared

MONDAY, OCTOBER 26, 2015 14:00–15:30
OMIC TECHNOLOGY PROVIDES NEW BIOMARKERS – ROOM E2

OP061 META-ANALYSIS OF 544 GASTRIC CANCER GENOMES IDENTIFIED NOVEL DRIVER GENES AND A PROGNOSTIC MUTATION SIGNATURE

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Introduction: Gastric cancer is not a single entity and its molecular classification is still evolving. Despite a decrease in both incidence and mortality owing to progresses in *Helicobacter pylori* eradication and cancer screening, gastric cancer remains the 7th most common cancer and the 3th leading cause of cancer death worldwide with a 5-year survival rate of 29.6%. Next-generation sequencing studies have identified novel driver genes in gastric cancer but their use in molecular typing and prognostication remains unestablished.

Aims & Methods: To characterize mutational processes operative in gastric cancer and to identify novel significantly mutated genes (SMGs) and prognosticators for patients with gastric cancers, we aggregated somatic mutational profiles and clinicopathological information of 544 gastric cancer patients from previous genomics studies. We further applied nonnegative matrix factorization (NMF) to decipher mutational signatures operative in gastric cancer, MutSigCV to discover new SMGs, and Kaplan-Meier survival and multivariate Cox regression analyses to identify prognostic mutation signatures.

Results: Gastric cancer could be classified into regular- (86.8%; average mutations per Mb: 2.5) and hyper-mutated (13.2%; average mutations per Mb: 33.7) subtypes based on mutation frequency. TpCpW mutations were significantly more frequent and associated with APOBEC expression in regular- but not hyper-mutated gastric cancer despite *APOBEC3B* mRNA levels were comparable. In regular-mutated gastric cancer, twelve reported (*TP53*, *ARID1A*, *CDH1*, *PIK3CA*, *etc.*) and six novel recurrently mutated genes (*FLG*, *COL14A1, BNC2, CNBD1, ITGAV, TP53BP1*) exhibited high mutation prevalence ($\geq$3.0%) and higher-than-expected number of non-silent mutations. Mutational profiling further identified two molecular subtypes in regular-mutated gastric cancer with distinct prognostic outcomes independent of TNM staging and Lauren classification. Genotoxic/oncogenic stress response (58.0%), histone modification/chromatin remodeling (28.9%) and growth factor receptor signaling (25.3%) were frequently altered by somatic mutations in regular-mutated gastric cancer. In diffuse-type gastric cancer, *CDH1* mutation was associated with shortened patients' survival independent of TNM staging.

Conclusion: Meta-analysis of 544 gastric cancer genomes has identified novel driver genes and a mutation signature predictive of patients' survival. *CDH1* mutation is an independent prognostic factor in diffuse-type gastric cancer.

Disclosure of Interest: None declared

OP062 A NOVEL GLYCOMIC-BASED SERUM BIOMARKER (GLYCOCIRRHOTEST) FOR RISK ASSESSMENT OF HEPATOCELLULAR CARCINOMA IN COMPENSATED CIRRHOSIS

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Introduction: Cirrhosis is a major risk factor for the development of hepatocellular carcinoma (HCC) with a yearly incidence ranging from 1 to 8%. EASL and AASLD guidelines recommend systematic screening with liver ultrasound at 6 months interval in cirrhotic patients. A glycomic-based test, called GlycoCirrhoTest (GCT), based on to the respective abundance of bisecting GlcNAc residues and triantenarry glycans on serum proteins, has shown a 79% sensitivity and 86% specificity for the diagnosis of cirrhosis among patients with chronic liver diseases.

Aims & Methods: The aim of the present study was to determine whether serum glycomics are predictive for the risk of HCC development in compensated cirrhosis.

Serum samples of 132 cirrhotic (Child A or B) patients collected between 1995 and 2005 were analysed. Seventy percent suffered of Hepatitis C. In the remaining patients, the cause of cirrhosis was HBV infection, alcohol and autoimmune diseases. Cirrhosis was confirmed by liver biopsy. The patients were followed until the appearance of a HCC, death or liver transplantation. Patients with HCC at the moment of serum sampling and during the first year were excluded. GCT was performed using capillary electrophoreses as previously described by Callewaert et al. (*Nature Medicine* 2004).
Results: After a median follow up of 4 years (IQR: 3.6–8.06), 35 (26.5%) of the patients developed a HCC. Mean follow up in the patients who did not develop HCC was 3.7 years (IQR: 3.4-9.9; ns). We observed a significant increase of the mean baseline GCT value in the patients who developed a HCC during follow up ($p < 0.001$) as compared to those who did not. ROC Curve analysis showed an AUC of 0.716 (95% CI: 0.611-0.820) for the prediction of HCC in the patients with a follow up of at least 1 year. An 0.1 increase in the value of the GCT was associated with a 27% increase in the risk for developing HCC (OR 1.27; 95%CI: 1.098-1.475). An optimal cutoff for the GCT was defined at 1.6 and the hazard ratio for the development of HCC was 3.88 (95% CI: 1.81-8.29) for patients with a baseline GCT above this treshold.
Conclusion: This study suggests that an analysis of the serum protein glycome could generate a useful biomarker for the identification of cirrhotic patients at high risk for the development of HCC up to 4 years before HCC development. GlycoCirrhoTest may help to stratify cirrhotic patients according to the risk of HCC and optimize screening.

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Disclosure of Interest: None declared

OP063 OVEREXPRESSION OF MIRNA221 AND 222 IN CANCER STROMA IS ASSOCIATED WITH MALIGNANT POTENTIALS IN COLORECTAL CANCER

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Introduction: Cancer stroma plays an important role in cancer development. Although a few study were reported on differential miRNA expression profile comparison between cancer stroma and normal stroma, the aberrant expression of miRNA in cancer stroma that related to cancer progression remains unclear.
Aims & Methods: The aims of this study is to investigate the miRNAs associated with liver metastasis in cancer stromal tissue of human colorectal cancer. Using a laser capture microdissection technique, we obtained cancer stromal tissues from primary lesion of 6 colorectal cancer patients with liver metastasis (CRCWLM) and 6 colorectal cancer patients without liver metastasis (CRCWOLM). These samples were analyzed by miRNA microarray to identify differentially expressed miRNAs in cancer stromal tissues of CRCWLM versus CRCWOLM. Results of microarray were further analyzed by quantitative real-time polymerase chain reaction (qRT-PCR). Furthermore, we examined 101 CRC samples whether miRNA expression status in stromal tissue could affect the clinicopathologic factors.
Results: Microarray analysis revealed that miR221 and miR222 were higher expressed in cancer stromal tissue of CRCWLM than in that of CRCWOLM, whereas the 4 miRNAs including miR659, 4470, 4669 and 5703 were lower expressed in CRCWLM. To confirm the microarrays findings, we measured the expression level of 6 miRNAs described as above in stromal tissues of 20 CRCWLM and 20 CRCWOLM, using qRT-PCR. Expression levels of miR221 and miR222 in cancer stromal tissue were significantly higher in CRCWLM than in CRCWOLM, while there was no difference in the expression of 4 down-regulated miRNAs. To examine the clinicopathological utility of stromal miR 221/222 expression in CRC patients, we measured miR 221/222 expression of cancer stroma and cancer cells in 101 CRC samples, using qPCR analysis. qPCR revealed that CRC patients with high miR221 expression level was related to liver metastasis, distant metastasis, venous invasion and shorter overall survival compared to CRC with low miR221 expression level ($P < 0.05$). Similarly, high miR222 expression level was related to liver metastasis, distant metastasis, depth of tumor invasion and shorter overall survival ($P < 0.05$). On the other hand, in cancer cells there is no correlation between clinicopathological factors and expression of miR221 and miR222.
Conclusion: Both miR-221 and miR-222 are two highly homologous microRNAs and many reports indicate that miR-221/222 may function as an oncogene in human cancer as an onco-miR. Our result suggested that overexpression of miR221 and miR222 in cancer stromal tissue is related to the malignant potentials to develop liver metastasis in patients with CRC.
Disclosure of Interest: None declared

OP064 EPIGENOME-WIDE DNA METHYLATION PROFILING IN INFLAMMATORY BOWEL DISEASE

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Introduction: Epigenetic alterations including DNA methylation may provide important insights into gene-environment interaction in complex immune diseases such as inflammatory bowel disease (IBD). Whilst whole tissue methylation changes may provide clinically useful biomarkers, epigenetic changes are cell-type specific. This study aimed to characterise the circulating methylome in IBD, and relate changes seen in whole blood to the methylation profile in separated leucocytes, gene expression data, as well as our previous data in childhood-onset disease.[1]
Aims & Methods: The Illumina 450k array was used to assess whole blood leucocyte DNA methylation at over 485,000 CpG sites across the genome in 240 patients (121 Crohn's disease[CD], 119 ulcerative colitis[UC]) and 191 controls. Whole blood data was analysed after correcting for batch effects and for the cellular composition of the samples. Differentially methylated sites discovered in whole blood were also investigated in immunomagnetically separated leucocytes (CD4+ & CD8+ lymphocytes, CD14+ monocytes). All participants were genotyped using the Illumina Omni Core Exome array.
Results: There were 446 differentially methylated positions (DMPs) meeting epigenome wide significance as defined as a Holm corrected p value of < 0.05 (uncorrected $p \leq 1.1 \times 10^{-7}$) in IBD cases versus control. No markers were significantly different between CD and UC.
There were 60 differentially methylated regions (DMRs) with unidirectional methylation change in 3 or more adjacent markers each achieving False Discovery Rate significance of $p < 0.05$. Of these, 5 were significant following more stringent Holm correction for the probes.
There was significant enrichment of methylation alteration around known susceptibility loci.[2] Linear Discriminant analysis using two CpG sites discriminated IBD cases and controls with high accuracy (area under curve 0.87)
Established as well as novel pathways pertinent to disease pathogenesis are strongly implicated. The most significant DMP in whole blood (RPS6KA2 [corrected $p = 1.1 \times 10^{-16}$] was also hypomethylated in monocytes in UC (uncorrected $p = 3.5 \times 10^{-6}$). The most significant DMR, VMP1/miR21 (most significant probe corrected $p = 4.9 \times 10^{-14}$) strongly replicates the same finding in our previous study. The gene encoding Beta-2 Integrin (ITGB2) was a hypermethylated DMR in IBD and more specifically CD (most significant probe corrected $p = 4.3 \times 10^{-4}$) compared with controls. Integration of genetic and epigenetic level data permitted identification of methylation quantitative trait loci.
Conclusion: This is the most detailed characterisation of the epigenome carried out in IBD to date and includes novel data exploring the circulating methylome in UC. The findings strongly validate this approach in complex disease, replicate and expand previous data, and provide clear translational opportunities.

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OP065 COMPREHENSIVE DNA METHYLATION ANALYSIS REVEALS A COMMON TEN-GENE METHYLATION SIGNATURE IN COLORECTAL ADENOMAS AND CARCINOMAS

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Introduction: Microarray analysis of promoter hypermethylation provides insight into the role and extent of DNA methylation in the development of colorectal cancer (CRC) and may be co-monitored with the appearance of driver mutations.
Aims & Methods: Colonic biopsy samples were obtained endoscopically from 10 normal, 23 adenoma (17 low-grade (LGD) and 6 high-grade dysplasia (HGD)), and 8 ulcerative colitis (UC) patients (4 active and 4 inactive). CRC samples were obtained from 24 patients (17 primary, 7 metastatic (MCRC)), 7 of them with synchronous LGD. Field effects were analysed in tissues 1 cm ($n = 5$) and 10 cm ($n = 5$) from the margin of CRC. Tissue materials were studied for DNA methylation status using a 96 gene panel. Expression levels

were assayed using whole genomic mRNA arrays. SFRP1 was further examined by immunohistochemistry. HT29 cells were treated with 5-aza-2' deoxycytidine to analyse the reversal of DNA methylation.
Results: More than 85% of tumor samples showed hypermethylation in 10 genes (*SFRP1, SST, BNC, MAL, SLIT2, SFRP2, SLIT3, ALDH1A3, TMEFF2, WIF1*), whereas the frequency of examined mutations were below 25%. These genes distinguished precancerous and cancerous lesions from inflamed and healthy tissue. The mRNA alterations that were caused by systematic methylation could be reversed by demethylation treatment.
Conclusion: Systematic changes in methylation patterns were observed early in CRC carcinogenesis, occuring in precursor lesions and CRC, often prior to the appearance of sporadic mutations. Thus we conclude that DNA hypermethylation is an early and systematic event in colorectal carcinogenesis, and it can be potentially reversed by systematic demethylation therapy.
Disclosure of Interest: None declared

OP066 DEVELOPMENT OF RECOMBINANT ANTIGEN MICROARRAY FOR AUTOANTIBODY BIOMARKER SIGNATURE ANALYSIS IN GASTRIC CANCER

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Introduction: According to GLOBOCAN data, Gastric cancer (GC) represents fifth most common type of cancer and third most common cause of cancer-related death worldwide. Over 80% of GC cases are detected at late stage when expected 5-year survival ranges from 4 to 20%. Hence, the development of a reliable and simple non-invasive biomarker assay for the early detection of GC among high-risk individuals is of paramount importance. Among other emerging biomarkers, circulating IgG class autoantibodies against tumour-associated antigens (TAAs) have been shown to have promising biomarker qualities for GC detection[1].
Aims & Methods: In our previous studies, we applied T7 phage-displayed antigen microarray (PDAM) technology to identify autoantibody biomarker signatures with relevance to GC. This resulted in the identification of GC-associated biomarker panel with promising diagnostic (AUC = 79%) and prognostic value[1]. Within the current study, in order to obviate the limitations of the PDAM system, we aimed to develop a recombinant TAA microarray that would be applicable for standartized large-scale autoantibody biomarker validation in independent patient and matched control cohorts. The selected GC antigen B cell epitope coding sequences were cloned in pFN19A (HaloTag® 7) T7 SP6 Flexi expression vector, expressed as His-HaloTag fusion proteins in *E. coli* and purified by using Protino® Ni-TED 150 Ni^{2+} columns. For microarray generation, the expressed antigens were printed in duplicate by Q-Array Mini microarray printer (Genetix) onto nickel chelate glass slides (Xenopore). Serum autoantibody signal was detected in 1:200 diluted GC patients' specimens, the protein amount in each spot was determined by using rabbit Anti-HaloTag® polyclonal antibody and respective fluorophore labelled secondary antibodies. Finally, preliminary analytical characteristics of the developed assay (i.e., reproducibility, limit of detection, dynamic range) was determined.
Results: In total, 105 antigen clones having most promising diagnostic and prognostic value for GC were selected for the expression and microarray development – these included clones from 15 Cancer-Testis antigens, 31 known TAAs and 46 novel antigens. According to the Western blot, 85% of the expressed proteins were shown to be soluble, and the obtained seroreactivity data showed that 92% of the expressed antigens retained their B cell epitopes exposed by using this expression system. The lower limit of antibody detection of the microarray platform was determined to be ~100 ng/ml. The dynamic range within the assay was set to be 7,000-15,000 MFI (mean fluorescence intensity) units basing on the linearity of analysed HaloTag and serum reactivity signal ratios. Intra-assay variation was determined to be within the range of 0.11-0.21 (mean 0.14), and inter-assay variation ranged from 0.12-0.36 (mean 0.19).
Conclusion: This study has resulted in the development of a robust platform applicable for serum autoantibody detection against a representative set of GC-associated antigens, which was shown to comply with the analytical and technical prerequisites of the serological assay to be applied for systematic autoantibody biomarker validation.

Reference

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Disclosure of Interest: None declared

OP067 PAIRED TRANSCRIPTOMIC AND PROTEOMIC PROFILING ANALYSIS OF THE INTESTINAL MUCOSA IDENTIFIES SIMILAR BIOLOGICAL PATHWAYS IN DIARRHOEA-PRONE IRRITABLE BOWEL SYNDROME

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Introduction: Altered intestinal barrier and mucosal inflammation are physiopathological characteristics in Irritable Bowel Syndrome (IBS). A transcriptomic analysis has previously guided us to identify a strong association between the transcript signature and immune activity and intestinal permeability in diarrhoea-prone IBS (IBS-D). However, a proteomic analysis with a similar strategy has not been performed so far.
Aims & Methods
Aim: To identify the proteomic profile and to assess whether mRNA changes translate into protein in the intestinal mucosa in IBS-D.
Methods: Total RNA and protein were obtained from jejunal mucosal biopsies from healthy volunteers (H; n = 5) and age-matched (range: 21-59 years) non-celiac, naïve IBS-D patients meeting Rome III criteria (n = 8). RNA was analyzed using Affymetrix GeneChip Human Genome HG-U133 Plus 2.0 array. Protein content was analyzed using 2D-difference gel electrophoresis (DIGE). Differential spots from the gel were picked and analyzed using Ultraflex TOF/TOF mass spectrometer. Mass fingerprint data were searched using Mascot algorithm and submitted to Ingenuity Pathway Analysis (IPA).
Results: RNA analysis showed a distinctive gene expression profile in IBS-D compared with H, with differences in canonical pathways and biological networks associated with mast cell function, intestinal permeability and tight junction (TJ) signalling ($P < 0.001$). Protein analysis revealed 139 spots differentially expressed ($P < 0.05$), of which 95 proteins were identified. The most significant pathways and functions associated with proteomic analysis included categories related to intestinal epithelial barrier modulation such as actin cytoskeleton signalling ($P < 0.003$) and caveolar-mediated endocytosis signalling ($P < 0.005$). Paired analysis of gene and protein profiles revealed association with the same canonical pathways, biological functions and disease mechanisms. Cellular assembly and cell-to-cell signalling were the most significant biological functions associated with IBS-D. Moreover, immunological, gastrointestinal and inflammatory diseases were among the most relevant disease mechanism associated with both IBS-D profiles ($P < 0.001$).
Conclusion: Distinctive mucosal proteomic profile in IBS-D patients identifies alterations in immune activation, mitochondrial dysfunction and cytosketelon signalling. Paired gene and protein expression analysis extends our previous results of dysfunctional tight junction signalling with altered cellular assembly and cell-to-cell signalling in IBS-D patients, supporting the loss of intestinal epithelia barrier function as central molecular mechanism in the disease.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 14:00–15:30
NEW TECHNOLOGIES IN GI ENDOSCOPY – ROOM E3

OP068 EFFICACY OF THE CRYOBALLOON FOCAL ABLATION SYSTEM FOR THE ERADICATION OF BARRETT'S OESOPHAGUS

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Introduction: Radiofrequency ablation (RFA) is currently the preferred ablation technique for eradication of Barrett's oesophagus (BO). However, this technique has drawbacks, such as the need for large controller units and multiple deployment steps. Cryoablation using the CryoBalloon Focal Ablation System (CbFAS) may be an attractive alternative.The CbFAS is a balloon-based system, which uses nitrous oxide as a refrigerant. It is designed to overcome the drawbacks of RFA, and earlier studies show that the CbFAS is feasible and safe for the eradication of BO. A recent dosimetry study demonstrated that 10 second ablations result in the most optimal effect (i.e., full conversion of BO to neo-squamous epithelium, without compromising safety). However, efficacy of 10 second ablations in a larger group of patients has not been investigated.
Aims & Methods: To assess the efficacy and performance of the CbFAS in patients with flat, dysplastic BO.
In this ongoing multi-centre, prospective, non-randomized trial, up to 40 patients will be enrolled. Eligible patients may have up to 2 BO islands that will be treated with 10-second ablations using the CbFAS.Follow-up (FU) endoscopy with photo documentation and biopsy of the treated area(s) is performed 6-8 weeks post-ablation. Primary outcome parameter is the percentage of completely eradicated BO islands at FU. Secondary outcome parameters are the percentage of BO islands with at least 50% eradication, device performance, and adverse events.
Results: As of May 2015, 16 patients were enrolled and treated (14 male, median BO C3M6). Eight patients (50%) underwent endoscopic resection (ER) of a visible lesion before ablation therapy, containing early adenocarcinoma in 5 patients (62%), HGD in 2 (25%), and LGD in 1 patient (13%). Worst pathology found, either in the ER-specimen or the baseline BO, was LGD in 8 patients (50%), HGD in 3 (19%) and early adenocarcinoma in 5 (31%). Thirteen patients (81%) had circumferential RFA-treatment prior to inclusion in this study.
23 ablations were performed in 16 patients; median procedure time was 15 (IQR 5-35) minutes. Device malfunction occurred in 4/16 (25%) procedures, but this did not hamper completion of the ablation. No adverse events occurred during the procedure. Mild pain was reported by 5 patients (33%) directly after the procedure; 1 patient reported mild pain during swallowing at two days post-procedure.As of May 2015, FU endoscopy was performed in 10 of 16 patients (14 treated areas). No strictures were detected. Complete eradication of BO islands, endoscopically and histologically, was observed in 12/14 (86%) treated areas. No buried glands were found on biopsy. In two patients, residual BO was observed at follow-up endoscopy, and confirmed by the presence of intestinal

metaplasia in biopsies. However, in one of these patients it was observed at the time of the procedure that the BO island was not completely ablated; in the portion of the island that was ablated, the BO was eradicated. In the other patient, residual BO (<50% of original size) was found after initial –endoscopically complete- ablation of the BO island.
Conclusion: Preliminary results suggest that cryoablation of BO islands using CbFAS during 10 seconds is effective and safe.
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OP069 A RANDOMIZED TRIAL COMPARING BIODEGRADABLE STENT PLACEMENT AND ENDOSCOPIC DILATION FOR RECURRENT BENIGN ESOPHAGEAL STRICTURES (DESTINY STUDY)

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Introduction: Endoscopic dilation is the standard of care for recurrent benign esophageal strictures (RBES). Esophageal stent placement is thought to prolong the effect of dilation and to reduce recurrences, but stents are associated with migration and require removal. Biodegradable (BD) stent placement might preclude these issues.
Aims & Methods: This multicenter, randomized study compared the efficacy and safety of BD-stent (SX-ELLA, Ella-CS, Czech Republic) placement to endoscopic dilation in patients with RBES. Patients with 1-5 previous dilations were randomized to BD-stent placement or dilation. Power calculation estimated a sample size of 66 patients. Primary outcome was the number of endoscopic dilations for recurrent dysphagia within 3 and 6 months post-procedure. Secondary outcomes were time to recurrent dysphagia, time to first dilation, safety and QoL. Dysphagia scores were recorded daily for one month and monthly thereafter for one year.
Results: A total of 32 patients were randomized to BD-stent placement and 34 patients to ongoing dilation. Baseline patient demographics and lesion characteristics were similar between the two groups. Dysphagia scores significantly improved in both groups at 3, 6 and 12 months compared to baseline ($p<0.001$ for all comparisons). In the BD-stent group, fewer dilations for recurrent dysphagia were required after 3 months (median: 0 [range 0-9] vs. 1 [range 011],$p<0.001$), and fewer patients required endoscopic dilation (87.5% vs. 43.6%, $p<0.01$). No differences between BD-stent placement and dilation were observed after 6 months for number of dilations (median: 1 [range 0-13] vs. 2 [range 0-13],$p=0.40$) or for number of patients requiring dilation at 6 months (38.8% vs. 31.1%, $p=0.05$) or 12 months (34.5% vs. 24.9%, $p=0.24$). Time to the first episode of recurrent dysphagia was significantly longer in the BD-stent group compared to the dilation group (median: 95 days vs. 30 days, $p=0.03$). Safety was not different between the two groups, with 8 procedure-related serious adverse events in each group ($p=0.90$). Most important serious adverse events included esophageal perforation (n = 2) in the dilation group and fistula formation (n = 2) in the stent group. At 6 months, patients in the BD-stent group scored better on the health state scale (median: 80 vs. 70, $p=0.03$) and more patients were able to perform normal levels of activity based on the WHO performance score (85.2% vs. 55.8%, $p=0.04$), compared to the dilation group.
Conclusion: BD-stent placement in patients with RBES prolonged time to recurrent dysphagia and was associated with a higher QoL compared to ongoing endoscopic dilation, while safety parameters were not different. These results suggest that BD-stent placement can be considered at an early stage in the treatment algorithm of RBES.
Disclosure of Interest: D. Walter: None declared, M. van den Berg: None declared, M. Hirdes: None declared, F. Vleggaar: None declared, A. Repici: None declared, P. Deprez: None declared, B. Viedma: None declared, L. Lovat: None declared, B. Weusten: None declared, R. Bisschops: None declared, E. O'Leary Conflict with: Employee for Cook Research Incorporated, J. van Hooft Financial support for research: Cook Medical, P. Siersema Financial support for research: Cook Medical

OP070 FULL-THICKNESS PERORAL ENDOSCOPIC MYOTOMY (POEM) FOR THE TREATMENT OF SIGMOID-TYPE ACHALASIA: A COMPARATIVE STUDY OF CONVENTIONAL AND MODIFIED POEM

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Introduction: POEM treatment of Sigmoid-type esophagus, especially of type S2, is a big challenge due to the technically demanding procedures and high incidence of complications.
Aims & Methods: This work is aimed to explore the feasibility of POEM in treatment of S-type achalasia and to provide experiences in prevention of gas-related complications by using a modified POEM method.A total of 23 S-achalasia patients from August 2011 to June 2014 in our department were included in the present study. Among those patients, six patients including one S2-achalasia underwent conventional full-thickness POEM; while seventeen patients including three S2-achalasia adopted an modified full-thickness POEM with operation changes in a) Creating tunnel entry by longitudinal incision combining with bilaterally perpendicular dissection; b) presetting tunnel routes by endoluminally submucosal injection of dye solution during tunnel creating process; c) increasing the width of the submucosal tunnel. Procedure-related parameters and adverse events, symptom relief and manometry outcomes were collected before and during periodical follow-up.
Results: All the S-achalasia patients have successfully undertaken either conventional or modified full-thickness POEM. The overall treatment success was achieved in 95.6% (22 of 23 cases) during follow-up. The overall mean lower esophageal sphincter pressures (15 of 23 cases) were 38.91 ± 5.83 mmHg and 12.38 ± 3.76 mmHg before and after treatment ($P < 0.01$). The mean Eckardt score decreased from 6.67 ± 1.97 to 0.50 ± 0.55 ($P < 0.001$) by conventional method, and from 7.47 ± 1.67 to 0.76 ± 0.75 ($P < 0.001$) by modified method. No significant differences were shown in the operation time, mytomy length, pre- and post-treatment values of symptom scores between two methods. Yet compared to conventional method, modified POEM decreased gas-related complications from the occurrence rate of 100% (6 of 6 cases) to 11.8% (2 of 17 cases).
Conclusion: POEM is feasible, safe and effective in treatment of S-type achalasia, including S2. Modified POEM method could prevent occurrence of gas-related complications. Yet further experiences and long-term results are warranted.

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Disclosure of Interest: None declared

OP071 INDIVIDUALIZED CHOICE OF SUCTION METHOD INTO APPLICATION CAP OF OVER-THE-SCOPE CLIP SYSTEM: COMPARISON OF SIMPLE SUCTION VERSUS TWINGRASPER IN MULTICENTER EXPERIENCES

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Introduction: The efficacy of over-the-scope clip (OTSC) for GI defects has been described. A successful key of OTSC depends on secure suction into the application cap of target lesion. The suction method includes three methods; simple suction (SS), twingrasper (TG) accessory device, and Anchor device. It seems unclear what kind of suction method should be applied to the target lesion with how type of characteristics.
Aims & Methods: The aim of this study was to investigate better choice of suction methods by comparing SS versus TG in the management of GI defects. The retrospective comparative study at 5 medical centers involved 56 consecutive patients with OTSC placement, dividing into two groups: 14 cases in SS-Group or 42 in TG-group. The primary outcomes were technical (TSR) and clinical success rate (CSR), procedure time, complication rate. Secondarily, the TSR and CSR regarding each parameters; indications, maximum defect size (D, mm), duration from onset, and the combined parameters in each indications were compared.
Results: Significant differences were observed between the two groups in only mean procedure time (SS, 5.9 vs.TG, 14.1 min). The CSR of SS with D≦10, immediate or acute in refractory bleeding was 100%, suggesting better situation of convenient SS. The CSR, 78.6% of SS despite technical success (TSR, 100%) had a tendency to decrease due to delayed leakage, compared to TG (TSR, CSR; 88.1%), revealing that TG assist is desirable for leak and fistula with defect of whole layer. However, OTSC using TG had some limitations in situations with D > 20, chronic, refractory bleeding and fistula.
Conclusion: Individualized choice of the suction method in OTSC system plays the most important role for OTSC success. Considering the size of defect, and

duration from onset in each indications may contribute to the improvement of OTSC success.

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Disclosure of Interest: None declared

OP072 A COMPARISON OF TWO FULL-THICKNESS ENDOSCOPIC CLOSURES: OVER-THE-SCOPE-CLIP (OTSC) VERSUS KING CLOSURE (ENDOLOOP) IN A RANDOMIZED LONG-TERM EXPERIMENTAL STUDY

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Introduction: There are several tools for endoscopic closure of gastrointestinal perforations. We have shown that both over-the-scope-clip (OTSC) and KING closure (endoloop + clips) are safe and effective and provide full-thickness closure but OTSC clip demonstrated inferior histological short-term outcomes [1].
Aims & Methods: To compare long-term effectiveness and macroscopic and histologic quality of healing of perforation closed with OTSC or KING closure. The main outcomes were the effectiveness, complication rate and histological response.
We conducted a randomized experimental study with 16 minipigs (average weight 43.2 ± 11.2 kg). A standardized perforation was performed on the anterior sigmoid wall using a needle knife followed by a 2 cm balloon dilation. KING closure (n = 8) was attained by approximation of an endoloop fixed to the margins of perforation with endo-clips. OTSC method (n = 8) was executed by deploying nitinol OTSC (OVESCO) clip over the defect. Pigs underwent a control rectoscopy 8 months after the perforation closure to assess the macroscopic quality of healing. Then, autopsy was performed and the rectosigmoid was sent for histopathological assessment.
Results: All closures were completed successfully without air leaks. The duration of closure was similar in both techniques (OTSC 17.8 ± 7.6 min vs. KING 19.6 ± 8.8 min). We found one small polyp-like formation (6.3%) in the KING group at autopsy. All other closures (93.7%) were healed with a flat scar without the presence of any foreign material or signs of leakage. Microscopically, no inflammatory or other changes were observed after KING closure. In the OTSC group, however, ulcers involving lamina muscularis mucosae were present in 2 pigs (25%), cryptal abscesses in 3 pigs (38%) and significant neutrophil accumulation in 7 pigs (88%). Giant cell granulomas, bridging, dysplasia or abundant scarification were not observed in either group.
Conclusion: Both OTSC closure and KING closure offer a long-term reliable seal of perforations without stenosis or fistulas. KING closure provides histologically superior healing.

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Disclosure of Interest: None declared

OP073 EFFECTIVENESS AND SAFETY OF ENDOSCOPIC RESECTION FOR RECTAL NEUROENDOCRINE TUMORS ACCORDING TO DIFFERENT RESECTION METHODS: A KASID MULTI-CENTER STUDY

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Introduction: Most rectal NETs can be treated by endoscopic resection because they are diagnosed at a small and early stage. However, optimal therapeutic methods have not been elucidated to date.
Aims & Methods: We are aimed to evaluate the effectiveness and safety of endoscopic resection for rectal NETs according to different resection methods through conducting a large, multicenter study. Patients with endoscopically resected rectal NETs, from January 2000 to November 2011 in 15 university hospitals were included in this study. Endoscopic resection methods were classified into three groups; (1) endoscopic mucosal resection (EMR) including conventional EMR methods; (2) modified EMR (mEMR) including EMR using a transparent cap (EMR-C), EMR using a ligation device (EMR-L), and precut EMR; (3) endoscopic submucosal dissection (ESD). End outcomes were determined by assessing resection margin status and complications.
Results: Of a total of 573 patients with rectal NETs, the mean age at diagnosis was 49.6 ± 11.6 years (male:female ratio = 1.4:1). The mean tumor size was 6.0 ± 3.3 mm (range 1.0 – 22.0 mm). Tumors were resected using conventional EMR (n = 369), EMR-L (n = 68), EMR-C (n = 41), precut EMR (n = 19), and ESD (n = 74). When classified into three groups, the tumor size was 6.2 ± 3.2, 4.7 ± 2.7, and 7.3 ± 3.9 mm in EMR, mEMR, and ESD group, respectively ($p < 0.001$). As for resection margin status, the complete resection rate of mEMR and ESD was superior to that of EMR ($p < 0.001$). However, in the overall complication rate including bleeding and perforation, there was no significant difference between groups.
Conclusion: On the basis of our results, as for en bloc resection and resection margin status, mEMR and ESD shows significantly superior efficacy compared to conventional EMR.
Procedure-related complications are independently associated with incomplete resection and deep invasion beyond submucosa, but not with treatment method.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 14:00–15:30
NASH: FROM BENCH TO BEDSIDE – ROOM E5

OP074 INCIDENCE AND RISK FACTORS FOR NON-ALCOHOLIC FATTY LIVER DISEASE IN AN URBAN, ADULT SRI LANKAN POPULATION – A COMMUNITY COHORT FOLLOW-UP STUDY

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Introduction: We previously reported a community prevalence of 33% for NAFLD in an urban, adult Sri Lankan population. We also found a significant association between patatin-like phospholipase domain containing 3 *(PNPLA3)* gene rs738409 polymorphism, and susceptibility to NAFLD in the same population, after testing 10 selected single nucleotide polymorphisms (SNPs) in a case-control study.
Aims & Methods: The aim of this study was to assess the incidence and risk factors for NAFLD in this population after seven years of follow-up. The study population consisted of 42-71-year-old adults, originally selected by age-stratified random sampling from electoral lists from Ragama, Sri Lanka. The target population was screened initially in 2007 and subsequently invited back for re-evaluation in 2014. On both occasions they were assessed using a structured interview, clinical and anthropometric measurements, liver ultrasound, and biochemical and serological tests. NAFLD was diagnosed on established ultrasound criteria for fatty liver (two out of three criteria: increased echogenecity of the liver compared to kidney and spleen, obliteration of the vascular architecture of the liver and deep attenuation of the ultrasonic signal), safe alcohol consumption (Asian standards: <14 units/week for men, <7 units/week for females) and absence of hepatitis B and C markers. Non-NAFLD controls were defined as subjects who did not have any of the ultrasound criteria for NAFLD. We also performed an updated case-control study to investigate associations of selected genetic variants with incident NAFLD [SNPs: *PNPLA3* (rs738409), *LYPLAL1* (rs12137855), *GCKR* (rs780094), *PPP1R3B* (rs4240624) and *NCAN* (rs2228603), *APOC3* (rs2854117 and rs2854116), *ADIPOR2* (rs767870) and *STAT3* (rs6503695 and rs9891119)].
Results: Of the 2985 original study participants, 2155 (72.2%) (1244 women and 911 men; mean age 59.2 years [SD, 7.7]) participated in the follow-up assessment. 1322 [mean age 58.9 years (SD, 7.6), 483 (53.0%) men and 839 (67.4%) women] had NAFLD. Out of 795 [466 (58.6%) women] participants who did not have NAFLD in the original study, 365 [226 (61.9%) women, mean age 58.6 years (SD, 7.9)] had developed NAFLD after 7 years, giving an annual incidence rate 6.6%. On multivariate analysis, increased waist circumference [OR 1.96(1.30 – 2.97), p = 0.001], BMI > 23 kg/m^2 [OR 2.93(1.99 – 4.30), $p < 0.001$] and raised plasma triglycerides (TG) [OR 1.49(1.03 – 2.13), p = 0.03] were independently predictive of incident NAFLD in this cohort, while raised BP and reduced

HDL, were not. In the updated association study involving 1310 cases and 427 controls, we found borderline association with NAFLD at two of the 10 candidate loci: rs4240624 at *PPP1R3B* and rs738409 at *PNPLA3* (one-tailed P = 0.044 and 0.033, respectively).
Conclusion: In this community cohort follow-up study in an urban, adult population in Sri Lanka, the annual incidence of NAFLD was 6.6%. Incident NAFLD was associated with features of the metabolic syndrome, and showed tendency of association at *PNPLA3* and *PPP1R3B* gene polymorphisms.
Disclosure of Interest: None declared

OP075 THE RECEPTOR TYROSINE KINASE MERTK IS INVOLVED IN THE HEPATIC FIBROGENESIS IN NAFLD

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Introduction: NAFLD comprises a spectrum of disease states, from steatosis (fatty liver) to non-alcoholic steatohepatitis (NASH) followed by progression to fibrosis, cirrhosis and hepatocellular carcinoma (1,2). Several genetic factors involved in NAFLD severity and progression have been identified through genome-wide association studies (GWAS) but their determination is still not sufficient to accurately predict the risk of progression of NAFLD. Mertk is a receptor tyrosine kinase with oncogenic properties that is often over-expressed or activated in various malignancies (3). In a recent GWAS study a SNP of Mertk (rs4374383 G > A) has been associated with fibrosis severity in patients with chronic hepatitis C (4), but currently there is no evidences on the involvement of Mertk in the hepatic fibrosis process.
Aims & Methods: Aim of this study was to assess the possible role of Mertk in the fibrogenic process in NAFLD. Genetic analyses were performed on specimens from patients, who underwent liver biopsy for suspected NASH without severe obesity. Human HSC were isolated from livers and cultured on plastic. The inhibitor used was UNC569 (5) C57BL6/J mice were treated with CCl4 for 6 weeks. Balb/C mice were fed with a methionine and choline deficient (MCD) diet for 8 weeks. Intrahepatic gene expression was assayed by qPCR.
Results: We found that Mertk rs4374383 AA genotype is associated with a lower prevalence of clinically significant fibrosis in patients with NAFLD and this polymorphism is associated with a decreased expression of Mertk. In murine models of hepatic fibrogenesis, we observed an increased hepatic expression of Mertk. In hepatic stellate cells (HSC) Mertk was found to be highly expressed and stimulation with a specific ligand, GAS6, resulting in a time-dependent activation of ERK1/2 and an enhancement of cell migration. Inhibition of Mertk induced apoptotic cell death of HSC. Finally analysis of the mRNA levels in liver specimens from patients with NAFLD, presenting different degree of liver fibrosis, showed that Mertk expression correlates with the score of fibrosis observed.
Conclusion: These data strongly suggest that Mertk could play an important role in fibrogenesis process and additional studies are needed to characterize this pathway in the pathogenesis of NAFLD.

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OP076 DUAL TARGETING OF MICRORNA-21 AND FXR AMELIORATES NAFLD PATHOGENESIS IN MICE

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Introduction: Non-alcoholic fatty liver disease (NAFLD) pathogenesis remains incomplete and effective therapeutic approaches are urgently needed. We and others identified microRNAs (miRNA/miRs) as novel pathogenic factors in NAFLD. In addition, nuclear receptors (NRs), namely peroxisome proliferator-activated receptors (PPARs) and the farnesoid X receptor (FXR) are currently under scrutiny as promising therapeutic targets for non-alcoholic steatohepatitis (NASH). In that regard, interim results from the NIH-funded FLINT clinical trial showed that obeticholic acid (OCA), a potent FXR agonist, has significant beneficial effects on NASH-induced liver damage.
Aims & Methods: In this study, we aimed to: 1) elucidate the role of miR-21 during NAFLD pathogenesis in mice, including modulation of PPARα, a miR-21-direct target; and 2) evaluate the therapeutic potential of a dual NR-targeting approach, namely activation of PPARα and FXR through miR-21 inhibition and OCA administration, respectively. C57BL/6 wild type (WT; n = 24) and miR-21 knockout (KO; n = 24) mice were fed either a standard diet (SD; n = 12) or a fast food diet (FF; n = 12) for 25 weeks. Six animals from each group were fed with OCA 10 mg/kg/day (provided by Intercept Pharmaceuticals, Inc.). In parallel, human liver biopsies were obtained from morbid obese NAFLD patients at different disease stages (n = 28). Liver samples were processed for histological analysis and quantification of miR-21 and pro-inflammatory cytokine expression by qRT-PCR, as well as NRs protein levels by immunoblotting.
Results: Our results showed that, after 25 weeks, WT FF-fed mice displayed increased liver/body weight ratio, macrovesicular steatosis and inflammatory infiltrates. Expression levels of TNF-α, IL-6, TLR4, IL-1β and NLRP3 were increased, consubstantiating steatohepatitis. Further, WT FF-fed mice exhibited increased miR-21 levels and decreased expression of the miR-21 target PPARα, a correlation also found in patients, and further increasing from steatosis to less and more-severe NASH. WT FF + OCA-fed animals displayed decreased steatosis and, interestingly, lower levels of miR-21 compared with WT FF-fed mice. In turn, KO FF-fed mice exhibited significantly reduced liver inflammation, as well as steatosis severity, in parallel with increased PPARα, comparing with WT FF-fed mice. Importantly, improvement of these histological, biochemical/metabolic and inflammatory parameters was augmented in KO FF + OCA-fed mice.
Conclusion: In conclusion, our results indicate that miR-21 downregulation, likely leading to increased PPARα, together with FXR activation by OCA, strongly ameliorate NASH in mice, highlighting the therapeutic potential of novel dual-targeting therapies for human NAFLD. (Supported by PTDC/BIM-MEC/0873/2012, SFRH/BD/88212/2012, SFRH/BD/91119/2012 and SFRH/BD/104160/2014, FCT, Portugal).
Disclosure of Interest: None declared

OP077 CXCL10 MEDIATES THE IMPAIRMENT OF AUTOPHAGOSOME-LYSOSOME SYSTEM THROUGH LYSOSOME DYSFUNCTION IN STEATOHEPATITIS

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Introduction: Autophagosome-lysosome system plays a crucial role in non-alcoholic steatohepatitis (NASH) progression. We recently demonstrated that chemokine CXCL10 is a key inflammatory mediator in NASH development. However, it is uncertain whether CXCL10 regulates autophagosome-lysosome system in the development of NASH.
Aims & Methods: We aim to delineate the underlying mechanism of autophagosome-lysosome impairment in CXCL10 induced NASH. The role of CXCL10 in autophagosome-lysosome system was investigated using CXCL10-knockout (KO) and C57BL/6 wild type (WT) mice. The effect of CXCL10 inhibition on autophagic flux was illustrated in C57BL/6 WT mice and hepatocytes (AML-12 and HepG2) administered with neutralizing anti-CXCL10 or control monoclonal antibodies (mAb). Lysosome function was assayed by LysoTracker Red staining and protein expression of lysosomal membrane glycoproteins. Mitochondrial function was monitored by flow cytometric analysis of MitoTracker staining and reactive oxygen species (ROS) detection.
Results: Impaired autophagic flux as indicated by accumulation of p62 and LC3-II proteins was significantly more pronounced in WT mice with severe steatohepatitis than in CXCL10-KO mice with mild steatohepatitis. Concordantly, autophagic flux impairment could be restored by CXCL10 inhibition using neutralizing anti-CXCL10 mAb both in AML-12 hepatocytes with steatohepatitis changes induced by methionine and choline-deficient medium and in HepG2 hepatocytes treated with palmitic acid. CXCL10 inhibition successfully restored autophagic flux not only in hepatocytes but also in mouse livers with steatohepatitis. Interference with autophagosome-lysosome fusion by bafilomycin A1 abolished the effect of anti-CXCL10 mAb in AML-12 cells with steatohepatitis, indicating the impairment of autophagic flux at the late stage by CXCL10. LysoTracker Red staining further demonstrated that anti-CXCL10 mAb treatment in AML-12 cells could restore lysosome acidification. The impaired lysosome function was further confirmed by reduced protein expression of lysosomal membrane glycoproteins (LAMP-1 and LAMP-2) in mice with genetic CXCL10 deletion and pharmacological CXCL10 inhibition. Moreover, CXCL10-induced autophagosome-lysosomal impairment was associated with ROS production, mitochondria dysfunction, polyubiquitinated proteins accumulation and endoplasmic reticulum stress.
Conclusion: We demonstrate for the first time that CXCL10 inhibits autophagic flux in the pathogenesis of steatohepatitis through eliciting lysosome dysfunction. CXCL10-induced lysosome impairment promotes experimental

steatohepatitis through mitochondria dysfunction and ubiquitinated protein accumulation.
Disclosure of Interest: None declared

OP078 GALECTIN-9 SUPPRESSES NONALCOHOLIC STEATOHEPATITIS-ASSOCIATED HEPATOCELLULAR CARCINOMA

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Introduction: Non-alcoholic steatohepatitis (NASH) is one of the most common causes of chronic liver disease and is considered to be a causative factor of cryptogenic cirrhosis and hepatocellular carcinoma (HCC). So far, various kinds of drugs have been used for the treatment of NASH, but these trials resulted in poor outcomes. Galectin-9 (Gal-9), a soluble β-galactoside-binding animal lectin, attenuates the inflammation via negative regulation of Th1-mediated immune responses. However, little is known about the effect for liver inflammation, and hepatocarcinogenesis.
Aims & Methods: The aim of this study is to determine therapeutic effects of Gal-9 during NASH-associated HCC using Stelic Animal Model (STAM) mice, a validated animal model for NASH-associated HCC, and Gal-9 knockout mice. Four-week-old male STAM were divided into 2 experimental groups and fed as follows: 1) high-fat diet (HFD) (control group); 2) HFD injected with 90 μg/mouse/day of mouse galectin-9 three times a week (Gal-9-treated group). After 12 weeks, mice were sacrificed and blood samples, livers, and bone marrow were collected. Samples were subjected to clinical parameters, histological study, mRNA and protein expressions for multiple genes. We also performed same procedure for Gal-9 knockout mice.
Results: Gal-9 significantly decreased transaminases and alkaline phosphatase. Histological examination revealed marked reduction of steatosis, ballooning, and inflammation in Galectin-9-treated group. In addition, mice treated with Gal-9 developed smaller area of liver fibrosis following fibrosis-related mRNA up-regulations. Furthermore, as for bone marrow derived macrophages, TNFα and CD14 were up-regulated in Gal-9 knockout mice as compared to those in control mice ($P < 0.05$). Moreover, Gal-9 significantly inhibited total number and size of HCC.
Conclusion: Gal-9 improved the clinical and histological development of NASH and reduced the number and size of HCC. Thereby, Gal-9 might be a potential therapeutic target for the treatment of NASH-associated HCC.

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Disclosure of Interest: None declared

OP079 PREDICTIVE VALUE OF FATTY LIVER INDEX FOR NON-ALCOHOLIC FATTY LIVER DISEASE: A POPULATION BASED STUDY

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Introduction: Fatty liver index (FLI) is a simple measure calculated based on body mass index (BMI), waist circumference (WC), and triglyceride (TG) and gamma glutamyl transferase (GGT) levels. The primary aim of this study is to determine the predictive performance of this index in the diagnosis of nonalcoholic fatty liver disease (NAFLD).
Aims & Methods: The data of approximately 5900 subjects, 16 years of age or older, participating in a baseline cohort study was used in the present study. Univariable and multivariable logistic regression analyses were conducted to determine the association between FLI and NAFLD. To determine the predictive performance of FLI in the diagnosis of NAFLD, ROC analysis was performed by which the optimal cutoff points of FLI were also determined based on calculated maximum values of the Youden index.
Results: The prevalence of NAFLD was shown to be 39.5% among men and 43.6% among women in this study. FLI was strongly associated with NAFLD, so that a one unit increase in FLI increased the chance of NAFLD 0.059% (OR = 1.059, [95%CI = 1.053-1.063]). Although FLI displayed accurate performance in the diagnosis of NAFLD (AUC = 0.868 [95% CI = 0.858 - 0.879]), its performance showed a lack of precision regarding WC (p-value = 0.2676). The optimal cutoff points of FLI in the diagnosis of NAFLD were 46.9 in men (sensitivity = 0.823, specificity = 0.775, Youden index = 0.598) and 53.7 in women (sensitivity = 0.824, specificity = 0.771, Youden index = 0.595).
Conclusion: FLI was shown to be an acceptable predictive measurement in the diagnosis of NAFLD; however, WC as a simple and more accessible index revealed a similar performance.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 14:00-15:30
NOVEL APPROACHES TO COLORECTAL CANCER - ROOM E6

OP080 DELTA-LIKE 4 INHIBITION HAS A CUMULATIVE EFFECT WITH ANTI-EGFR THERAPY ON APCMIN/+ MOUSE TUMOR INITIATION

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Introduction: Colorectal cancer (CRC) is the third most common malignancy and mutations in the *Adenomatous polyposis coli (Apc)* gene are needed for the initiation of the hereditary CRC familial adenomatous polyposis (FAP) syndrome and most sporadic CRC (Fearnhead, Wilding et al. 2002). One of the strategies to treat CRC is the anti-epidermal growth factor receptor (EGFR) therapy (Vokes and Chu 2006). Notch signalling is another important pathway in CRC development (Qiao and Wong 2009) and it has been demonstrated that Delta like 4 (Dll4)/Notch is a key regulator of tumor angiogenesis (Liu, Fan et al. 2014). There is a cross talk between Notch and EGFR signaling in several types of cancer (Dai, Ma et al. 2009). However this was never demonstrated in CRC.
Aims & Methods: Our aim was to confirm the effect of Dll4 inhibition in the $Apc^{Min/+}$ mouse model of CRC (Yamada and Mori 2007) and to evaluate if the combination of anti-Dll4 and anti-Egfr therapies seemed beneficial in this setting. For that we tested the dominant-negative fusion protein Dll4-Fc alone and in combination with the anti-Egfr tyorsine kinase inhibitor erlotinib hydrochloride in the $Apc^{Min/+}$ model.
Results: We found that in the $Apc^{Min/+}$ model, besides the known role on angiogenesis, Dll4 seems to have an additional effect maintaining the proliferative state and inhibiting the differentiation of tumor-initiating cells. Furthermore Dll4-Fc associated to an anti-Egfr therapy had a cumulative effect inhibiting the tumor initiation and an additional role inhibiting the $Apc^{Min/+}$ tumor volume. Moreover anti-Egfr therapy led to Notch activation, while Dll4-Fc inhibited Egf/Egfr pahtway in the tumors.
Conclusion: Our results indicate that Dll4 inhibition, and mainly the association of anti-Dll4 therapy with anti-Egfr treatment, should be considered to treat CRC at initial stages and as chemoprevention on patients predisposed to this disease such as FAP patients.

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Disclosure of Interest: None declared

OP081 GRP78 HETEROZYGOSITY IN THE INTESTINAL EPITHELIUM PROTECTS AGAINST ADENOMA FORMATION

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Introduction: In the intestinal epithelium, differentiation of healthy stem cells is required for normal organ function. Perturbed stem cell differentiation underlies tumorigenesis. We have previously shown that endoplasmic reticulum (ER) stress, by knockout of the critical chaperone *Grp78*, results in forced differentiation of intestinal epithelial stem cells and may thereby protect against tumorigenesis. ER stress-induced stem cell differentiation occurs through activation of the unfolded protein response (UPR). However, since no stem cells remain upon deletion of *Grp78*, this situation is incompatible with normal organ function. Previously, *Grp78* heterozygosity has been used to induce moderate levels of ER stress. We set out to determine the phenotype of heterozygous deletion of

intestinal epithelial *Grp78*. In addition, this model enables long-term recombination and analysis of intestinal tumorigenesis.

Aims & Methods: For inducible heterozygous deletion of *Grp78*, we crossed $Grp78^{fl/+}$ mice with inducible intestinal epithelium specific *Cre deleter* mice ($Ah1^{Cre}$ or $Villin^{CreERT2}$) to obtain $Grp78^{fl/+}$ animals with heterozygous recombination in intestinal epithelial cells (IEC; $Grp78^{fl/+(IEC)}$). For adenoma studies, we used heterozygous intestinal epithelium specific deletion of tumor suppressor gene *Apc*, which results in development of multiple adenomas throughout the intestine and colon ($Apc^{fl/+(IEC)}$). To monitor recombination efficacy, we crossed *LacZ* reporter alleles into all mice. Upon staining with X-gal, all recombined cells become blue.

Results: We first analyzed the phenotype of $Grp78^{fl/+(IEC)}$ animals and *Grp78* wildtype littermate controls during homeostasis. Counting X-gal stained sections, recombination in all animals was excellent with >95% of crypts recombined. Compared to controls, proliferation in $Grp78^{fl/+(IEC)}$ animals was unaltered, as judged by BrdU incorporation. Additionally, gene-expression analysis by means of quantitative RT-PCR for intestinal epithelial stem cell markers showed no change in *mRNA* levels of stem cell markers *Lgr5*, *Olfm4* or *Ascl2* compared to controls. We found no changes in the expression of a set of UPR target genes showing that heterozygous deletion of *Grp78* has no observable phenotype in a situation of homeostatic epithelial turn over. We next analyzed adenoma numbers in $Grp78^{fl/+}$-$Apc^{fl/+(IEC)}$ animals and $Apc^{fl/+(IEC)}$ controls. After 100 days, $Grp78^{fl/+}$-$Apc^{fl/+(IEC)}$ animals had a marked reduction in adenoma burden compared to $Apc^{fl/+(IEC)}$ mice (1.43 vs. 3.33; $P = 0.0054$).

Conclusion: Heterozygous deletion of *Grp78* from the intestinal epithelium results in unaltered proliferation. Maintenance of stemness in these animals is not affected as judged by RNA expression of stem cell markers. However, adenomagenesis is markedly reduced in compound heterozygous $Grp78^{fl/+}$-$Apc^{fl/+(IEC)}$ animals. These results show that induction of moderate levels of ER stress by perturbation of a single *Grp78* allele results in protection against intestinal tumorigenesis without affecting the healthy stem cell pool.

Disclosure of Interest: None declared

OP082 DELTA-LIKE 4/NOTCH SIGNALING BLOCKADE INHIBITS THE DEVELOPMENT OF IBD-ASSOCIATED COLORECTAL CANCER IN MOUSE MODEL

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Introduction: Colorectal cancer (CRC), one of the most frequent cancers, can develop as a complication of inflammatory bowel diseases (IBD) (Mattar, Lough et al. 2011). The Notch pathway plays a central role in intestinal homeostasis and in CRC development (Miyamoto and Rosenberg 2011). We know that Dll4/Notch signaling is a key regulator of tumor angiogenesis (Liu, Fan et al. 2014). However a putative role for Dll4 in the development of IBD-derived CRC (colitis associated cancer or CAC) has yet to be addressed.

Aims & Methods: Our objective was to analyze Dll4/Notch expression and the effect of Dll4/Notch inhibition in IBD and in CAC. We assessed the expression of Dll4 and other Notch pathway members by immunohistochemistry and the effect of Dll4 inhbition using genetical ($Dll4^{+/-}$) and pharmacological (Dll4-Fc) strategies in the azoxymethane plus dextran sodium sulphate (AOM + DSS) IBD-associated CRC (CAC) mouse model (Neufert, Becker et al. 2007).

Results: Dll4/Notch expression was strongly detected in IBD and in CAC. The inhibition of Dll4 led to a significant reduction in the average number and volume of tumors by several mechanisms. Specifically, Dll4 blockade promoted immature and dysfunctional tumoral angiogenesis and apoptosis and inhibited tumor proliferation. Additionally, it decreased the number of Leucine-rich G-protein coupled Receptor 5 (Lgr5) positive tumor stem cells and promoted Paneth and goblet cell differentiation. Furthermore the observed inhibition of carcinogenesis was associated with reduced colitis and tumor inflammation by decreasing the number of immune cells (macrophages, dendritic cells, neutrophils and helper and cytotoxic T cells) and the expression of important inflammatory mediators, such as *iNos*, *Cox-2*, *Tnf-α*, *Il-6, Il-17a, Ifn-γ* and *Il-4*. Dll4 inhibition also decreased the expression of the CAC promoter *Nfkb2,* upregulated the CAC inhibitor *Tgf-β,* increased the number of regulatory T cells and inhibited the proinflammatory M1 macrophage polarization in the tumors.

Conclusion: Our findings show that additionally to the known Dll4 blockade action on angiogenesis, it also seems to inhibit CAC initiation and progression through its effect on reducing inflammation and promoting stem cell differentiation. Furthermore, we believe that this therapy could be also useful to treat IBD and therefore to prevent CRC initiation.

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Disclosure of Interest: None declared

OP083 MEK5/ERK5 SIGNALLING CONTROLS COLON CANCER CELL SENSITIVITY TO 5-FLUOROURACIL THROUGH A P53 DEPENDENT MECHANISM

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Introduction: We have recently shown that MEK5 and ERK5 expression is increased in human colon adenomas and adenocarcinomas, and that ERK5 expression correlates with tumor stage progression. Moreover, ERK5 has been suggested to play a role in the suppression of p53 function. In turn, p53 is known to be a major determinant of the balance between apoptosis and cell cycle progression following exposure to 5-fluorouracil (5-FU), the most widely used chemotherapeutic agent for colon cancer treatment. Thereby, we hypothesized that MEK5/ERK5 signalling inhibition could sensitize colon cancer cells to 5-FU-induced cytotoxicity through a p53-dependent mechanism.

Aims & Methods: In the present study, we aimed to investigate the role of MEK5/ERK5 signalling in colon cancer cell proliferation and sensitivity to 5-FU. For this purpose, HCT116 and SW620 cell lines expressing a constitutively active (CA) or a dominant negative (DN) form of MEK5 were produced by lentiviral transduction, followed by sorting of stably transduced cells. Alternatively ERK5 activity was blocked in HCT116 p53 wild-type ($p53^{+/+}$) and null ($p53^{-/-}$) isogenic cell lines using the pharmacological inhibitor XMD8-92.

Results: Our results demonstrate that CAMEK5 increased cell proliferation ($p < 0.05$), as well as KRAS expression ($p < 0.01$), in both HCT116 and SW620 cells. In turn, 5FU exposure markedly decreased the levels of endogenous KRAS/MEK5/ERK5 expression and/or activation ($p < 0.05$). In the HCT116 model, DN-MEK5 increased cell death following 5-FU exposure, associated with increased caspase-3/7 activation and apoptosis ($p < 0.05$). Conversely, CA-MEK5 reduced 5-FU-induced cytotoxicity and apoptosis ($p < 0.05$). Moreover, DN-MEK5 increased the expression of p53 ($p < 0.05$) and its transcriptional targets p21 and Puma ($p < 0.01$). Interestingly, ERK5 inhibition by XMD8-92 increased the response of HCT116 $p53^{+/+}$ cells to 5-FU ($p < 0.05$), but failed to sensitize HCT116 $p53^{-/-}$ cells to the cytotoxic effects of this chemotherapeutic agent, suggesting a p53-dependent mechanism mediating 5-FU sensitization following ERK5 inhibition. Finally, ERK5 inhibition by XMD8-92 increased the antitumoral effects of 5FU in a HCT116 subcutaneous xenograft model ($p < 0.05$).

Conclusion: Overall, our results indicate that MEK5/ERK5 pathway overactivation may contribute to CC aggressiveness and chemoresistance, suggesting ERK5-targeted inhibition via siRNA, miRNA or small-molecule inhibitors may provide a promising therapeutic approach for CC treatment.

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Disclosure of Interest: None declared

OP084 SUCCESSFUL SELECTIVE ERADICATION OF COLORECTAL CANCER CELLS BY ADENOVIRUS-BASED DELIVERY OF TOXINS

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Introduction: *K-Ras* gene mutation is an early event in the development of colorectal cancer (CRC) and occurs in ~50% of CRC cases. We propose a strategy that exploits the Ras hyperactive pathway, rather than inhibiting it as was tried and failed many times. We have previously reported that recombinant adenovirus, carrying a pro-apoptotic gene under the regulation of Ras-responsive elements (Ets/AP1), suppressed the growth of cancer cells displaying hyperactive K-Ras (*Biomed Pharm,* 2005, *Cancer Gene Ther,* 2012, *Exp Cell Res,* 2012). TA systems are evolutionarily successful entities that are prevalent in lower organisms and play important roles in a diverse range of cellular activities

Aims & Methods

Aim: To establish a tight control and improved ras responsive element based on the bacterial MazEF system.

Methods: Efficient vectors for cancer-directed gene delivery were constructed and cloned into a "first generation" ΔE1/ΔE3 human type-5 adenoviral-vector. Virus particles were produced, their titer was calculated by the End-Point Dilution Assay (EPDA) and their potency was tested. Cell death was measured qualitatively by using the fluorescent microscopy and colony formation assay, and was quantified by MTT. FACS analysis using annexin V and RedDot2 dyes was performed for measuring apoptosis and dead cells, respectively. *In vivo* tumor formation was measured in xenograft model. Ad-Py4-SV40-MazEF and

Ad-ΔPY4-CMV-MazEF viruses (1×10^9pfu) or PBS were administrated intraperitoneal twice with a 3-day interval between injections.
Results: Adenovirus therapy induced massive cell death, in a dose-dependent manner; 73% with a titer of 10 MOI in cells with activated K-Ras as compared to 22% in tumor cells having the WT K-Ras. The cytotoxic effect was confirmed qualitatively by colony formation assay. In the absence of K-ras-responsive DNA element increase expression of MazE, the anti-toxin, protected normal cells from any possible internal or external leakage of the system and confirmed the selectivity, specificity and safety of the targeting system. FACS analysis confirmed massive cell death, 55% apoptosis and 82% dead cells, following infection with the full toxin-antitoxin encoding viruses. Control viruses lacking the K-ras responsive element a modest toxicity was seen (18% and 10%, respectively). Impressive tumor shrinkage was demonstrated *in vivo* following treatment with Ad-Py4-SV40-MazEF-encoding adenovirus (61%) without any toxic or side effects. Ad-ΔPY4-SV40-MazEF treated mice (control group) tumor volume was reduced only by 27% ($P < 0.05$). No growth inhibition was seen following injection of PBS.
Conclusion: A proof-of-concept for a novel cancer gene therapy by exploiting aberrant K-Ras hyperactive pathway was successfully demonstrated. The lack of toxicity holds promise for effective and safe therapy of human cancers carrying K-Ras mutations.
Disclosure of Interest: None declared

OP085 CONTRIBUTION OF MIRNA-143 AND MIRNA-145 TO CETUXIMAB-MEDIATED CELLULAR CYTOTOXICITY IN COLON CANCER CELLS

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Introduction: Only 10-20% patients with metastatic colorectal cancer benefit from cetuximab treatment. miRNAs, regulators of gene expression, have been associated with differential chemosensitivity in numerous cancer types. miR-143 and miR-145 are reported as downregulated in colon cancer, and their forced expression promotes apoptosis and suppresses tumorigenesis. In this context, we hypothesise that miR-143 and miR-145 may play a role in modulating cell sensitivity to cetuximab-induced apoptosis.
Aims & Methods: We aimed to evaluate the effect of miRNA-143 and miRNA-145 overexpression in the sensitivity of colon cancer cells to cetuximab-mediated cellular cytotoxicity, and its role in cetuximab-induced apoptosis. We produced miR-143, miR-145 and empty vector control overexpressing cell lines in KRAS mutant HCT116 cells, and evaluated viability and proliferation of cells exposed to cetuximab. Further, cetuximab-mediated cellular cytotoxicity was evaluated using the xCELLigence system and LDH assays, in cells exposed to cetuximab, and/or peripheral blood mononuclear cells (PBMCs) isolated from human healthy donors as effector cells. Apoptosis was detected by Guava Nexin flow cytometry assay, evaluation of nuclear morphology following Hoechst staining, and by caspase-3/7 activity.
Results: Our results show that miR-143 and miR-145 overexpression sensitized HCT116 colon cancer cells to cetuximab, resulting in 40% reduction of cetuximab IC_{50}, compared to control ($p < 0.01$), and also reduced cell proliferation and migration ($p < 0.05$). Overexpression of miR-143 and miR-145 triggered cetuximab-mediated cellular cytotoxicity ($p < 0.01$) by increasing apoptosis, displaying increased nuclear fragmentation, caspase-3/7 activation and PARP cleavage ($p < 0.01$). Following rituximab (anti-CD-20 antibody) and PBMCs treatment, no antibody dependent cellular cytotoxicity was seen in HCT116-derived cells ($p < 0.01$). In addition, overexpression of miR-143 negatively regulated Bcl-2 protein, which was further reduced upon treatment with cetuximab and PBMCs in cells overexpressing miR-143 and miR-145 ($p < 0.01$). Further, Bcl-2 silencing reduced HCT116 cell viability with a concomitant increase in cell death and cetuximab-mediated cellular cytotoxicity, compared to control siRNA ($p < 0.05$). Moreover, inhibition of granzyme B, a serine protease involved in effector cell-mediated granule secretory pathway, abrogated cetuximab-mediated cellular cytotoxicity, reducing caspase-3/7 activity in HCT116-derived cells ($p < 0.01$). In turn, caspase inhibition reduced the cytotoxic effect of PBMCs and cetuximab in HCT116 cells overexpressing miR-143 and miR-145 ($p < 0.01$).
Conclusion: Collectively, restoration of miR-143 and miR-145 could sensitize cancer cells to cetuximab by stimulating cells for apoptosis induced by cetuximab-mediated cellular cytotoxicity.
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Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 14:00–15:30
OBESITY: POTENTIAL SOLUTIONS – ROOM B3

OP086 IMPACT OF A 2-WEEK VERY LOW CALORIE DIET ON FATTY ACID SENSING AND TRANSPORT, INCRETIN HORMONES AND LIPID PROFILE IN MORBIDLY OBESE HUMANS

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Introduction: Human obesity is associated with increased expression of the fatty acid (FA) transporter CD36 in the small intestine but reduced expression of the G-protein coupled FA receptor GPR119 (Little et al. *AJP* 2014). We previously showed that a two-week very low-calorie diet (VLCD) reduced expression of small intestinal sweet taste receptors and glucose transporters in the morbidly obese (Nguyen et al. *EUGW* 2014, abstract).
Aims & Methods: This study examined the effects of VLCD on small intestinal FA sensors and CD36, as well as incretin hormones, lipid profile and body weight in the morbidly obese. 10 non-diabetic, morbidly obese subjects (2M:8F; 45 ± 3yrs, BMI: 46 ± 3kg/m^2) were studied before and after a 2 week VLCD (750kcal/day). On each occasion, endoscopic duodenal biopsies were collected at baseline to assess relative expression of CD36, free FA receptors (FFAR) 1, 2, 3 and 4 transcripts by QT-PCR. Blood glucose and plasma concentrations of glucose-dependent insulinotropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1), and insulin were also measured over 270 mins following an intraduodenal (ID) glucose infusion (30 g over 30 min). Insulin resistance was assessed by HOMA-IR score.
Results: Expression of CD36 ($-22 \pm 7\%$; $P = 0.03$), body weight (-5.6 ± 0.5kg, $P < 0.001$), plasma low density lipoprotein (LDL: -4.8 ± 2.1 μM; $P = 0.001$) and triglycerides (-36.3 ± 11.8μM; $P = 0.10$), as well as ID glucose-stimulated insulin (-4.6 ± 0.4; $P = 0.03$) and GIP (-4.6 ± 0.4; $P = 0.03$) were lower after 2 weeks VLCD, but plasma high density lipoprotein (HDL: $+45.2 \pm 8.5$μM; $P = 0.02$) was increased. There were no differences in the expression of FFAR 1, 2, 3, and 4, or ID glucose-stimulated plasma GLP-1 concentration after VLCD. The reduction in CD36 expression correlated with the reduction in plasma insulin ($r = 0.61$; $P = 0.04$) and HOMIR score ($r = 0.57$, $P = 0.05$), whilst the changes with plasma GIP correlated positively with the changes in body weight ($r = 0.72$; $P = 0.01$), plasma LDL ($r = 0.63$; $P = 0.03$) and inversely with HDL ($r = -0.67$; $P = 0.02$).
Conclusion: This study is the first to show that dietary intake can alter transcriptional control of the small intestinal FA transporter CD36 in morbidly obese subjects. Reduced CD36 expression after VLCD was linked to improved insulin resistance, while the reduction in plasma GIP may be important in mediating the improvement in lipid profile and body weight.
Disclosure of Interest: None declared

OP087 A RANDOMIZED CONTROLLED MULTICENTER STUDY OF AN INCISIONLESS OPERATING PLATFORM FOR PRIMARY OBESITY (POSE) VS. DIET-EXERCISE ALONE: THE MILEPOST STUDY

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Introduction: ***Pose***™ is a minimally invasive procedure used to treat Class I and II obesity. During the procedure, an endoscopist or bariatric surgeon per-orally places full-thickness plications in the gastric fundus and distal body to modify gastric capacity and function. The effect of these full thickness plications is believed to reduce fundal accommodation, accelerate the passage of food from fundus to antrum, and alter antral motility, thus slowing total gastric emptying. By so doing, the patient experiences a feeling of fullness sooner and may stay full longer. The purpose of this study was to compare safety, satiety, and weight loss outcomes of subjects undergoing ***Pose*** plus diet and exercise to those following diet and exercise alone.
Aims & Methods: A prospective, multi site, open label, randomized controlled trial was conducted in 3 EU countries. Following Ethics approval, 44 subjects (mean age 38) were enrolled and randomized with baseline BMIs between 30 to 40 in a 3:1 (treatment: control) ratio. The treatment group received ***Pose*** with diet and exercise guidance. The control group received diet and exercise guidance only. Following the procedure, diet was advanced to full solids over 4-6 weeks to allow time for suture plication healing. The control group was instructed to follow the same diet progression up through 6 weeks post randomization. After 6 weeks, all subjects were counseled to follow a diet that provides a specified maximum number of calories (1500-1800) with a targeted amount of protein and minimum quantity of liquids throughout the duration of the study. Both groups were followed at regular intervals (1 week post-procedure or randomization and at 1, 2, 3, 6, 9, and 12 months. Primary outcome measures were: change in mean % total body weight loss (TBWL) (6 and 12 months post randomization) and changes in liquid gastric capacity from baseline at 2, 6, and 12 month time points. To evaluate changes in capacity, a validated satiety test was employed to measure the volume of nutritional drink ingested by the subject and time to reach satiation. At the 12 month time point the control subjects can choose active treatment if they have remained in the study and complied with the follow-up visit schedule.
Results: Groups were comparable (BMI 36.2 treatment vs 37.1 control). There was a significant reduction in mean %TBWL in treatment 12.5% ($n = 31$) versus control 4.6% ($n = 9$) at 6 months ($p < .003$). Gastric capacity change is statistically significant for the treatment group between baseline and 6 months ($p < .001$) but not for the control group ($p = .103$). There were no serious adverse events related to device or procedure.
Conclusion: ***Pose*** provides a safe and superior weight loss solution over diet and exercise alone. The significant reduction in gastric capacity tolerated at 6 months in the treatment group provides ongoing evidence to support how ***Pose*** can affect satiety through durably impacting gastric anatomy and function.
Disclosure of Interest: R. Turro Financial support for research: USGI Medical, J. W. Greve Financial support for research: USGI Medical, K. Miller Financial support for research: USGI Medical

OP088 GASTRIC MUCOSAL DEVITALIZATION PROMOTES WEIGHT LOSS AND IMPROVES METABOLIC PROFILE: A POTENTIAL ENDOSCOPIC OBESITY THERAPY

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Introduction: The gastric mucosa is increasingly recognized as an important regulator of hunger and food intake. This is evidenced by studies demonstrating that the effects of vertical sleeve gastrectomy (VSG) are independent of gastric restriction and weight loss. Therefore, could a method of selectively ablating the gastric mucosa be a potential metabolic therapy?

Aims & Methods

Aims: To investigate whether gastric mucosal devitalization can affect weight, lipid metabolism and glucose homeostasis in a diet induced rat model of obesity.

Methods: Four week old male Sprague-Dawley rats received a high fat diet (HFD) for 11 weeks to induce a previously validated obesity phenotype. Rats were randomized into 3 groups: APC, VSG and sham. A rat model of gastric mucosal devitalization was developed by opening and mobilizing the stomach and using argon plasma coagulation (APC) to ablate 80% of the gastric mucosa. VSG was accomplished by performing a J-shaped resection of 80% of the stomach. Sham rats received a laparotomy and mobilization of the stomach. HFD was resumed at day 2 ad libitum for another 54 days.

Results: APC rats had a significant reduction in body weight as well as visceral and subcutaneous adiposity compared with sham rats. Furthermore, APC rats had a significant reduction in triglycerides and total cholesterol (Table 1). Total free fatty acid levels were significantly reduced in APC compared with sham rats. Fasting glucose, fasting insulin and insulin resistance (HOMA-IR) were significantly reduced in APC compared with sham rats (Table 1). We found that compared to sham, APC rats had a significant lowering of daily food intake. Energy expenditure (assessed by body temperature measurement) was similar between the APC and sham rats. The aforementioned findings were also seen when VSG was compared with sham rats (Table 1). Therefore, these results indicate that a therapy selectively targeting the gastric mucosa can reduce weight, decrease food intake, improve lipid metabolism and improve glucose homeostasis in the absence of gastric restriction.

8 weeks post op	Sham N = 20	APC N = 20	VSG N = 20	P
Body weight [g]	646 ± 32	509 ± 56 *	571 ± 29 *	0.023
BMI [g/cm2]	0.81 ± 0.02	0.72 ± 0.05 *	0.76 ± 0.02 *	0.036
Fat mass visceral [g]	25.5 ± 8.8	9.9 ± 5.4 *	12.8 ± 6.8 *	ns
Fat mass subcutaneous [g]	16.1 ± 2.2	8.9 ± 3.94 *	12.3 ± 2.0 *	ns
Triglyceride [mmol/L]	1.67 ± 0.99	0.71 ± 0.25 *	0.86 ± 0.52 *	ns
Total Cholesterol [mmol/L]	3.82 ± 1.29	2.24 ± 0.38 *	2.11 ± 0.4 *	ns
LDL Cholesterol [mmol/L]	1.15 ± 0.82	0.95 ± 0.31	1.02 ± 0.38	ns
Total Free Fatty Acids [mmol/L]	1.03 ± 0.23	0.68 ± 0.10 *	0.81 ± 0.11 *	0.047
Food Intake [g/d]	22.7 ± 0.41	18.6 ± 0.33 *	20.3 ± 1.95 *	0.015
Fasting glucose [mmol/L]	7.4 ± 0.29	6.8 ± 0.16 *	6.8 ± 0.3 *	ns
Fasting Insulin [ng/mL]	1.93 ± 0.66	0.76 ± 0.48 *	0.67 ± 0.24 *	ns
HOMA-IR	2.9 ± 1.0	0.8 ± 0.4 *	0.7 ± 0.3 *	ns

Conclusion: Gastric mucosal devitalization using APC results in a significant reduction in weight and improvement in metabolic profile. We propose that a minimally invasive procedure, such as endoscopic gastric mucosal devitalization, be investigated as a potential new therapy for obesity.

Disclosure of Interest: V. Kumbhari: None declared, M. Heinrich: None declared, N. Schlichting: None declared, S. Lehmann: None declared, H. Till: None declared, M. Khashab Financial support for research: Cook Medical, Consultancy: Boston Scientific, Olympus America, Xlumena, A. Kalloo Consultancy: Apollo Endosurgery, Shareholder: Apollo Endosurgery, A. Oberbach: None declared

OP089 INTRAGASTRIC BALLOON: A BRAZILIAN MULTICENTRIC STUDY OF 3545 CASES

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Introduction: The intragastric balloon has been used for more than 10 years in Brazil as an endoscopic method for assisting weight loss, and alongside multidisciplinary team support, the results have been satisfactory.

Aims & Methods: To assess the efficacy and complications of the weight loss with IGB in patients seen at the 5 private centers. A total of 3545 patients with IGB implanted from 2009 to 2014 were analyzed from a prospective fed databank. A liquid filled IGB with a volume in-between 620 to 700 ml was used. Initial BMI started at 27 kg/m2 (as approved by Brazilian health authorities) and were followed up by a multidisciplinary team during implant. IGB maximum period implant was 08 months. Statistical analysiswas performed according to sex and degree of excess weight (overweight and grade I, II and III). Data were analyzed using Student t-test, and andTukey post-test. The level of significance was set at $p < 0.05$.

Results: 205 patients (5.78%) were excluded from the analysis: 110 (3.1%) due to early removal, 39 (1.1%) due fail on weight loss or weight gain, 56 (2.2%) due to incomplete data. There were also spontaneous hyperinflation on 0.34% (n = 12) and balloon spontaneous deflation or leakage in 0.62% (n = 22). Incidence of complications not leading to removal were 5.95% Complications other happened as fungal contamination in in 4.54% (n = 161); WernickKorsakoff syndrome 0.05% (n = 2) and pregnancy during implant period on 0.39% (n = 14). The incidence of complications with IGB removal was 0.028% (n = 1): gastric perforation and upper digestive bleeding. On the 3340 remaining patients, 2271 (68%) were women and 1069 (32%) were men. Mean age was 35.72 years. The patients showed a significant weight loss, with a significantly lower final BMI (28.58 ± 7.14 kg/m2; range: 18.69-37) than the initial BMI (34.83 ± 5.13 kg/m2; range: 27-76.12) Percent EWL was higher in the overweight group (142.69%EWL), followed by obesities grades I (78.72%), II (61.51%) and III (47.13%) sequentially.

Conclusion: The intragastric balloon has been established as an valid endoscopic therapeutic option for weight loss, especially in patients with overweight and obesity grades I and II.

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Disclosure of Interest: None declared

OP090 THE FIRST PROCEDURELESS GASTRIC BALLOON: A PROSPECTIVE STUDY EVALUATING SAFETY, WEIGHT LOSS, METABOLIC PARAMETERS, AND QUALITY OF LIFE

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Introduction: Traditional gastric balloons for weight loss require endoscopy for placement and removal. Elipse™ (Allurion Technologies, Wellesley, MA USA) is the first procedureless gastric balloon. The balloon is swallowed, resides in the stomach for 3 months, and is then excreted.

Aims & Methods: The objectives of this study were to assess the safety of Elipse™ and to measure its effects on weight loss, metabolic parameters, and quality of life in up to 50 patients. We report the complete results of the first 8 patients treated at the time of abstract submission.

Each patient swallowed one Elipse™ device which was filled with 550mL of filling fluid through a thin delivery catheter that was then removed. Each device was designed to remain in the stomach for 3 months and then reproducibly open and pass during the 4th month. Weight was measured every 2 weeks, and metabolic parameters were assessed at baseline and at trial exit. The Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire was administered at baseline and trial exit to measure the effects of weight loss on Physical Function (PF), Self-Esteem (SE), Sexual Life (SL), Public Distress (PD), Work (W), and Overall (O).

Results: Eight patients were enrolled with a mean BMI of 34.3 kg/m^2. All 8 patients successfully swallowed the Elipse™ device. As expected with balloon therapy, all patients experienced nausea and vomiting during the first 48 hours. There were no other adverse events. At 3 months, weight loss was statistically significant. The mean percent total body weight loss was 6% (range: 2.4% - 9.7%, $p < 0.01$) and mean percent excess weight loss was 25.4% (range: 6.5% - 47.3%, $p < 0.01$). All 8 balloons were uneventfully excreted in the stool. Mean waist circumference and hemoglobin A1c (HgbA1c) were reduced by 6cm

($p < 0.01$) and -0.15% ($p < 0.05$), respectively. Improvements were also seen in triglycerides, HDL, LDL, ALT, and AST. At trial exit, IWQOL-Lite mean scores improved across all domains: +10.5, +14.4, +1.9, +9.6, +6.9, and +9.1 for PF, SE, SL, PD, W, and O, respectively. An improvement of greater than 7.7 in any domain is considered statistically significant.
Conclusion: This study demonstrates clinically significant weight loss with Elipse™, the first procedureless gastric balloon. The weight loss was similar to that seen in prior studies of endoscopically placed balloons. There were no serious adverse events. In addition, Elipse™ therapy led to a significant improvement in waist circumference, HgbA1c, and overall quality of life.
Disclosure of Interest: E. Machytka Financial support for research: Allurion Technologies, R. Chuttani Shareholder: Allurion Technologies, M. Bojkova: None declared, T. Kupka: None declared, M. Buzga: None declared, K. Stecco Consultancy: Allurion Technologies, S. Levy Shareholder: Allurion Technologies, S. Gaur Shareholder: Allurion Technologies

OP091 OPTIMAL TIMING FOR ENDOBARRIER RE-IMPLANTATION: AN EXPLORATORY STUDY

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Introduction: EndoBarrier (EB) therapy involves the endoscopic placement of a removable, impermeable liner that anchors in the duodenum and bypasses the first two feet of the upper bowel, replicating features of gastric bypass. Clinical data has demonstrated weight loss and improvements in glucose control after 12 months of EB therapy in obese subjects with or without type 2 diabetes mellitus. The feasibility of repeat EB treatment is often questioned.
Aims & Methods: This study aimed to determine the feasibility of a potential EB re-implant with evaluation of optimal timing for re-implantation. Subjects were eligible ($n = 21$) for re-implant if they completed 12 months of initial EB treatment. Upper-endoscopy was performed at explant and prior to re-implant to evaluate the feasibility of re-implantation. Lanza scale was used to grade the mucosal injury observed by upper endoscopy.
Results: 19 subjects (mean age 38.5 yrs, mean BMI 37.2 kg/m^2, mean body weight 93.4 kg, 73.7% non-diabetic) underwent endoscopic evaluation after the initial EB was explanted. All subjects had duodenal pseudopolyps; 6/19 subjects had a Lanza score of 2 or less, and one subject had a score of 3 (6 to 10 erosions).
Of the 13 subjects suitable for re-implant at 8 months, 12/13 subjects had pseudopolyps and 9/13 subjects had no visible mucosal injury. 11/13 subjects were successfully re-implanted. At 12 months, among the 8 subjects remaining to be re-implanted, all had pseudopolyps and all but one subject (score of 4) had no visible mucosal injury. These 8 subjects were successfully re-implanted.
With a 12 month time lapse between the initial explant and re-implant, all subjects (8/8) completed sequential EB therapy with no early device removal. With an 8 month time lapse between the initial explant and re-implant, 45% (5/11) of subjects had early device removal. The early device removal in 5 subjects was due to abdominal pain (2), device migration (2), and GI bleed (1). Four of five subjects required hospitalization.
Regardless of the wait time between initial and second implant (8 months vs 12 months), subjects benefited from EB re-implantation by renewed weight loss (mean weight loss 6.5 ± 1.1 kg, mean percent excess body weight loss 30.1 $\pm 23.1\%$). Furthermore, the implant procedure time trended to be less for subjects who waited 12 months as compared to 8 months (20.4 ± 10.6 mins vs. 29.2 ± 14.3 mins, respectively, $p = 0.06$).
Overall, adverse events (AEs) were classified as either mild (84%) or moderate (16%), with the majority of AEs related to GI symptoms.
Conclusion: This exploratory study suggests sequential EB placement is feasible with careful interim assessment. The optimal timing for re-implantation after the initial EB treatment appears to be approximately 12 months, but these findings warrant additional clinical evaluation.
Disclosure of Interest: N. Quezada: None declared, F. Pimentel Financial support for research: GI Dynamics, Inc., E. Chiquette Conflict with: Employee, P. Wenten Conflict with: Consultant, K. Malomo Conflict with: Employee, A. Escalona Financial support for research: GI Dynamics, Inc., D. Maggs Conflict with: Employee

MONDAY, OCTOBER 26, 2015 15:45–17:15
LONG-TERM MEDICAL MANAGEMENT OF IBD – ROOM A2

OP092 EVOLUTION AFTER ANTI-TNF DRUG DISCONTINUATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD): A MULTICENTER LONG-TERM FOLLOW-UP STUDY

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Aims & Methods: 1) to assess the risk of relapse after anti-TNF discontinuation; 2) to identify the factors associated with relapse; 3) to calculate the response rate to re-treatment with the same anti-TNF after relapsing, and 4) to evaluate the safety of re-treatment with these drugs.
Retrospective, observational, multicenter study. Crohn's disease (CD) or ulcerative colitis patients who had been treated with anti-TNFs and in whom these drugs had been withdrawn after having achieved clinical remission were included
Results: 1,055 patients were included (50% women, mean age 42 years, 69% CD). The cumulative incidence of relapse was 44% (95%CI = 41-46%): 15% at 6 months, 24% at 1 year, 38% at 2, 46% at 3, and 56% at 5 years after anti-TNF withdrawal. The incidence rate of relapse was 18% per patient-year (95%CI = 17-20%). In the multivariate analysis, the variables associated with a higher risk of relapse were younger age at anti-TNF discontinuation (HR = 0.9, 95%CI = 0.97-0.99), treatment with adalimumab (ADA) (vs. infliximab) (HR = 1.3, 95%CI = 1.02-1.6), and the elective discontinuation of anti-TNFs (HR = 1.7, 95%CI = 1.1-2.6) or the discontinuation of anti-TNFs due to adverse events (HR = 1.9, 95%CI = 1.2-2.9) (vs. top-down strategy). The treatment with IMMs (vs. no treatment) after anti-TNF discontinuation was associated with lower risk of relapse (HR = 0.7, 95%CI = 0.6-0.9). 69% of patients who relapsed were re-treated with the same anti-TNF; 75% of them achieved remission at the end of follow-up; 11% presented adverse events, all mild.
Conclusion: The incidence rate of relapse after anti-TNF drug discontinuation was 18% per patient-year. The predictive factors for relapse were the lack of IMM maintenance treatment after anti-TNF is stopped, younger age, treatment with ADA, and the elective discontinuation of anti-TNFs or the discontinuation of anti-TNFs due to adverse events. Re-treatment of relapse with the same anti-TNF was effective and safe.
Disclosure of Interest: None declared

OP093 LONG-TERM OUTCOME AFTER INFLIXIMAB WITHDRAWAL FOR SUSTAINED REMISSION IN CROHN'S DISEASE

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Introduction: The long-term outcome of Crohn's disease (CD) patients after infliximab (IFX) withdrawal is not well established. The aim of this study was to describe the long-term outcome of the patients previously included in the STORI trial studying infliximab cessetion in patients with sustained corticosteroid-free remission on IFX and antimetabolites.
Aims & Methods: Clinical notes of the patients included in STORI were retrospectively reviewed. The following clinically significant events were recorded: need for surgery, active perianal lesions, treatment modification including need for corticostereroids, infliximab, adalimumab or other biologic.
Results: 17/20 GETAID centres involved in the STORI trial participated in this retrospective study, representing 94/115 STORI patients. Long-term data were available in 85/94 (9 patients lost to follow up, including 5 early relapsers in STORI). Median follow-up from STORI inclusion was 79 months. A medical treatment was restarted in 64 (85%) patients after a median time of 29 months (IFX in 54, Adalimumab in 9, steroids in 1); eleven (13%) patients underwent surgical resection after a median of 59 months (before resuming any medical treatment in 6 patients); nine (11%) developped perianal lesions after a median of 55 months (after resuming anti-TNF in 6 cases). At maximal follow up, 13 hadn't experienced any significant event and 32 were still under IFX or Ada without surgical resection.
Conclusion: The vast majority of patients stopping IFX for sustained remission under antimetabolites + IFX had to restart a treatment over the long term. Almost one quarter develop tissue damage (surgical resection and perianal fistula). A controlled trial is necessary to properly assess benefits and risks of this strategy.

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OP094 OPTIMIZATION OF THIOPURINE THERAPY IMPROVES REMISSION RATES AFTER CESSATION OF ANTI-TNFA IN CROHN'S DISEASE

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Introduction: Biologics are effective in treating Crohn's disease but are expensive. Also, many patients develop immune responses or experience effect loss. Studies have shown remission rates at 12-months of 51-67%[1,2] when halting biologic treatment in patients in clinical remission.
Thiopurines (azathioprine (AZA) or 6-mercaptopurine (6-MP) are used to maintain remission but lack of efficacy and intolerance are common problems. Optimizing thiopurine therapy with measurements of metabolites and initiation of combination therapy with allopurinol (ALLO) improves efficacy and decreases intolerance.
In this study on patients with Crohn's disease in clinical remission, we optimized thiopurine treatment prior to cessation of anti-TNFα (infliximab (IFX)/adalimumab (ADA)), and evaluated remission rates at 6- and 12-months follow-up.
Aims & Methods: Physicians were instructed how to optimize thiopurine treatment using measurements of metabolite levels and combination therapy. When the patients had reached a level of 6-thioguaninenucleotide of 150-200 pmol/$8x10^8$ and were in clinical remission (Harvey Bradshaw Index (HBI) < 5), biologics were discontinued. During follow-up, relapses, defined as the need to restart of biologics, were recorded. Data on remission or relapse was obtained six and twelve months after stopping biologic therapy.
Results: 32 patients with luminal Crohn's disease had their thiopurine therapy optimized, were in clinical remission, and discontinued biologics. At inclusion, the median (IQR) age was 34 years (26-41), median disease duration was 7.2 years (3.8-12.5), median durations of biological therapy before discontinuation were 1.7 years (1.2-3.2 (IFX)) and 1.5 years (1.3-4.8 (ADA)). We found a median 6-TGN of 205 pmol/$8x10^8$ (178-261), MeMP 1124 pmol/$8x10^8$ (171-1156), and fecal calprotectin 100 mg/kg (30-158). 1(3%) patient received 6-MP, 3 (9%) 6-MP/ALLO, 16 (50%) AZA, and 12 (38%) AZA/ALLO.
97.0% (31/32) were in clinical remission six months after stopping biologic treatment, and 90.0% (26/29) patients were in remission after twelve months. Three patients had not yet completed one year follow-up.
We did not find any predictive risk factors for relapse (disease duration, length of biological therapy, smoking, fecal calprotectin, leucocytes, C-Reactive Protein or hemoglobin).
Conclusion: In this study, optimizing thiopurine treatment prior to stopping biologic treatment leads to at least 30% higher remission rates than shown in other studies with non-optimized patients.[1,2] No predictive factors for relapse were identified. Optimization has previously been shown to decrease side effects and intolerance. It is possible that optimizing thiopurine therapy in patients with Crohn's disease might alter the disease prognosis and decrease the need of biological therapy. Prospective studies will further clarify the future position of thiopurine optimization in IBD therapy.

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Disclosure of Interest: None declared

OP095 ADJUNCTIVE ALLOPURINOL IN THIOPURINE NON-RESPONDERS OPTIMISES 6TGN AND IMPROVES CLINICAL OUTCOMES IN IBD: THE MULTICENTRE, PROSPECTIVE, DOUBLE BLIND, DOSE-RANGING AAA STUDY

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Introduction: 15% of IBD patients who do not respond to azathioprine (AZA) or mercaptopurine (MP) are shunters. They preferentially metabolise MP to 6-methylmercaptopurine (6MMP) instead of the efficacious 6-thioguanine nucleotides (6TGN).
Aims & Methods: This multicentre, prospective, double-blind, dose-ranging, randomised trial aims to show that low-dose allopurinol–thiopurine achieves steroid-free clinical remission and minimises toxicity; and to compare outcomes of allopurinol 50 vs 100mg. Inclusion criteria were: clinically active or steroid-dependent IBD; thiopurine shunters with 6TGN <260pmol/$8x10^8$ RBCs and 6MMP:6TGN ratio ≥ 20; total leucocyte count $\geq 3.5x10^9$/L. Patients were randomised to a blinded dose of 50 or 100mg allopurinol and 25% of their screening thiopurine dose. Thiopurine doses were then optimised, aiming for 6TGN >260. The primary endpoint was steroid-free clinical remission after 24 weeks (SFR24) using the Harvey Bradshaw Index and the Simple Clinical Colitis Activity Index. An intention-to-treat analysis was performed.
Results: 73 patients were enrolled: 46 had Crohn's disease and 27 ulcerative colitis. Mean doses for AZA reduced from 164mg at screening to 67mg at week 24 and 6MP from 88mg to 45mg (both $p<.001$). Significantly greater thiopurine dose reductions were seen in the 100mg allopurinol arm than the 50mg arm (63-65% vs 35-53% reduction, $p=0.006$ and 0.008). 39 patients [53% (95% CI 42–65)] achieved SFR24 with no difference in rates of SFR24 between 50 and 100mg arms ($p=.913$). 6TGN increased from 177 ± 14 to 402 ± 16 ($p<.001$). 6MMP decreased from 9949 ± 485 to 1235 ± 547 ($p<.001$) and 6MMP:6TGN ratio fell from 64 to 4 ($p<0.001$). There was no significant difference in 6TGN between allopurinol arms, however mean 6MMP was significantly higher in the 50mg arm (1987 vs 483, $p=0.023$). Hepatitis decreased with ALT improving from 52 ± 6U/L to 27 ± 6U/L ($p<.001$). 26 of 32 patients (81%) were able to cease steroids ($p=.011$). Total leucocyte count decreased from mean $7.1x10^9$/L to $5.9x10^9$/L ($p<.001$). Only two transient episodes of mild leucopenia occurred in 1 patient, resolving with a reduced thiopurine dose. Significant reductions in faecal calprotectin occurred in steroid dependent CD patients from mean 864ug/g to 122ug/g ($p=.043$). Significant reductions in CRP occurred in UC patients from mean 6.1mg/L to 3.6mg/L ($p=.019$). 15 serious adverse events occurred; 2 (dental abscess and perianal abscess) were possibly related to the drug combination.
Conclusion: Allopurinol-thiopurine combination safely and effectively optimises 6TGN and concurrently reduces 6MMP. Optimisation of thiopurine metabolites improves disease outcomes without additional toxicity. No clinically significant differences were seen between allopurinol groups. It has been prospectively validated as a therapeutic intervention for IBD patients who are shunters.
Disclosure of Interest: None declared

OP096 FIRST EXPERIENCE OF SWITCHING BETWEEN ORIGINATOR AND BIOSIMILAR INFLIXIMAB IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Inflammatory bowel disease incidence in children is on the rise. In relative to more cases biological treatment is needed. Recently, biosimilar infliximab (IFX) was authorized in European Union what may lead to switching patients. First experiences of such switch are described.
Aims & Methods: 32 paediatric patients with diagnosis of Crohn Disease (CD) and 7 of Ulcerative Colitis (UC) from 3 academic hospitals who were switched from originator to biosimilar infliximab (Remsima) were included in the study. Patient characteristics, disease severity (PCDAI for CD; PUCAI for UC), laboratory values (CRP, ESR, platelet count, haemoglobin level) was recorded. Mean, median and range values were calculated. Adverse events were recorded before and after the switch.

Abstract number: OP096

	Originator INF start	At 2nd last originator INF infusion	At last originator INF infusion	At switch (before 1st biosimilar infusion)	Before 2nd biosimilar infusion	Before 5 biosimilar infusion
Week	-	W -16	W -8	W 0	W +8	W +32
No. patients	32	32	32	32	32	18
PCDAI	47,8(52,5;2.5-65)	7,4(3.8;0-32,5)	7(5;0-30)	8,8(5;0-35)	7.2(5;0-30)	7,1(5;0-42,5)
CRP	1,4(0.9;0-6,5)	0.6(0.3;0-2,3)	0.6(0.4;0-3,8)	0.6(0.3;0-3,8)	0.6(0.3;0-2,1)	0.6(0.2;0-2,3)
ESR	28(23;3-80)	14(9;2-63)	15(10;2-59)	14(9;1-63)	14(8;0-75)	10(7; 1-35)
Platelets	389(392; 169-630)	302(305; 112-543)	299(288; 171-635)	304(282; 183-804)	325(315; 175-854)	294(272; 152-493)
Hb	12,3(12.3;10.3-14.4)	13,1(13.3;10.4-16,7)	13,1(12.9;10.3-15.6)	13.1(13.1;10.4-16.4)	13.3(13.3;11.2-16,4)	13(12,3; 9,8-15,8)

Results: Mean age of patients at diagnosis of CD was 11.2y (2.7-15.3), of UC patients was 12.3y (8.5–14.8). Mean time from CD diagnosis to the start of current biological treatment was 1.8y (range:1 week–5y) and from UC 1.7y (median 0.55y, range 0.5-4.8y). Mean number of originator IFX infusions before the switch to biosimilar in CD group was 9.9 (8; 4-29); in UC 5.1 (5;1-12). At originator IFX qualification patients mean PUCAI was 42.9 (median 45, range 10-65). CRP, ESR, platelet count were elevated for 1,5,4 patients, respectively. PUCAI decreased for all patients after first dose: 12.5 (10; 0-35). At switch mean PUCAI was 16.4 (20; 0-30). CRP, ESR, platelet count were elevated for 3,2,2 patients, respectively. Before 2 and 4 dose of Remsima mean PUCAI was 11 (0; 0-40) and 2 (0;0-5), respectively.
For CD patients data before and after switch were presented in the Table as mean(median; range).
There was no infusion reactions observed in CD group after originator of biosimilar INF treatment. In UC group during first biosimilar IFX dose infusion-related reactions (skin erythema) was observed for 2 patients, which was not observed for the originator. Antihistaminic treatment caused resolution of symptoms and the full dose of IFX was delivered. The occurrence of sporadic mild adverse events did not differ before or after switching and was consistent with IFX molecule safety profile.
Conclusion: Switching form originator to biosimilar infliximab in children with CD seems to be safe.
Disclosure of Interest: None declared

OP097 ANTI-REMICADE ANTIBODIES CROSS-REACT WITH THE BIOSIMILARS REMSIMA AND INFLECTRA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Remicade (INN-infliximab, IFX) has proven to be effective in inducing and maintaining remission of Crohn's disease and ulcerative colitis. The link between the serum trough concentration and the clinical outcome has been demonstrated repeatedly and has led to the introduction of therapeutic drug monitoring (TDM) for treatment optimization. In September 2013, the European Medicines Agency issued the marketing authorisation of a biosimilar of Remicade, CT-P13, under trade names Remsima and Inflectra.
Aims & Methods: 1) To evaluate binding of a panel of 55 mouse monoclonal antibodies, generated toward Remicade, to Remsima and Inflectra; 2) to quantify biosimilars in the Ridascreen IFX monitoring assay (R-Biopharm); 3) to compare titers of the antibody response of patients that developed anti-Remicade antibodies toward Remsima and Inflectra.
The reactivity of a panel of monoclonal antibodies, including MA-IFX6B7 and MA-IFX10F9, toward the biosimilars was tested using a sandwich ELISA and mixed model analysis was used to determine dissimilarity between Remicade and the biosimilars. Schuirmann's two one-sided *t*-test (TOST) was used to analyse the similarity between the detection of biosimilars and Remicade in the Ridascreen IFX monitoring assay using four quality control samples. Bridging assays to determine anti-biosimilar antibodies were developed according to the protocol of the bridging ELISA of Remicade using MA-IFX10F9 as calibrator.[1]
Serum of 18 patients previously treated with Remicade was analysed for anti-drug antibodies toward Remicade, Remsima and Inflectra using their respective bridging ELISA.
Results: Using mixed model analysis, no evidence for different reactivity of IFX6B7 and IFX10F9 toward Remsima and Inflectra versus Remicade was found ($p > 0.05$). TOST demonstrated an equally well quantification of the biosimilars and Remicade in the Ridascreen IFX monitoring assay. Quantification of anti-IFX antibodies in serum of patients treated with Remicade revealed highly correlated titers toward the biosimilars as compared to Remicade (Spearman $r = 0.9963$, $p < 0.0001$).
Conclusion: This study describes an assay to perform TDM of the IFX biosimilars. TDM provides a basis for personalised dosing based on predictive models, an approach which is expected to further increase cost efficacy. We have demonstrated that anti-drug antibody titers toward Remicade correlate with titers toward Remsima and Inflectra.

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OP098 UPPER GASTROINTESTINAL BLEEDING SECONDARY TO PEPTIC ULCER DISEASE – CAN WE CONTINUE TO REDUCE ITS INCIDENCE?

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Introduction: In the last decades the incidence of Peptic Ulcer Disease (PUD) progressively decreased in the western world, but it still remains as an important factor of morbidity and mortality. The reduction allowed by the improvement of socio-economic conditions and the decrease in incidence of *Helicobacter pylori* infection, was partially outweighed by the advanced age of patients and the iatrogenic effect of modern medicine.
Aims & Methods: (1) To assess the number of potentially preventable hospitalizations due to upper gastrointestinal bleeding secondary to PUD; (2) identification of the factors that led doctors to prescribe proton pump inhibitors (PPIs) in clinical practice; (3) and the accordance with the current guidelines for gastroprotective therapy.
Retrospective analysis of all patients admitted to our center between 2009 and 2013, with upper gastrointestinal hemorrhage secondary to endoscopically proven PUD. According to the guidelines of the American College of Gastroenterology and the American Heart Association for gastroprotective therapy, patients were divided into low and high-risk groups. Demographic, comorbidities and medication data were recorded. From published studies, we assumed the 50-85% potential effect of PPIs in preventing hemorrhage secondary to PUD.
Results: We identified 348 patients (high-risk:133), with a mean age of 72 years, a male sex preponderance ($n = 249$) and a mean age adjusted Charlson comorbidity index of 5. The percentage of patients doing antiaggregation was 35% (dual antiaggregation: 14%); non-steroidal anti-inflammatory: 24%; anticoagulation: 13% and corticosteroids: 5%; 18% of patients had past history of PUD. PPIs were identified in 14% of patients, however only 26% of the patients in the high-risk group were doing gastroprotection. Although it was not statistically significant ($p = 0.065$), we identified a trend for concomitant gastroprotection prescription if the factor that led the patient to belong to the high-risk bleeding group was an initial prescription from a hospital doctor, instead of one from a general practitioner (21% versus 10%). In 30% of patients, the factor for belonging to the high-risk group was self-medication. Assuming that all high-risk patients should do gastroprotection, it was estimated that about 49-83 admissions could be prevented (14-24% of admitted patients).
When analyzed the factors that led doctors to prescribe gastroprotective therapy, the only variable that was statistically associated and in agreement with the current guidelines was antiagregation plus antiagregation/ anticoagulation ($p = 0.027$; $OR = 2.64$). In univariate analysis, other statistically associations were identified (not in line with current guidelines): age ≥ 65 years, anticoagulation, use of cox-2 inhibitors, aspirin and clopidogrel, but in the multivariate analysis, the only variable associations that prevailed were anticoagulation ($p = 0.001$; $OR = 3.48$) and clopidogrel ($p = 0.000$; $OR = 6.71$).
Conclusion: The high percentage of self-medication and the low obedience to the current guidelines (especially in general practitioners), led that up to 25% of hospital admissions secondary to peptic ulcer hemorrhage could be preventable.
Disclosure of Interest: None declared

OP099 INTERNATIONAL, MULTICENTRE PROSPECTIVE STUDY COMPARING RISK SCORING SYSTEMS FOR PATIENTS PRESENTING WITH UPPER GASTROINTESTINAL BLEEDING

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Introduction: Several risk scoring systems have been developed for the assessment of patients with upper gastrointestinal bleeding (UGIB). However, only few of these have been externally validated in international studies.
Aims & Methods: We compared the ability of five risk scoring systems to predict: 1. Need for hospital-based intervention or mortality, 2. Rebleeding within 7 days, 3. Length of hospital stay (LOS), and 4. 30-day mortality.
We performed a prospective study on consecutive patients presenting with UGIB at six centres in United States, Scotland, England, Denmark, Singapore, and New Zealand over 12 months. Using area under receiver operating characteristics curves (AUROC) we compared the discriminative abilities of the pre-endoscopic scores: Glasgow Blatchford score (GBS), AIMS65, and admission Rockall score (ARS) and the post-endoscopic scores: the full Rockall (FRS) and PNED scores to predict outcome.
Results: 3171 patients were included. Median age was 65 years, and 58% were male; 45% needed hospital-based intervention or died, 5% rebled, median LOS was 3 days, and mortality was 7%. In the prediction of need for intervention, or death, GBS had the highest discriminative ability (AUROC 0.89) when compared to AIMS65 (AUROC 0.70; $p < 0.0001$), PNED (AUROC 0.70;

$P < 0.0001$), FRS (AUROC 0.69; $P < 0.0001$) and ARS (AUROC 0.69; $P < 0.0001$). The PNED was best (AUROC 0.85) at predicting rebleeding, compared with GBS (AUROC 0.71; $P < 0.0001$), FRS (AUROC 0.62; $P < 0.0001$), AIMS65 (AUROC 0.62; $P < 0.0001$), and ARS (AUROC 0.62; $P < 0.0001$). All risk scores had poor discriminative abilities for predicting LOS > 3 days (all AUROCs < 0.70). PNED (AUROC 0.80) and AIMS65 (AUROC 0.79) had better discriminative abilities for mortality than ARS (AUROC 0.76; $P < 0.02$), FRS (AUROC 0.72; $P < 0.03$), and GBS (AUROC 0.70; $p < 0.0001$). All of these findings were consistent across all sites.

Conclusion: This large international study shows that GBS has the best accuracy for predicting need for hospital-based intervention or mortality. PNED and AIMS65 are best at predicting 30-day mortality. Apart from PNED (which includes data on rebleeding) all scores were poor at predicting rebleeding, and no score could accurately predict LOS.

Disclosure of Interest: None declared

OP100 WEEKEND ADMISSION INCREASES MORTALITY OF UPPER GASTROINTESTINAL BLEEDING PATIENS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Upper gastrointestinal bleeding (UGIB) mortality has remained stable in recent years despite advances in endoscopic and pharmacological treatment. The studies identify factors such as severity of the bleeding, advanced age and high comorbidity as predictors of mortality. However, the finding of additional modifiable factors associated with mortality could allow establish measures to reduce mortality in UGIB. The "weekend effect" is defined as an increased mortality rate in patients presenting to hospitals on the weekend.

Aims & Methods: To evaluate if admission weekend increases rebleeding, the need for surgery and mortality in UGIB by performing a systematic review and meta-analysis.The search was conducted in PubMed and ISI Web of Knowledge (until February 2014) to identify studies comparing mortality in patients with UGIB admitted on weekend versus weekday admission. We used a model of fixed and random effects with odds ratio (OR) to determine differences for rebleeding, need for surgery and mortality. Publication bias was assessed using the method of Egger and Macaskill. Heterogeneity between studies was analyzed using the statistical I2, Q and Tau 2. The quality of the publications was evaluated using the STROBE statement criteria.

Results: Seventeen studies including 1,038,106 patients met the inclusion criteria. Compared to patients admitted on weekdays, patients with UGIB admitted on weekends had higher mortality (OR 1.12; 95%CI:1.07-1.18) and higher rates of surgical intervention (OR 1.18; 95%CI:1.11-1.26. However, weekend admission did not significantly increased rebleeding rates: (OR:1.23; 95%CI:0.98-1.53). The subgroup analyses evaluating variceal and non-variceal upper gastrointestinal bleeding separately found that Weekend admission increased mortality (OR:1.14; 95CI%(1.07-1.21)and the need for surgery (OR:1.23; 95%CI:1.07-1.4) but not rebleeding (OR 1.10 (95%CI 0.73 -1.67) in non-variceal upper gastrointestinal bleeding. Regarding variceal upper gastrointestinal only the mortality was significantly elevated (OR1.06; 95%CI:1.00-1.12).

Conclusion: Patients with UGIB admitted on the weekend show worse outcomes in terms of mortality and need for surgery than those admitted on a weekday. As the rebleeding rate is not increased, our study may suggest that poorer management of comorbidities due to the lower level of staffing and the decreased intensity of care provided in hospitals during the weekend may account for this finding.

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Disclosure of Interest: None declared

OP101 TITLE: THE EFFECT OF OFF-HOUR HOSPITAL ADMISSION ON MORTALITY FOR PATIENTS WITH UPPER GASTROINTESTINAL HEMORRHAGE: A SYSTEMIC REVIEW AND META-ANALYSIS

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Introduction: Controversies abound upon the impact of non-office hour admission on clinical outcomes for patients with upper gastrointestinal hemorrhage (UGIH). This study aimed to evaluate the relationship between off-hours admission and clinical outcomes for UGIH.

Aims & Methods: We conducted literature search on Medline, Embase, Scopus, and Cochrane until November 2014. All manuscripts or abstracts that reported the association between hospital admission time and outcomes for patients with UGIH would be identified without restriction to language and study design. We used the Newcastle-Ottawa scale to determine the quality of the included studies. Clinical outcomes included mortality, time to receive endoscopy, length of hospital stay, need for surgery, rebleeding rate, and length of hospital stay were assessed. A randomized effect model was used for the meta-analysis. Heterogeneity was evaluated by calculating I2 statistic and Q test.

Results: We recruited 16 studies with an average of 7.81 points on quality scale into the meta-analysis, including 519,521 cases of UGIH. Patients with UGIH who were admitted during off-hours had a significantly higher mortality (OR 1.08, 95% CI 1.03-1.12). Moreover, those with non-variceal UGI bleeding had significantly increased risk of mortality when admitted during off-hours (OR 1.08, 95%CI 1.03-1.15; OR 1.07, 95%CI 1.02-1.12). However, for studies conducted in hospitals where there was an off-hours endoscopist on-call rota, the mortality rate for patients admitted during off-hours became insignificant (OR 1.10, 95%CI 0.89-1.36). Patients in the off-hour group were less likely to be treated by early endoscopy with 24 hours after admission (OR 0.74, 95% CI 0.63-0.86).

Conclusion: Patients with non-variceal UGI bleeding and admitted during off-hours had significantly higher mortality, while this impact can be offset among hospitals with on-call endoscopist rota.

Disclosure of Interest: None declared

OP102 WHAT ARE THE RISKS OF UPPER GASTROINTESTINAL BLEEDING AMONG PEOPLE OVER THE AGE OF 65 WHILE BEING PRESCRIBED NSAIDS OR ASPIRIN? A POPULATION BASED COHORT STUDY FROM ENGLAND

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Introduction: Limited knowledge exists on the impact of interactions between hazardous prescriptions on the risk of upper gastrointestinal bleeding (UGI).

Aims & Methods: This study aims to precisely determine the population level absolute rates of UGI bleeding associated with NSAID/aspirin use in relation to interactions with other drugs and comorbidities. Our study population consisted of individuals over the age of 65 years registered within primary care data (Clinical Practice Research Datalink – CPRD) linked to secondary care data (Hospital Episode Statistics-HES) between 1998 and 2010. NSAIDs/Aspirin exposure was defined in a time varying manner. The absolute rate (AR) of UGI bleed among those exposed to NSAIDs/aspirin was calculated and compared to those not exposed to NSAIDs/aspirin using a Cox regression model adjusted for PPI use. We then stratified by the presence of comorbidities and any exposure to drugs previously known to be associated with UGI bleed (anticoagulants, clopidogrel, steroids, SSRI and anti-cirrhotic drugs).

Results: Our study population consisted of 376,586 individuals of whom 39% received an NSAID or Aspirin prescription at least once during the study period. Overall there were 8,410 UGI bleeds and the risk of GI bleed associated with NSAIDs/Aspirin exposure was 208 per 10,000 person-years (Table 1; 95% Confidence Interval (CI) 192-226). This corresponded to a 1.5% absolute excess risk and a 3-fold risk relative (95%CI 3.04-3.60) compared to those not exposed to NSAIDs/Aspirin. These estimates remained broadly similar when stratified by comorbidity and receipt of other prescriptions known to increase UGI bleed risk.

Table 1: Absolute rate of GI bleed per 10,000 and hazard ratio by drug use stratified by NSAIDs exposure

Variable	NSAIDs exposed			NSAIDs unexposed			HR (adjusted)*	95% CI		Rate difference
	Rate	95% CI		Rate	95% CI					
Overall rate	208.3	192.2	225.8	55.6	54.6	56.9	3.31	3.04	3.60	152.7
Male	241.0	215.8	269.2	64.9	62.9	67.0	3.26	2.92	3.65	176.1
Female	180.6	160.6	203.1	48.5	47.0	50.1	3.36	2.98	3.80	132.1
No Comorbidity[1]	169.4	150.6	190.5	46.8	45.4	48.2	3.30	2.92	3.73	122.6
At least 1 comorbidity[1]	312.0	254.9	381.9	81.8	77.0	86.9	3.62	2.93	4.46	230.2
≥2 comorbidities[1]	244.2	214.5	278.6	68.5	65.9	71.3	3.20	2.78	3.67	175.7
No prescriptions[2]	170.9	152.9	191.1	46.9	45.6	48.2	3.29	2.93	3.69	124
At least 1 prescription[2]	226.9	194.0	265.3	74.7	71.3	78.3	2.90	2.46	3.41	152.2
≥ 2 prescriptions[2]	265.1	306.2	433.0	115.9	108.8	123.4	2.98	2.48	3.59	149.2

*HR adjusted for age, gender, comorbidity and concurrent PPI use when not stratified by those variables [1]Ulcer, varices, UGI cancer, GI neoplasm, angiodysplasia, Cirrhosis, Gastric/oesophageal/duodenitis, Mallory Weiss Syndrome, H-pylori, Alcohol consumption, Crohn's disease, liver failure, Ascites, Portal hypertension, Encephalopathy, Ascetic complications [2]Anticoagulant, Clopidogrel, Coxib, SSRI, Anti-cirrhotic drugs and oral steroids.

Conclusion: During exposure to NSAIDs/aspirin individuals have a 1.5% per annum excess absolute rate of UGI bleed compared to those unexposed to these drugs, corresponding to an estimated number needed to harm per NSAIDs/Aspirin prescription of 67. The excess risk remains broadly similar when stratified by comorbidities and other drugs previously associated with GI bleed suggesting limited interaction between them.
Disclosure of Interest: None declared

OP103 MAINTENANCE OF ANTITHROMBOTIC THERAPY POST ENDOSCOPY FOR ACUTE UPPER GASTROINTESTINAL BLEEDING IS ASSOCIATED WITH IMPROVED CLINICAL OUTCOMES

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Introduction: Antithrombotic drugs (antiplatelets and anticoagulants) are often stopped following acute upper gastrointestinal bleeding (AUGIB). In the UK, NICE (National Institute of Health and Care Excellence) have recently advocated resuming aspirin after AUGIB,[1] but their position on non-aspirin antithrombotics is less clear.
Aims & Methods: We aimed to assess if maintenance of antithrombotic therapy following AUGIB correlated with improved clinical outcomes. We identified patients on antithrombotic therapy who underwent gastroscopy for suspected AUGIB at University Hospital Birmingham whilst on antithrombotic therapy between May 2013 and November 2014 and performed follow-up until March 2015. Clinical outcomes were measured after endoscopy and discharge, and included cause-specific mortality, thrombotic events, rebleeding, and any adverse event (any of the above). Exclusion criteria included failure of haemostasis, death <24 hours of endoscopy, and end of life care. Patients were stratified according to whether antithrombotics were maintained or discontinued. Data comparisons were performed using Fisher's Exact and *t*-test, with Kaplan-Meier analysis to estimate follow-up outcome. *p*-values (two-tailed) were significant if <0.05.
Results: 132 patients were included for analysis, of which 118 survived until discharge. Antithrombotic use consisted of aspirin monotherapy (43%), oral anticoagulants (27%), dual antiplatelet therapy (DAPT) [16%], thienopyridine monotherapy (10%), and other (4%). Antithrombotic maintenance, defined as resumption within 72 hours of endoscopy or prior to discharge, was observed in 51%. Older age, aspirin monotherapy and peptic ulcer disease were significant predictors of antithrombotic discontinuation, whereas DAPT use and warfarin use for metallic heart valve were significant predictors of maintenance. Mean follow-up after discharge was 286 days. The overall mortality rate was 22%, with in-hospital mortality of 11%. Our rebleeding rate over this follow-up period was 8.2%. Overt bleed-related mortality ($n=3$) was overshadowed by cardiovascular mortality ($n=16$) [$p=0.005$]. Mortality during inpatient AUGIB (33%) was significantly higher than those admitted with AUGIB (14%). Discontinuation of antithrombotic therapy post endoscopy was associated with increased thrombotic events (RR 5.5, $p<0.001$), reduced rebleeding (RR 0.5, $p=0.35$), and increased incidence of any adverse event (RR 2.1, $p=0.005$). Discontinuation post discharge was associated with reduced survival ($p=0.03$), increased thrombotic events ($p=0.01$) and any adverse event ($p=0.006$). Discontinuation of aspirin monotherapy was observed in 67%, but did not reach significance for thrombosis ($p=0.24$) or adverse outcome ($p=0.15$). However, thrombotic events were significantly higher in the discontinued oral anticoagulant ($p=0.01$) and non-aspirin monotherapy subgroups ($p=0.002$).
Conclusion: In our patient group, mortality from thrombotic causes following AUGIB is high. Maintenance of antithrombotic therapy, including non-aspirin regimens, appears to be associated with improved thrombotic outcomes and reduced mortality.

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Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 15:45-17:15
ADVANCES IN CAPSULE ENDOSCOPY AND ENTEROSCOPY - ROOM E1

OP104 MAGNETICALLY ASSISTED CAPSULE ENDOSCOPY IN THE UPPER GASTROINTESTINAL TRACT: A RANDOMISED TRIAL OF CONTROL AND PREPARATION

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Introduction: Delayed gastric emptying can be a significant factor in incomplete small bowel capsule endoscopy (SBCE). This has been addressed by using prokinetic agents, albeit with the need for cannulation or intramuscular (IM) injections and the small risk of adverse drug reactions. Recently a manoeuvrable small bowel (SB) capsule has become available using a handheld magnet to control movement. In this study we have compared this technique with a standard protocol to determine if control using a magnet can be demonstrated by the achievement of a readily definable and in terms of small bowel examination, a clinically useful end point: entry into the duodenum.
Aims & Methods: Single centre, randomised controlled trial involving 122 patients attending for SBCE using MiroCam Navi (Intromedic, Seoul, Korea) between February 2014 and February 2015. Patients were randomised to either the standard (control) group or the steerable capsule (intervention) group. The control group were mobilised for 30 minutes after ingestion of the capsule, followed by IM metoclopramide 10mg if the SBCE had failed to enter the SB. The intervention group ingested a gastric distention volume of 1000mls of water with 5 drops of simethicone prior to SBCE. Positional change and magnetic steering was used to manipulate the SBCE into the duodenum. If unsuccessful after 30 minutes, the patient transferred to the standard protocol. Outcome measures: gastric transit time (GTT), capsule endoscopy completion rate (CECR), gastric visibility and distention (as measured on a 1-4 scale). Secondary outcome measures: first pyloric image, relationship of body habitus to GTT and CECR and patient comfort scores. For the primary outcome measures; 60 patients per group were required to achieve 80% power, assuming a completion rate of 70% for the control protocol, improving to 90% with the intervention. Ethics: 13/YH/0358
Results: 122 patients were recruited (61 to each group: 34 men, mean (SD) age 49.6 ± 17.8 years, range 20-85 years). 2 patients were excluded due to gastric retention of the capsule. GTT was longer in the intervention group but this did not reach statistical significance (median 23 vs 51 minutes Mann-Whitney $U=1487$, $p=0.116$). There was no significant difference in CECR between the two groups (χ^2 $p=0.395$). Gastric mucosal clarity and distention were significantly better in the intervention group ($p<0.0001$ and $p<0.0001$ respectively). Similarly the first pyloric image was seen significantly sooner in the intervention group ($p=0.029$), suggesting that magnetic control hastens capsular transit to the gastric antrum but is unable to impact upon duodenal passage. Examining the intervention sub-group: no correlation between body mass index (BMI) or waist-hip ratio (WHR)and GTT was demonstrated ($r=0.002$ and $r=5.98$ respectively). Similarly no significant difference between WHR ($p=0.938$) or BMI ($p=0.507$) and CECR was noted.
Conclusion: Magnetic steering of a small bowel capsule is unable to overcome pyloric contractions to enhance gastric emptying. However mobility, image clarity and distention within the gastric cavity was significantly better in the intervention group, suggesting that with further improvements this technique could potentially be harnessed to enable capsular examination of the gastric cavity.
Disclosure of Interest: None declared

OP105 SMALL BOWEL IMAGING IN CROHN'S DISEASE: MEASURING THE TRUE ACCURACY OF PROXIMAL AND DISTAL SMALL INTESTINAL DISEASE ACTIVITY USING TOTAL ENTEROSCOPY IN PATIENTS WITH ESTABLISHED AND SUSPECTED CROHN'S DISEASE

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Introduction: Small bowel imaging, such as MR enterogprahy (MRE), CT enterography (CTE), and capsule endoscopy (CE) are used not only for detecting small intestinal (SI) Crohn's disease (CD), but also for assessment of mucosal healing; however, previous studies have relied on ileocolonoscopy alone as the reference, not taking into account the full length of the SI.
Aims & Methods: The aim of this study was to assess the accuracy of SI imaging using total enteroscopy (TE) as the gold standard. This is a single-center retrospective chart review of patients with established and suspected CD status post TE via double balloon enteroscopy (DBE) and small bowel imaging. CD activity was defined as positive if $\geq$1:aphthous lesion, small ulcer, large ulcer, ulcerated mucosa, and/or stenoses. For imaging, CD was defined as presence of wall thickening, increased contrast enhancement, or hyperemia, and/or presence of stenoses. Disease location was defined as proximal (duodenum to proximal ileum) or distal (proximal ileum to terminal ileum). Using TE as the gold standard, sensitivities, specificities, positive predictive values (PPV) and negative predictive values (NPV) were calculated.
Results: 2146 DBEs were performed between 2004-2014 with 611 TEs achieved in 337 patients; 71 TEs were achieved in one direction. 55 patients (M36:F19, 51yo) identified with CD (30 suspected and 25 established) underwent 109 DBEs for 58 TEs. 11 DBEs required balloon dilation. 2 DBEs were performed for capsule retrieval. There were 0 perforations, pancreatitis. 18 patients underwent CE with a median Niv score of 5.5. CTE, MRE, and SBFT compared to other imaging modalities, such as CT and MRI, detected CD activity with 66.7% vs 47% sensitivity, and stenoses were detected with 50% vs 62% sensitivity. On the other hand, CE detected CD activity with 75% sensitivity and 50% specificity, and stenoses were detected with 83% sensitivity and 100% specificity. When evaluating the proximal vs distal SI, MRE, CTE, and SBFT had 42% vs 63% sensitivity. Alternatively, the PPV for proximal vs distal CD for CE was 100% vs 70.8%. Because of TE there was maintenance of therapy in 7, escalation of therapy in 10, resection/lysis of adhesions in 4, IBS in 6, de-escalation of therapy in 2, symptom improvement post balloon dilation in 3, diagnosis of CD in 18,

CD ruled out in 5, and other concomitant diagnoses in 7 (celiac sprue, NSAID enteropathy, carcinoid, Meckel diverticulum).

Table1: Diagnostic Accuracy of CTE/MRE/SBFT for Small Intestinal CD

	sensitivity	specificity	ppv	npv	lr	p-value
all crohn's disease activityn = 42	0.6667	0.2083	0.3871	0.4545	0.8421	0.4832
stenosesn = 32	0.5000	0.4091	0.2778	0.6429	0.8462	0.7120

Conclusion: CTE/MRE/SBFT sensitivities for SI CD activity are lower than expected, and may not be as reliable as TE in assessing isolated small intestinal CD activity. Additionally, in comparison, CE has overall excellent accuracy for total small intestine. However, both modalities were less sensitive for detecting proximal SI CD, and deep enteroscopy could be preferred.
Disclosure of Interest: N. Mann Lecture fee(s): Given Imaging, Consultancy: Given Imaging, L. Jamil: None declared, S. Lo: None declared

OP106 COLOR-BASED SEGMENTATION OF CAPSULE ENDOSCOPY IMAGES FOR AUTOMATED LESION SIZE MEASUREMENTS

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Introduction: Accurate & objective measurement of the size of gastrointestinal (GI) lesions in capsule endoscopy (CE) is essential. Currently, measurement is based on subjective estimations relative to the diameter of the bowel lumen. Color carries important information for lesion discrimination[1]; we developed a novel color-based CE image segmentation method & evaluated its capacity for lesion size measurement.
Aims & Methods: Images of GI lesions (various types/sizes) with MiroCam® (IntroMedic® Co., Seoul, South Korea) - available online from **KID** database (*Dataset 1*)[2]. Size reference standards were made by manual annotation. Automatic image segmentation was performed by Simple Linear Iterative Clustering (SLIC), capable of grouping pixels of similar color into contiguous clusters of pixels (regions), called superpixels[3]. The algorithm uses the CIE-Lab color space representation instead of the standard RGB used in CE[1]. The components of this space represent lightness (L), the quantity of red ($a > 0$) or the quantity of green ($-a > 0$), the quantity of yellow ($b > 0$) or the quantity of blue ($-b > 0$) of a pixel. The superpixels are clustered using the k-means algorithm into three clusters using chromatic information only from component a. The method considers that a user specifies a point belonging to an abnormal image region of interest (ROI). Thereafter, the method estimates from each neighboring superpixel of the selected superpixel i.e. the one containing the selected point, the dissimilarities (Euclidean distances) of the color feature vectors composed of the mean values of a and b, with: a) the respective vectors of the selected superpixel (d1); and b) the mean of the respective vectors obtained from all superpixels that do not belong to the cluster of the selected superpixel (d2). Then the neighboring superpixel is considered to belong to the abnormal region of interest if d1.
Results: The algorithm was evaluated for the segmentation of 7 different types of GI lesions. Accuracy of the measurements was assessed comparing the area of the lesion (as identified by the method) with the reference standard area of each lesion. Average accuracies obtained for the measurement of angioectasias, aphthae, chylous cysts, lymphangiectasias, polypoid lesions, stenoses, and ulcers were 98.6%, 92.8%, 94.3%, 99.1%, 80.0%, 82.9%, and 94.8%, respectively. Comparatively, using the well-known color space proposed by Ohta (I1I2I3) for image segmentation instead of CIE-Lab[1] the results were lower; 97.1%, 92.1%, 92.6%, 97.8%, 75.2%, 78.8%, 91%, respectively. Due to color dependency, in cases where the abnormal ROI has observable color variations, our method presents lower accuracy.
Conclusion: A novel method for accurate size measurement of lesions in CE is proposed & evaluated on a publicly available dataset of CE images; overall accuracy of approx. 92%. These results call for the development of a novel measurement tool embedded in the CE reading software.

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Disclosure of Interest: None declared

OP107 EVALUATION FOR THE CLINICAL EFFICACY OF COLON CAPSULE ENDOSCOPY IN THE DETECTION OF LATERALLY SPREADING TUMOR

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Introduction: With the advancement of technology used in PillCam COLON 2 capsule endoscopy (CCE2), there have been marked improvements in diagnostic rates for CCE2 in the detection of colonic polyps and colorectal cancer. However, a limited data have been reported about laterally spreading tumor (LST) in the colorectum.
Aims & Methods: This study compared CCE2 with optical colonoscopy (OC) for the detection of LST. We performed a prospective, single-academic center study comparing CCE2 with OC (the gold standard for comparison) in a cohort of patients with LSTs by diagnostic OC performed within 3 months prior to CCE2 at Hiroshima University Hospital. Patients underwent an adapted colon preparation, and colon cleanliness was classified into inadequate and adequate. We focused on the sensitivity and the specificity of CCE2 for detecting LST. All LSTs were resected by endoscopic resection and confirmed histopathological diagnosis. The recorded capsule videos were reviewed by the 2 independent investigators without any information of patients and OC. LSTs were dived into LST-granular type (LST-G) and LST-non granular type (LST-NG) based on detailed observation during chromoendoscopy with indigo carmine dye spraying as previously reported.
Results: A total of 21 LSTs (7 LST-Gs and 14 LST-NGs) in 30 patients (mean age, 59.5 years) were included in the study. The average size of LST was 27 ± 15 mm (10-60 mm) in diameter. Histopathological diagnosis of LST was as follows; tubular adenoma (TA) 12 cases (57%), sessile serrated adenoma/polyp (SSA/P) 4 (19%) cases, Tis carcinoma 1 case (5%), and T1 carcinoma 4 cases (19%). The existed location of LSTs was cecum 1 case (5%), ascending colon 6 cases (29%), transverse colon 6 cases (29%), descending colon 1 case (5%), sigmoid colon 3 cases (13%), and rectum 4 cases (19%). The capsule was excreted within 10 hours after ingestion and before the end of the lifetime of the battery in 100% of the patients. The colon cleanliness was adequate in all cases (100%). The sensitivity and specificity of CCE2 for detecting LSTs were 81% and 100%, respectively. For detecting LST-G, the sensitivity and specificity of CCE2 were 71% and 100%, respectively. For detecting LST-NG, the sensitivity and specificity of CCE2 were 86%and 100%, respectively. The 4 false-negative cases of CCE2 were 1) LST-G, 18mm, cecum, TA, 2) LST-G, 20mm, sigmoid colon, TA, 3) LST-NG, 25mm, transverse colon, SSA/P, and 4) LST-NG, 20mm, transverse colon, SSA/P, respectively.
Conclusion: The use of CCE2 allows visualization of the LST in most cases, however its sensitivity for detecting LST (especially located in the transverse colon or SSA/P) is low as compared with the use of OC.
Disclosure of Interest: None declared

OP108 CAPSULE ENDOSCOPY IS SUPERIOR TO MULTIDETECTOR CT SCAN FOR EVALUATION OF SMALL BOWEL DISORDERS: A META-ANALYSIS

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Introduction: Capsule endoscopy and multidetector CT scan are diagnostic tools for evaluation of small bowel (SB) disorders, including obscure GI bleeding (OGIB). Studies comparing the diagnostic yield of these tests for SB lesions have shown conflicting results.
Aims & Methods
Aims: The aim of this study was to compare the diagnostic yield of capsule endoscopy (CE) and multidetector CT scan (MDCT) for small-bowel (SB) lesions using meta-analysis.
Methods: We performed a recursive search of studies comparing CE with MDCT for evaluation of SB disorders. MDCT in different studies included CT angiogram (CTA), CT enterography (CTE) or CT enteroclysis (CTEC). Data on diagnostic yield of CE and MDCT for small bowel lesions were extracted, pooled, and analyzed. Odds ratio (OR) and 95% confidence intervals (CIs) using pooled data for the yield of CE and MDCT for SB lesions were calculated using a random effects model (REM) for analyses since several of the outcome measures had significant heterogeneity. Funnel plots and Galbraith plots were consulted to determine potential publication bias, and all study results were determined to be appropriate for combined analysis
Results: Ten studies compared CE and MDCT (CTE-4 studies, CTEC-3 studies, CTA-2 studies, and both CTA and CTE-1 study) in patients with suspected SB disorders, including OGIB, Crohn disease or SB tumor. The SB findings on CE and MDCT were confirmed on deep enteroscopy, surgery, or mesenteric angiogram in 9 studies (this information was not provided in 1 study). The pooled overall yield for SB findings was significantly higher with CE (49.7%; n = 409) compared with MDCT (29.7%; n = 461) (odds ratio 1.96; 95% CI 1.14-3.37; REM). Seven studies compared CE and MDCT in patients with OGIB (73% with overt OGIB based upon data from 5 studies). The pooled overall yield was significantly higher with CE (50.4%; n = 329) than MDCT (32%; n = 350); (OR 2.17; 95% CI 1.13-4.18; REM). Ten studies reported vascular, inflammatory lesions and polyps/tumors; the pooled overall yield of CE (12.4%; n = 409) was significantly higher than MDCT (3.4%; n = 461) only for vascular lesions (OR 3.38; 95% CI 1.68-6.78; REM). The pooled overall yield of CE and MDCT for inflammatory lesions was 12.9% (n = 409) and 8.4% (n = 461), respectively (OR 1.61; 95% CI 0.93-2.80; REM).

The pooled overall yield of CE and MDCT for polyps/tumors was 13.6% (n = 409) and 15.1% (n = 461), respectively (OR 0.85; 95% CI 0.57-1.28; REM).
Conclusion: CE has a significantly higher yield than MDCT for SB lesions in patients with suspected SB disorders, including OGIB. Among the SB lesions, CE has a significantly higher yield than MDCT for only vascular lesions. There is no difference between the tests for detection of inflammatory lesions or tumors/polyps. CE should therefore be considered the first test of choice for SB evaluation. MDCT may be indicated in patients with a contraindication for CE, and those with a negative CE but high clinical suspicion for a SB lesion.
Disclosure of Interest: S. Pasha Financial support for research: Covidien, Capsovision, Consultancy: Covidien, R. McLemore: None declared, A. Hara: None declared, M. Crowell: None declared, J. Leighton Financial support for research: Covidien, Capsovision, Consultancy: Covidien, Olympus

OP109 MONITORING AND ENDOSCOPIC TREATMENT OF SMALL INTESTINAL POLYPS IN PEUTZ-JEGHERS SYNDROME: A 12-YEARS FOLLOW-UP

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Introduction: Small intestinal polyps screening in Peutz-Jeghers (PJ) syndrome has evolved during the last decade since new non-invasive technologies have arisen such as capsule endoscopy (CE), MR enterography (MRE) or CT enterograhy (CTE). Polypectomy during double balloon (DBE) or spiral enteroscopy (SE) has become the first line treatment, replacing push enteroscopy (PE), and surgery is less frequently needed.
Aims & Methods: Our aims were: 1/ to describe diagnostic yields of CE and imaging techniques for small intestine polyps screening and 2/ to evaluate therapeutic yield of DBE or SE in PJ syndrome. We conducted a retrospective study based on a cohort of PJ syndrome patients followed-up in a French tertiary center within a specialized network. Between 2002 and 2014, 23 patients (M/F = 14/9, mean age = 35 years old (8-58), history of small intestine surgical resection 17/23 = 74%) with PJ syndrome were followed-up in our center. Small intestinal polyp screening was performed every 2 to 3 years using CE and/or MRE and/or CTE. Endoscopic treatment using mainly DBE or SE was attempted for polyps greater than one centimeter seen during screening. In case of endoscopic treatment failure, or incomplete treatment, surgical enteroscopy or surgical resection was performed.
Results: During a mean follow-up of 62 months (2-132), 21/23 patients (91%) had 39 CE procedures (1.9 CE/patient (1-4)), 13/23 patients (57%) had 21 radiologic exams with CTE (n = 11) or MRE (n = 10) (1.6 exam/patient (1-3)) and 23/23 had 46 small bowel endoscopies (39 per-oral and 7 per-anal) using DBE (n = 29), SE (n = 15) or PE (n = 2) (2 exams/patient, (1-6)). Diagnostic yield for polyp detection was 92% for CE and 90% for both radiologic techniques. Small bowel endoscopic polypectomy allowed the resection of 189 polyps measuring 5 to 60mm (8 polyps/patient (1-45)) and was considered as complete in 17/23 patients (74%). Neither severe bleeding nor perforation was noted. Surgical enteroscopy was performed in 4/23 patients (17%) allowing a supplementary resection of 58 polyps (14 polyps/patient (7-25)), measuring between 5 and 40mm. Surgical treatment by small intestine resection was indicated in 2/23 patients (9%), the first one because of a large jejunal polyp of 6 cm that was not feasible with DBE and the second one because of a recurrence of an anastomotic flat polyp. This actual rate of surgical resection was statistically different from that observed initially in our cohort (9% vs 74%, $p < 0.001$).
Conclusion: CE and small intestine imaging by MRE or CTE have an excellent diagnostic yield (90%) for small bowel polyp screening in PJ syndrome. Endoscopic polypectomy by DBE or SE is sufficient in 90% of cases when combined to surgical enteroscopy. Indication for surgical resection has become very rare, but remains a good alternative for difficult cases or complex post-surgical recurrences.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 15:45-17:15
IRRITABLE BOWEL SYNDROME: WHAT CAN SCIENCE TELL US? - ROOM E4

OP110 EXPLORING THE GENETIC ARCHITECTURE OF IBS THROUGH GWA STUDIES OF > 25,000 INDIVIDUALS FROM GENERAL POPULATION COHORTS

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Introduction: A heritable component of Irritable bowel syndrome (IBS) has been demonstrated, but gene-hunting efforts have so far been scarce. Exploiting its high prevalence, we seek to identify IBS risk genes through genome-wide association studies (GWAS) of general population samples.[1]
Aims & Methods: Following our recent report of the first GWAS of IBS in the Swedish population[2], we are now studying several other population-based cohorts, and aim for later comprehensive meta-analyses. So far, the following cohorts have been included (total N > 25,000): SALT (Sweden), SHIP-trend (Germany), Northern Finland Birth Cohort 1966 (Finland), TwinsUK (UK) and LifeLine-Deep (The Netherlands). IBS cases and asymptomatic controls were identified using epidemiological data and symptom-based Rome III criteria. Upon stringent quality controls (QC), genotype and HapMap2 imputed data for 1.8-6.6 million markers and 823-5,332 individuals from different cohorts were used for association testing with logistic regression under an additive model adjusted for gender.
Results: Association testing comparing IBS cases and controls identified several chromosomal regions providing GWAS signals of suggestive ($P < 5x10-5$) significance in individual cohorts, with large heterogeneity across datasets. Genes from shared pathways map to these regions, including those involved in prostaglandin synthesis, circadian clock, neuropeptide transmitters and others. Meta-analysis of data from these cohorts is under way.
Conclusion: It is a long and winding road to the identification of unequivocal IBS risk genes and associated variants. This requires massive sample size and replication of results across different populations, as well as a conclusive validation of findings in the clinical settings through case-control studies. Our approach holds the promise to overcome these limitations, and through large international collaboration we are gathering the numbers that are ultimately necessary to identify true IBS genetic risk factors with adequate statistical power. Overall, the set of association signals identified in independent GWA studies, and the later meta-analysis with additional incoming datasets, provide the first solid foundation for major follow-up efforts and further replication in independent case-control studies.

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Disclosure of Interest: None declared

OP111 INTESTINAL MICROBIOTA IN PATIENTS WITH IBS - HIGH THROUGHPUT SEQUENCING OF THE MUCOSA AND LUMINAL MICROBIOTA

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Introduction: Alterations in the intestinal microbiota is emerging as an important factor in the pathogenesis of irritable bowel syndrome (IBS). The luminal microbiota (LM) and the mucosal-associated microbiota (MAM) are two distinct ecosystems and are thought to have different metabolic and immunological functions. However, most of the studies investigating the intestinal microbiota in IBS have focused on analysis of fecal samples and the very few studies that investigate the MAM have used samples collected following preparation for endoscopic procedures.
Aims & Methods
Aim: To characterize and compared the intestinal LM and MAM in IBS patients and healthy controls (HC) that did not receive a bowel cleansing.
Methods: Fresh fecal samples and colonic mucosal biopsies were collected from 16 IBS subjects before (fecal) and during (mucosa) a flexible sigmoidoscopy of an unprepared bowel. Characterization of bacterial communities was done using high throughput pyrosequencing of the 16S rRNA gene (V1-V3). Microbial richness and diversity were calculated using the Shannon index of diversity. Normalized percentages of the core microbial taxa (present in ≥25% of samples of either niche) were compared, and adjusted for multiple comparisons using a false discovery rate (FDR) at 0.1.
Results: Similar to what we have recently reported in HC, patients with IBS demonstrated: 1. Significant microbial population differences between LM and MAM (ANOSIM: $R = 0.3$, $P = 0.001$) 2. A significantly tighter clustering in the LM compared to the MAM (average weighted UniFrac distances- 0.26 ± 0.04 vs. 0.42 ± 0.11, $P < 0.001$, respectively) and 3. Higher diversity in the LM compared to the MAM (Shannon diversity index: 4.79 ± 0.5 vs 4.26 ± 0.8, $P < 0.05$) 4. The abundance of dominant phyla in the LM and MAM niches was significantly different: *Firmicutes* (41% vs. 28%, FDR < 0.001, respectively), *Actinobacteria* (20% vs. 12%, FDR < 0.001, respectively) and *Proteobacteria* (11% vs. 20%, FDR < 0.001, respectively).
The abundance of 56 genera differed significantly (FDR < 0.1) between the two niches. All genera belonging to the *Proteobacteria* and *Bacteroidetes* phyla, were more abundant in the MAM compared to the LM in HC and in IBS patients. However, while in HC all six genera of the *Actinobacteria* phylum were more abundant in the LM niche and most (23 out of 34) of the genera of the *Firmicutes* phylum were more abundant in the MAM niche, in IBS patients only a few of the genera of the Actinobacteria (3 out of 9) and *Firmicutes* phyla (6 out of 28) were more prominent in the MAM niche.
Conclusion: The intestinal LM and MAM are significantly different from each other in composition and diversity both in IBS and HC. IBS and HC are different in both LM and MAM. These two microbial niches should be investigated independently in order to better understand the role of the intestinal microbiota in the pathogenesis of IBS.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 15:45–17:15
NEW WAYS OF ASSESSMENT IN CROHN'S DISEASE – ROOM E3

OP112 INVESTIGATING THE SMALL BOWEL IN PEDIATRIC CROHN'S DISEASE: PROSPECTIVE COMPARATIVE STUDY BETWEEN SMALL INTESTINE CONTRAST ULTRASONOGRAPHY AND MAGNETIC RESONANCE IMAGING

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Introduction: Small bowel (SB) assessment is a cornerstone for the proper management of pediatric Crohn's disease (CD). Magnetic resonance imaging (MRI) is now considered the gold-standard for the evaluation of SB. However, MRI is an expensive technique, it requires a strong patient's compliance and need a considerable amount of oral contrast to ensure an adequate distension of the intestinal lumen. Small intestine contrast ultrasonography (SICUS) is a, non-invasive and low-cost imaging modality in CD, and it is generally well tolerated by pediatric patients (pts).

Aims & Methods: To compare the diagnostic accuracy of SICUS and MRI in detecting presence, site and extension of SB disease and in assessing stricturing complications in pediatric pts with suspected or known CD. Pts referred to our Pediatric Gastroenterology and Liver Unit for suspected CD or for relapse of a known CD were prospectively enrolled, from January 2012 to December 2014. All pts underwent SICUS, MRI and ileo-colonoscopy according to previously published methods *. The examinations were performed by different operators unaware of the results of other techniques. To allow the comparative study the SB was subdivided into three sections: jejunum, ileum, terminal ileum. The statistic concordance (k) between the two techniques in detecting presence and site of SB lesions was calculated according to Landis and Koch criteria**. For the terminal ileum (TI) sensitivity (SE) and specificity (SP) were assessed too, having ileo-colonoscopy as reference standard. Comparative evaluation of the extension (cm) of disease in the different SB segments was assessed using one-way ANOVA with Kruskal-Wallis post-test.

Results: Sixty-six consecutive pts (median age 13; range 7-18), with suspected (23) or known (43) CD were included. The overall concordance (k) between SICUS and MRI in assessing the presence of SB lesions was high: $k = 0.94$ (ES 0.06; 95%CI 0.8-1). The k for segments was: 0.67 (ES 0.1, 95%CI 0.4-0.8) for jejunuum, 0.91 (ES 0.06, 95% CI 0.76-1) for ileum and 0.91 (ES 0.06; 95%CI 0.8-1) for TI. SE and SP of SICUS and MRI in assessing TI lesions respectively were 98% and 100% and 93% and 92%. One-way ANOVA showed no difference in assessing the extension of lesions between SICUS and MRI in the different SB segments. The k between SICUS and MRI for the presence of SB strictures was 0.62 (ES 0.1, 95% CI 0.4-0.8). SE and SP of SICUS and MRI in detecting strictures of the TI respectively were 100% and 100% and 92% and 87%. MRI provided 7 false positive results, not detected at SICUS nor confirmed at endoscopy.

Conclusion: The diagnostic performance of SICUS is comparable to that of MRI in pediatric CD. Due to its capability to provide a dynamic evaluation of the SB, SICUS is useful in assessing strictures, probably with higher accuracy than MRI. Thus, SICUS might represent a first-line diagnostic tool in pediatric CD, able to reduce costs and to post-pone or even avoid more invasive and expensive investigations.

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Disclosure of Interest: None declared

OP113 DIAGNOSTIC PERFORMANCE OF MR ENTEROGRAPHY IN 'ROUTINE CLINICAL PRACTICE' FOR THE ASSESSMENT OF TERMINAL ILEUM IN CROHN'S DISEASE: MARGINALLY INFERIOR RESULTS WITH A COMPLEMENTARY ROLE

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Introduction: Magnetic resonance enterography (MRE) in Crohn's disease (CD) management has been rapidly growing in importance during recent years. MRE has the advantages of providing high soft tissue contrast, obtaining static and dynamic images, and avoiding ionizing radiation. Prospective studies perfomed in highly academic centers by dedicated radiologists with the state-of-the-art technique yields a diagnostic accuracy of 91%. A systematic review reported per-patient sensitivity and specificity of MRI for the diagnosis of CD as 78% and 85%, respectively.[1]

Aims & Methods: The objective of this study was to evaluate the accuracy of MRE for detecting terminal ileal involvement in CD compared to the gold-standard ileocolonoscopy in the 'real-life setting'. A total of 156 patients (mean age 37 ± 11, 94 male) were included in this study, and underwent both MRE and ileocolonoscopy within a 60-day period. Patients with ileocolonic (n:35) and ileal (n:53) CD constitutes 'terminal ileum affected group'. CD patients without ileal involvement (n:47), and ulcerative colitis patients without backwash ileitis (n:21) constitutes control group (normal terminal ileum). All MRE images were evaluated by on-duty radiologists, and not consulted by an expert working in abdominal MR imaging. Colonoscopic SES-CD (<3 inactive), and MRE simple activity scores (SEAS) were calculated.

Results: MRE showed 75% accuracy (71% sensitivity, 80% specificity, 82% positive predictive value, 67% negative predictive value) for detecting ileal disease in routine clinical practice. MRE was false negative in 23 patients (16%). In two patients with a diagnosis of CD according to MRE findings, colonoscopic biopsies revealed lymphoma and adenocarcinoma. A statistically significant positive correlation was found between MRE SEAS scores and SES-CD scores ($r = 0.412$; $P < 0.01$). For SEAS score, a cut off level of ≥ 2 has the best diagnostic performance for discrimating active from inactive disease (accuracy 75%, sensitivity 77%, specificity 73%).

Conclusion: MRE has marginally inferior diagnostic performance in general practice when compared to results in well-designed studies. Diagnostic performance of MRE seems dependent on the experience of radiologists and state-of-the art technique. False negativity/positivity, and unexpected tissue diagnosis of malignancy in two patients (1%) underlies the importance of ileocolonoscopy, and complementary nature of the cross-sectional imaging.

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Disclosure of Interest: None declared

OP114 A SIMPLE ULTRASONOGRAPIC SCORE FOR THE ACCURATE DETECTION OF INFLAMMATORY ACTIVITY IN CROHN'S DISEASE

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Introduction: Cross-sectional imaging is central in the diagnosis and management of Crohn's disease (CD), an immune-mediated disease of the small and large bowel that often leads to transmural damage. Safe, non-radiation based modalities are preferred, given young age of onset. Ultrasound is accurate in detection of disease activity, however a simple validated score for inflammatory activity is not widely used.

Aims & Methods: The aim of this study was to evaluate the sonographic grey scale parameters that contribute most to disease activity and devise a clinically applicable score. This was an IRB-approved, single-center prospective study evaluating patients with established Crohn's disease treated with adalimumab. Patients were evaluated with ileocolonoscopy (scored using validated indices, Simple Endoscopic Score and Rutgeert's Score) and ultrasound within 2 weeks of endoscopy at time zero and either at 6 or 12 months depending on clinical indication. Clinical indicators (Harvey Bradshaw Index/ HBI) and serologic inflammatory markers (C-Reactive Protein/ CRP) were collected at each time point. The ability of HBI and CRP to predict disease activity was determined by comparison with endoscopy and ultrasonography using Fisher's exact test. An US score was developed based on ordinal logistic regression using a proportional odds model. The final model included only variables with p values ≤ 0.05. Disease severity was classified according to endoscopic score with the most significant grey scale variables weighted to classify individuals into different severity levels. ROC curves were plotted to demonstrate the discriminative and predictive capacity of the scoring system developed.

Results: A total of 63 patients were included, 24 had 2 endoscopic examinations, while 39 had 1, giving a total of 87 US and endoscopic comparisons. The average age was 40.7 years, with 28 females and 35 males. The most common disease distribution was ileocolonic 59% (37/63), with 30% (19/63) having terminal ileal and 8% (5/63) with isolated colonic disease. HBI and CRP were found to have no significant association with endoscopic ($p = 0.188$, 0.156 respectively) or ultrasonographic ($p = 0.138$, 0.273 respectively) findings. Three grey scale parameters were significantly associated with inflammatory activity, including bowel wall thickness ($p = 0.046$) mesenteric inflammatory fat ($p = 0.006$) and lymph nodes ($p = 0.028$). Based on the novel score, the ROC curve for distinguishing patients with inactive or mild disease from those with active disease was 0.89 while distinguishing normal from any activity was 0.81.

Conclusion: A simple sonographic score comprising three parameters can be used to accurately reflect disease activity, as seen on gold standard endoscopy. Thus, ultrasound may be a surrogate to endoscopy to guide disease management and this score may increase standardization of sonographic CD activity measurement across centers.

Disclosure of Interest: None declared

OP115 THE ROLE OF ULTRASOUND ELASTICITY IMAGING IN PREDICTING ILEAL FIBROSIS IN CROHN'S DISEASE PATIENTS

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Introduction: Bowel wall fibrosis is associated with a complicated disease behavior and a reduced efficacy of anti-inflammatory therapies in patients with Crohn's disease (CD). The quantitative assessment of fibrosis severity in CD-affected areas, and their differentiation from inflammatory lesions, can be of great help in clinical decision-making.
Aims & Methods: The aim of the study was to evaluate the feasibility, reliability and reproducibility of Ultrasound Elasticity Imaging (UEI) towards the assessment of ileal fibrosis in patients with CD.
Twenty-three consecutive patients with ileal or ileocolonic CD, elected for surgical resection of the terminal ileum, underwent bowel ultrasound and UEI. Twenty inflammatory CD patients without complications were enrolled as controls. Bowel wall stiffness was evaluated with UEI by means of color scale and quantitative strain ratio measurement. Bowel wall thickness, stratification pattern and vascularization were evaluated at bowel ultrasound. The severity of bowel wall fibrosis and that of acute and chronic inflammation were evaluated on histological sections by both semi-quantitative and quantitative image analysis, and used as a reference standard.
Results: The UEI strain ratio measurement was significantly correlated with the severity of bowel fibrosis at both semi-quantitative and quantitative histological image analysis: it was characterized by an excellent discriminatory ability for severe bowel fibrosis (AUROC: 0.917; 95% CI: 0.788-1.000). UEI strain ratio measurements were characterized by an excellent inter-rater agreement with with ICC at 0.90 (95% CI 0.75-0.96). At multivariate analysis, bowel wall fibrosis resulted the only independent determinant of strain ratio ($R^2 = 0.75$, $p < 0.0001$). The ileal strain ratio of inflammatory CD patients was significantly lower than in operated CD patients with severe fibrosis (1.2 ± 0.6 vs 2.4 ± 0.5, $p = 0.0005$).
Conclusion: The results show that UEI is a reliable highly reproducible technique, which can be complementary to bowel ultrasound examination in CD patients, as it can accurately identify small bowel segments affected by advanced fibrosis, without being influenced by the severity of intestinal inflammation.

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Disclosure of Interest: None declared

OP116 FAECAL CALPROTECTIN IN PATIENTS WITH SUSPECTED SMALL BOWEL CROHN'S DISEASE: CORRELATION WITH SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: Faecal calprotectin (FC) is a stool biomarker recommended as a simple, non-invasive test to distinguish between inflammatory bowel disease (IBD) and functional bowel disorders. Despite a good correlation with colonic inflammation, FC is felt to be less accurate at identifying small bowel (SB) inflammation. Small bowel capsule endoscopy (SBCE) has a high sensitivity for detecting SB mucosal inflammation. We investigated the correlation between FC and SBCE in patients with suspected IBD.
Aims & Methods: We prospectively correlated the findings of SBCE with FC levels in patients under investigation for suspected IBD. Patient demographics, clinical symptoms, medications and blood parameters: haemoglobin (Hb), albumin, ESR and CRP were collected. SBCE findings including Lewis scores were analysed against FC values and final diagnosis.
Results: 127 patients were included, mean age 42 years (range 18-75 years), 85 female. Presenting symptoms included: a combination of diarrhoea, abdominal pain and bloating (74%), diarrhoea alone (13%), abdominal pain alone (12%), rectal bleeding (1%). Median time from FC measurement to SBCE was 62 days. 12% had a family history of IBD, 14% were current smokers. 6 patients with a diagnosis of colonic pathology were excluded.
Results are presented in the table. Of the 14 patients (23.0%) with FC > 100mg/kg, 14 had clinically significant SB findings (12 SB ulcers, 2 villous atrophy) and mean FC levels 468mg/kg (range 112-1010mg/kg). A definitive diagnosis was made in 10 patients (9 Crohn's disease, 1 NSAID enteropathy), the remaining 10 patients are undergoing further evaluation. FC > 50mg/kg was significantly associated with clinically relevant SBCE findings (χ^2 $p = 0.02$). FC had a sensitivity 81%, specificity 40%, positive predictive value 42% and negative predictive value (NPV) 80%. Receiver operating curve analysis showed an area under the curve (AUC) of 0.626 for FC, similar to CRP (AUC 0.638) but better than ESR (AUC 0.524) and Hb (AUC 0.545). Albumin most closely correlated with an AUC 0.686. Multiple logistical regression showed serum albumin to be the only variable significantly associated with positive SBCE ($p = 0.032$). Lewis score significantly correlated with FC value ($r = 0.793$, $p < 0.05$).

Table 1

FC Level	< 50mg/kg	51-100mg/kg	> 100mg/kg
Total	40	20	61
Normal SBCE	38	16	47
SBCE suggestive of IBD (or coeliac disease)	2	4	14
Definitive diagnosis	1	2	7

Conclusion: With a reasonable sensitivity and NPV, FC could be most effectively utilised to screen out patients where further SB investigation is unnecessary. However, in our series 1 patient with FC < 50mg/kg had SB Crohn's disease. Thus at best, FC can be only be recommended as an adjunct to clinical decision making, when patient factors and other biochemical parameters are also taken into account.
Disclosure of Interest: None declared

OP117 FAECAL CALPROTECTIN MEASUREMENT AND INFLIXIMAB TROUGH LEVELS PREDICT THERAPEUTIC EVOLUTION CD PATIENTS IN CLINICAL REMISSION

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Introduction: The deep remission notion (clinical remission and mucosal healing) is an important objective for patients under treatment. The appearance of inflammation and pharmacological biomarkers could be a non-harmful way of predicting the evolution of Crohn's disease (CD). The aim of our study was to offer a predictive model for relapse in CD patients presenting clinical remission undergoing infliximab (IFX) treatment.
Aims & Methods: It was a prospective monocentric study that included all CD patients on IFX maintenance treatment (5mg/kg) and in clinical remission (CDAI < 150) for at least 16 weeks, between 2011 and 2014. On the day of the IFX infusion, all of these patients underwent a faecal calprotectin assay (Buhlmann technique), a CRP assay and pharmacological assays of IFX (ELISA technique, Theradiag). TLI (> 2µg/ml) and ATI (<20ng/ml) were considered therapeutic as well as CRP levels < 5mg/l and faecal calprotectin levels < 250 mg/g of stools. All of the patients included were followed up for a minimum of nine months. A CDAI score was calculated at each IFX infusion. A patient was defined in loss of response to IFX (LOR) when the CDAI was above 220, resulting in a change of treatment deemed necessary by the physician (IFX optimisation, change of medical treatment including the use of corticosteroids, surgery).
Results: 119 patients (mean age: 34 +/- 12 years, M:F sex ratio 1.2, mean duration of evolution of the disease 7.8 years) were included. The mean follow-up period was 20.4 months. 17% of the patients were on combotherapy (IFX and azathioprine). During follow-up, 37 patients (31.1%) out of the 119 relapsed, 78% within the first 6 months (mean period: 4.6 months). While the clinical characteristics of the relapsed and non-relapsed patients were similar, a univariate analysis isolated four significant factors predicting LOR: (CRP > 5mg/l ($p = 0.043$), ATI > 20ng/ml ($p < 0.001$), LTI > 2 µg/ml ($p < 0.001$) and calprotectin > 250 µg/g stools ($p < 0.001$)). After logistic regression, two independent factors were linked to a loss of clinical response: LTI < 2µg/ml (OR: 4.34; 95% CI: 1.28-10.7; $p = 0.001$) and faecal calprotectin > 250µg/g stools (OR: 3.5; 95% CI: 1.5-8.7; $p = 0.001$). In light of these results, a training cohort of 55 patients was isolated randomly in order to implement a predictive model for LOR in patients on IFX and in clinical remission. The combination of calprotectin > 250µg/g stools and TLI < 2µg/ml enabled to be predicted LOR in 95% of the cases within 6 months. This model was validated on the test cohort of 64 patients with a PPV of 95% and an NPV of 95%.
Conclusion: In IFX-treated CD patients and in clinical remission, a combination of TLI (< 2µg/ml) and faecal calprotectin (>250µg/g of stools) enable the prediction of clinical recurrence within 6 months in 95% of cases. Intervention studies are needed to assess the impact of treatment modification in this group of patients.
Disclosure of Interest: X. Roblin Lecture fee(s): MSD; Theradiag, G. duru: None declared, L. Clavel: None declared, E. Deltedesco: None declared, J. M. Phelip: None declared, L. Peyrin Biroulet: None declared, S. Paul: None declared

MONDAY, OCTOBER 26, 2015 15:45-17:15
INSIGHTS INTO CHOLESTATIC LIVER DISEASE - ROOM E5

OP118 BILIARY BILE ACID AND PHOSPHOLIPID COMPOSITION IN PSC: EFFECT OF DISEASE SEVERITY AND UDCA THERAPY

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Introduction: Primary sclerosing cholangitis (PSC) is chronic cholestatic liver disease of unknown origin, characterized by inflammation and strictures of intra- and extrahepatic bile ducts, leading to liver cirrhosis and development of biliary dysplasia and cholangiocarcinoma. Several pathogenetic mechanisms has been suggested including the toxic bile acids induced inflammation and fibrosis of biliary epithelium. Ursodeoxycholic acid (UDCA), has widely been used to treat PSC demonstrating amelioration of cholestatic liver enzymes.
Aims & Methods: Aims of the study were to analyze: 1) bile acid, phospholipid and cholesterol content in bile in relation to disease severity in PSC, compared to controls, 2) the effect of UDCA therapy 20mg/kg/day on bile acid composition 3) the patient and disease severity related factors on bile composition.
Patients and methods: The study population consists of PSC patients naïve for UDCA therapy (n = 21), patients on UDCA therapy (n = 154) and controls (n = 27) referred for ERCP for confirming or excluding the diagnosis of PSC or for biliary dysplasia surveillance. During ERC bile sample was aspirated using balloon catheter and immersed immediately in liquid nitrogen (-196°C) and stored in -20°C. The total bile acids, cholesterol and phospholipids were analyzed by gas-liquid chromatography and the content of individual bile acids: deoxycholic (DCA), chenodeoxycholic (CDCA), cholic acid (CA), lithocholic (LCA) and UDCA were analyzed. The amount were expressed as molar percentages (mM%) of total bile acids. Blood samples were drawn at the time of ERCP for analysis of live enzymes. Cholangiographic findings were scored according to the modified Amsterdam score (mAm score).
Results: In total 175 PSC patients with adequate bile sample were included. The mean age of UDCA naïve patients was 34.0 ± 12.9 vs 40.9 ± 12.7 years in UDCA users, and 44.9 ± 14.8 years in controls, p = 0.020. Concomitant IBD was present at 86% vs 71% of patients, respectively. 1) Compared to controls, no differences were found in total bile acid concentration (mM%), or between individual bile acids. Phospholipid concentration were also similar in controls and in PSC patients. 2) UDCA therapy was associated with markedly increased of UDCA in bile (9.7± 19.0 vs. 49.1± 22.2%, p < 0.001), with significant reduction of biliary cholesterol content, while the total bile acid and phospholipid content remained unchanged. Proportion of both the primary bile acids, DCA (13.4 ± 13.1, vs 7.0 ±7.2%, p = 0.00222) and CDCA (31.8 ± 12.3 vs 18.3 ± 8.0%, p < 0.001) were markedly reduced. Of the secondary bile acids, CA mM% dropped from 43.5 ± 16.9 to 23.4 ± 16.1%, p < 0.0001, but LCA remained unchanged. No correlation was found between the disease severity judged by ERC findings (mAm score) and biliary bile acid changes during UDCA therapy. In multivariate analysis colectomy was associated with decrease with LCA (t = -2.63, p = 0.010) and DCA (t = -2.50, p = 0.014) and increase of CA (t = 3.04, p = 0.003).
Conclusion: No differences were found in biliary bile acid or phospholipid composition between controls and PSC patients, suggesting that they do not play significant role in the pathogenesis of PSC. UDCA therapy was associated with significant reduction of primary bile acids, but also with reduction of more toxic secondary bile acids. Disease progression during UDCA therapy did not impact bile acid composition.
Disclosure of Interest: None declared

OP119 ALKALINE PHOSPHATASE (ALP), BILIRUBIN AND THE RISK FOR LIVER TRANSPLANT AND LIVER-RELATED DEATH IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS (PBC)

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Introduction: Previous work created and validated a predictive model of liver transplant and liver-related death in PBC patients in the UK [Carbone et al, 2015]. Predictors included bilirubin µmol/l; ALP U/l; albumin g/l, platelets per 10^9/l and ALT. Risk was calculated as: = 1 – (0.87^EXP(-0.35*(((ALP/1500)^-0.5)-2.296) – (0.024*(((ALT/500)^-1)-7.901)) + 1.127*(LN(bilirubin/170)+2.62) + 2.954*((albumin/35^-1)-0.851) - 0.532*(platelets/150-1.854)).
Aims & Methods: The aim was to calculate absolute risk reduction (ARR) and number needed to treat (NNT) associated with fixed percent ALP reductions using an algorithm for predicting liver transplant or liver-related death in PBC patients. ALT was set at 120; albumin at 50; and platelets at 150. Bilirubin varied as a function of upper limit of normal (ULN): 17 (1X ULN), 34 (2X ULN) and 51 (3X ULN). Baseline ALP was set at 500, 400, 300 and 200. We applied 20%, 40% and 60% reductions to each baseline ALP level. We calculated 15-year absolute risk (AR), ARR, and NNT.
Results: Baseline risk for liver-related death or liver transplant increased dramatically as a function of bilirubin. Across bilirubin levels, ARRs were higher and NNTs lower at lower baseline ALP. At bilirubin = 34 and ALP = 200, a 40% ALP reduction produced a 10% ARR for liver transplant or death from liver disease; NNT = 10. A 60% ALP reduction lowered risk by 19%; NNT = 5. At baseline ALP = 500, a 40% ALP reduction yielded ARR = 7% (NNT = 14); 60% reduction ARR = 13% (NNT = 8). At a bilirubin of 20, the NNTs at baseline ALP = 500 were 50 (20% ALP reduction), 20 (40% reduction) and 9 (60% reduction).

		Bilirubin 17								
		20% ALP reduction			40% ALP reduction			60% ALP reduction		
Baseline ALP	AR	AR	ARR	NNT	AR	ARR	NNT	AR	ARR	NNT
500	45%	43%	2%	50	40%	5%	20	34%	11%	9
400	43%	40%	3%	33	37%	6%	17	31%	12%	8
300	40%	37%	3%	33	33%	7%	14	27%	13%	8
200	34%	31%	3%	33	27%	7%	14	22%	12%	8
		Bilirubin 34								
500	73%	70%	3%	33	66%	7%	14	60%	13%	8
400	70%	67%	3%	33	63%	7%	14	56%	14%	7
300	66%	63%	3%	33	58%	8%	13	50%	16%	6
200	60%	56%	4%	25	50%	10%	10	41%	19%	5
		Bilirubin 51								
500	87%	85%	2%	50	82%	5%	20	77%	10%	10
400	85%	83%	2%	50	79%	6%	17	73%	12%	8
300	82%	79%	3%	33	75%	7%	14	67%	15%	7
200	77%	73%	4%	25	67%	10%	10	57%	20%	5

Conclusion: These data demonstrate the importance of early intervention in PBC. Preventing bilirubin from rising above ULN had the greatest impact in terms of lowering risk for adverse liver outcomes. The data show similar results for ALP: the greatest reduction in risk for liver transplant and liver-related death resulted from decreasing ALP at lower baseline levels. These results support the need to treat PBC early, to stabilize bilirubin at the lowest level possible and to treat to the lowest achievable ALP.

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OP120 NOVEL PROGNOSTIC MODEL FOR PRIMARY SCLEROSING CHOLANGITIS: THE IMPORTANCE OF INCLUDING LABORATORY VALUES

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic, cholestatic liver disease, without effective drug treatment options. The only curative option is liver transplantation (LT). It is important to be able to make an indication of prognosis, for purposes of patient counseling, management and adequate timing of LT. Many biomarkers of disease progression have been assessed, recent literature indicates the independent prognostic ability of alkaline phosphatase (ALP) over time.
Aims & Methods: Aim of this study was to create a prognostic model consisting of disease phenotypical as well as biochemical variables.
692 PSC patients were identified in a large population based PSC cohort from the Netherlands. Variables of PSC phenotype, biochemistry results and long term follow-up data were retrieved from patient records. Clinical endpoints were development of cholangiocarcinoma, LT, or PSC-related death. Laboratory values were transformed by log transformation, missing values were imputed by multiple imputation. All variables were assessed as potential predictors of survival by univariate analysis. To calculate the prognostic index (PI), Cox proportional hazards model was developed and internally validated with bootstrap.
Results: The median follow-up time was 85 months (range 0-468 months). All phenotypical variables and biochemistry results were considered for the model. After variable selection by LASSO, multivariable Cox models were fitted, and parameters estimated from 20 imputation datasets were averaged. The following formula was created:
PI = 1.374*PSC type(0/1)[1] + 0.023*Age at diagnosis PSC - 2.643*logAlbuminxULN^2 + 2.029*abs(logTrombocytesxULN-0.5)^2 + 0.544*logAspartate aminotransferase(AST)xULN^2 + 0.683*logAlkakaline phosphatase(ALP)xULN^2 + 0.430*logTotal bilirubinxULN^2
1: PSC type: Large duct = 1; Small duct = 0
2: xULN = times upper limit of normal
The PI yielded a c-statistic of 0.7180 (0.7080 after adjusted for optimism with 1000 times bootstrap).

Conclusion: By using a population-based PSC cohort, we were able to create a prognostic model based on PSC type, age at diagnosis PSC, albumin, thrombocytes, AST, ALP and total bilirubin. Internal validation using bootstrap showed adequate performance. The inclusion of biochemistry could facilitate the dynamic prediction of PI over time.
Disclosure of Interest: None declared

OP121 A SURVEY OF DRUG-INDUCED LIVER INJURY (DILI) CASES IN JAPAN

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Introduction: Drug-induced liver injury is an important cause of acute liver injury and the incidence of drug-induced liver injury seems to be increasing with the increase in the numbers of new drugs.
Aims & Methods: We retrospectively surveyed Japanese DILI cases until February 2015 from 25 hospitals.
Results: The total of 234 cases (97 cases of male and 137 cases of female) were distributed between 17 and 84 years old (average 57 years old), and were classified to 154 cases (66%) of the hepatocellular type, 32 cases (14%) with the mixed type and 48 cases (20%) with the cholestatic type according to the type of liver injury. The percentage of the hepatocellular type was increased compared to previous studies. Eosinophilia (>5%) was observed in 62 cases (26%). Drug-induced lymphocyte stimulation test (DLST) was performed in 136 cases (58%), and was positive in 67 cases (49%). According to the diagnostic scale of the Digestive Disease Week (DDW)-Japan 2004 (*Hepatol Res* 2005; 32: 250), 197 cases (93%) were diagnosed as highly probable and 13 cases (6%) as possible. Among DILI cases, 18% occurred within 7 days, 27% occurred within 14 days, 52% occurred within 30 days, 70% occurred within 60 days, 77% occurred within 90 days after starting drug administration. Percentages of causal drugs were as follows; 12% by antimicrobial drugs, 10% by anti-inflammatory drugs, 9% by drugs for the gastrointestinal system and drugs for the psychiatry and neurological system, 8% by anti-cancer drugs and dietary supplements. To clarify whether genetic factors are involved in the susceptibility of DILI, genetic association study was performed using DILI patients and healthy controls. Specific HLA types and several single nucleotide polymorphisms (SNPs) were significantly associated with the susceptibility of DILI on their type (the hepatocellular type, the mixed type, the cholestatic type).
Conclusion: Further storage of DILI cases and DNA samples will accelerate the characteristics of DILI cases in Japan.
Disclosure of Interest: None declared

OP122 HYBRID DRAINAGE USING A NASOBILIARY TUBE FOR TREATING ACUTE CHOLECYSTITIS

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Introduction: Emergency or early laparoscopic cholecystectomy is the standard treatment for patients with acute cholecystitis. However, in cases with hospital situations or because of patients' conditions, conservative treatment with antibiotics, followed by drainage and elective surgery may be performed as an alternative. For such cases, we developed a hybrid gallbladder drainage procedure that facilitates both external and internal drainage in a single session.
Aims & Methods
Aims: To prospectively evaluate efficacy and safety the hybrid gallbladder drainage in acute cholecystitis.
Methods: Patients with mild or moderate cholecystitis diagnosed according to the Tokyo guidelines 2007 (TG07) were enrolled if they wished to undergo elective surgery. The procedure was performed as follows: 1) place the nasobiliary drainage (NBD) tube in the gallbladder under endoscopic guidance, 2) lavage the gallbladder using 100-200 mL saline without removing the scope, 3) insert the guidewire through the NBD tube, 4) remove the NBD tube while measuring the length from the fundus of the gallbladder to the papilla, 5) cut the tube to the measured length, and 6) insert the trimmed tube into the gallbladder for internal drainage. The main outcome measurements were procedural success rate, clinical success rate, complication rate, procedure time, and duration of hospital stay.
Results: In all, 54 patients (median age, 69 years [range, 34-92], male: 27, female: 17) were included. Cholecystitis was mild in 18 patients (33%) and moderate in 36 patients (67%). The procedure was successful in 43 patients (80%). The total time taken for the procedure was a median of 54 min (range, 13-120). The cut length of the NBD tube was 25 cm (range, 17-35). A minor complication of bile leak from the cystic duct occurred in 2 patients (3.7%). The procedure was unsuccessful in 11 patients of the total 54 patients: complications occurred in 2 and the technical failure in 9, all of whom required percutaneous transhepatic gallbladder drainage (PTGBD). Among the 43 patients in whom the procedure was successful, 42 (98%) showed clinical success. Delayed elective cholecystectomy was performed in 48 patients (89%), and recurrent cholecystitis was not observed during the waiting time of a median of 42 days (range 9-138). The median duration of hospital stay was 8 days (range, 2-76). The duration of hospital stay in patients with procedural success was significantly shorter than in those with procedural failure (7 versus 14.5 days, $P < 0.01$).
Conclusion: Hybrid drainage using the nasobiliary tube for acute cholecystitis is efficient and safe. This procedure may be alternative if emergency/early surgery is impossible because of various causes.
Disclosure of Interest: None declared

OP123 POSTOPERATIVE ANTIBIOTIC USE IN THE TREATMENT OF ACUTE CHOLECYSTITIS: A RANDOMIZED, MULTICENTRE, NONINFERIORITY TRIAL

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Introduction: Acute calculous cholecystitis is a common diagnosis in the surgical practice with a clear indication for surgery. Among surgeons, there is no consensus regarding the use of extended antibiotic prophylaxis and it's use is mainly dependent on the clinical condition of the patient, perioperative findings and the surgeon's preference.
Aims & Methods: To determine the effect of extended antibiotics on postoperative infection rate in patients undergoing cholecystectomy, we conducted a multicentre randomized non-inferiority trial. We hypothesized that extended postoperative antibiotic treatment would not decrease the infectious complication rate. Based on a noninferiority margin of 5% and power of 80%, 78 patients were required in each groups. Patients with acute calculous cholecystitis undergoing cholecystectomy were eligible, provided that the APACHE-II score was 6 or less. Study participants were randomly assigned to a single pre-operative prophylactic dose of cefazoline (2000mgs) 15-30 minutes prior to incision (group A), or postoperative antibiotic treatment (cefuroxime 750mgs 3dd and metronidazole 500mgs 3dd intravenously during three days) in addition to a single prophylactic dose (group B). Primary endpoint was the occurrence of postoperative infections (wound infection, intra-abdominal abscess, pneumonia, urinary tract infection). Secondary endpoints were other postoperative complications, hospital stay and total costs. Analysis was by intention-to-treat.
Results: Between 2012 and 2014 a total of 156 patients were randomized in 6 teaching hospitals: 76 patients in group A and 80 patients in group B. Male/female ratio, age and APACHE-II score (average 3.5) were comparable between groups. Primary endpoint occurred in 3 patients (4%) in group A and in 3 patients (3.8%) in group B (RR 1.04, 95% CI 0.22-4.99; $p = 0.99$). Other postoperative complications occurred in 4 and 5 patients respectively (NS).
Conclusion: In patients with mild calculous cholecystitis, extended postoperative antibiotic treatment did not lead to a decrease of infectious complications.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 15:45-17:15
NORMAL AND ABNORMAL UPPER GI FUNCTION - ROOM E6

OP124 ANTICIPATORY FEAR MODULATES PERCEPTUAL AND NEURAL RESPONSES TO SUBSEQUENT GASTRIC PAIN IN HEALTH

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Introduction: Malfunction of descending pain modulatory pathways is believed to be playing an important role in the pathophysiology of pain-predominant functional gastrointestinal disorders such as Functional Dyspepsia (FD). Results from studies that combine neuro-imaging techniques with psychophysical methods suggest this 'top-down' modulation of pain transmission is heavily influenced by affective and cognitive psychological processes such as anticipatory fear. However, studies on the effect of anticipation on visceral pain perception are currently sparse, particularly for gastric pain.
Aims & Methods: We aimed to investigate the relationship between anticipatory fear and the subsequent perception of gastric pain, both at behavioural and neural level. We hypothesized a positive association between anticipatory fear and subsequent responses to gastric pain.
Fifteen healthy volunteers (5 men, mean age: 31.8 ± 2.27) participated in this study. Brain responses during cued certain (100% chance of receiving the painful stimulus) and safe anticipation (0% chance of receiving the painful stimulus, control condition) and subsequent gastric balloon distension at individually titrated pain threshold ($certain_{pain}$) or no balloon distension ($safe_{no\_pain}$, control condition) were measured using functional magnetic resonance imaging (fMRI). Ratings of anticipatory fear and pain intensity were collected using visual analogue scales (0-10) during scanning. Robust regression was used to test the association between anticipatory fear and pain intensity ratings. The relationship between anticipatory brain activity and pain intensity ratings and, vice versa, between anticipatory fear ratings and brain responses during the subsequent pain induction were investigated using SPM8 (whole-brain voxel-based analysis with voxel-level threshold of $p_{uncorr} < .005$ combined with a cluster-level threshold of $p_{FWE\text{-}corr} < .05$).

Results: Subjects rated fear significantly higher during certain compared to safe anticipation (3.93 ± 0.59 and 0.35 ± 0.13, respectively). Pain intensity ratings during subsequent pain induction were also higher ($certain_{pain}$: 5.78 ± 0.45; $safe_{no\_pain}$ 0.18 ± 0.06). Average anticipatory fear ratings during certain compared to safe anticipation were positively associated with average pain ratings during $certain_{pain}$ compared to $safe_{no\ pain}$ ($\Delta certain_{pain} - safe_{no\ pain}$) ($\beta = 0.37 \pm 0.23$, $p < .001$). Significant positive correlations of brain responses during certain anticipation with subsequent pain ratings were found in the insula, basal ganglia, anterior, mid- and posterior cingulate cortex , ventrolateral and –medial prefrontal cortex. Vice versa, fear ratings during anticipation were positively correlated with brain activity during subsequent gastric pain in the insula, midcingulate cortex and caudate nucleus.
Conclusion: This study demonstrated for the first time that behavioural and brain responses (at the level of the ''visceral pain neuromatrix'') during anticipatory fear are associated with increased perceptual and neural responses to gastric pain induction. This may explain how (anticipatory) fear impacts on visceral sensitivity and symptom reporting in FD.
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OP125 GPR84 PLAYS A ROLE IN THE PATHOGENESIS OF REFLUX DISEASE

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Introduction: Gastro-esophageal reflux disease (GERD) is one of the most common disorders in gastroenterology. Patients present with or without increased acid exposure indicating a non-uniform etiology. Thus the common treatment with proton pump inhibitors (PPIs) fails to control symptoms in up to 40% of patients.
Aims & Methods: To further elucidate the pathophysiology of the condition and explore new treatment targets, transcriptomics, proteomics and histological methods were applied to a surgically induced sub-chronic reflux esophagitis model in Wistar rats[1,2] after treatment with either omeprazole (PPI) or STW5, a herbal preparation shown to ameliorate esophagitis without affecting refluxate pH. The normal human esophageal squamous cellline HET-1A and human endoscopic biopsies were used to confirm our findings to the G-protein coupled receptor (GPR)84 in human tissue.
Results: Both treatments reduced reflux-induced macroscopic and microscopic lesions of the esophagi as well as known pro-inflammatory cytokines. Proteomic and transcriptomic analyses identified CINC1-3, MIP-1/3α, MIG, RANTES and IL-1β as prominent mediators in GERD[2]. Most regulated cyto-/chemokines are linked to the TREM-1 signaling pathway. The fatty acid receptor GPR84 was one of the most highly up-regulated genes in esophagitis (32.5x) but significantly decreased in treated groups, a finding supported by Western blot and immunohistochemistry in both rat tissue and capsaicin treated HET-1A cells. GPR84 was also found to be significantly up-regulated in patients with grade B reflux esophagitis.
Conclusion: The expression of GPR84 in esophageal tissue and its potential involvement in GERD are reported for the first time. IL-8 (CINC1-3) and the TREM-1 signaling pathway are proposed, besides GPR84, to play an important role in the pathogenesis of GERD.

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Disclosure of Interest: H. Abdel-Aziz Conflict with: employee of Steigerwald Arzneimittelwerk GmbH, M. Schneider: None declared, W. Neuhuber: None declared, A. M. Kassem: None declared, S. Khailah: None declared, H. Gamaleldeen: None declared, A. Khairy: None declared, M. Khayyal: None declared, T. Efferth: None declared, G. Ulrich-Merzenich: None declared

OP126 ENDOSCOPIC STOMACH VOLUME ESTIMATION FOR BARIATRIC ENDOLUMINAL GASTROPLASTY: ANIMAL VALIDATION STUDY

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Introduction: The shape of stomach is variable among individuals and conditions, so estimation of stomach volume is still difficult even though the recent development of various imaging modalities (CT or MRI). We proposed the possibility of endoscopic stomach volume estimation previously (*Digestive Disease Week* 2014, Mo1154). In this study, we aimed to validate the accuracy and value of endoscopic stomach 3D reconstruction and volume estimation using extracted porcine stomachs.
Aims & Methods: Three extracted porcine stomachs were used to test the accuracy of endoscopic stomach volume estimation. First, internal dimensions of porcine stomachs were measured using endoscopic guide-wire. Then, 3D stomach models were reconstructed using 3D graphic software (Cinema4D R12, MAXON Computer, Germany). Stomach volumes were estimated from the reconstructed 3D models and these results were compared with the real volumes measured by filling the stomach with water. Second, we performed bariatric gastroplasty using our novel endoscopic suture device (Endoscopy 45(8): 655-660), aiming to reduce the stomach volume by 30%. In this step, we took advantage of previously constructed 3D stomach model by simulating the most suitable gastroplasty for predetermined volume reduction. After gastroplasy, real volume of deformed stomachs were measured by filling with water.
Results: Stomach volume estimation by endoscopy was relatively accurate (mean error was about 10% of stomach volume). In addition, planned bariatric gastroplasty for predetermined stomach volume reduction by endoscopic suture device was possible with the help of simulation using 3D graphic software, which was not feasible by random suturing.
Conclusion: Endoscopic stomach 3D reconstruction and volume estimation was useful, accurate method, which can be used for the future tailored bariatric treatment.

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Disclosure of Interest: None declared

OP127 THE EXPRESSION OF RECEPTORS FOR NEUROTROPHINS AND NEUROTROPHIC FACTORS IN THE VAGAL AND SPINAL AFFERENT NEURONS INNERVATING THE STOMACH IN THE RAT

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Introduction: TRPV1-positive primary afferent neurons innervating the stomach have chemosensory and/or nociceptive function thus playing an important role in reflex regulation and perception. Neurotrophins and neurotrophic factors are often produced in inflammation and can induce neural plasticity that contributes to reflex dysregulation and pain. However, the neurotrophic regulation of afferent neurons innervating the stomach is incompletely understood.
Aims & Methods: Here we address the hypothesis that the vagal nodose and spinal dorsal root ganglia (DRG) neurons innervating the rat stomach have distinct expression profiles of receptors for neurotrophins and neurotrophic factors. Nodose and DRG neurons retrogradely traced following DiI injection into the stomach wall (along the major curvature) were individually analyzed by single cell RT-PCR. We evaluated the expression of mRNA for receptors TrkA, TrkB, and TrkC for neurotrophins from the NGF family (NGF, BDNF and NT-3, respectively), and the GFL co-receptor subunits GFRalpha1, GFRalpha 2, and GFRalpha 3 for the neurotrophic factors from the GDNF family (GDNF, neurturin and artemin, respectively).
Results: Total 142 nodose and 31 DRG neurons labeled from the stomach in 25 rats were analyzed. 93/142 gastric nodose neurons were positive for TRPV1. The gastric nodose TRPV1+ neurons often expressed receptors consistent with chemosensory function including TRPA1 (11/21), adenosine A1 receptor (13/27), bradykinin B2 receptor (8/21), and serotonin 5-HT3 receptor (11/27). In contrast, gastric nodose TRPV1- neurons that probably have mechanosensory function virtually lacked these receptors. The gastric nodose TRPV1+ neurons nearly uniformly expressed TrkB (23/27), often expressed GFRalpha1 (10/18) and occasionally expressed GFRalpha2 (6/18) and TrkA (8/27), but essentially did not express GFRalpha3 (2/27) and TrkC (0/45). In comparison, the gastric DRG TRPV1+ neurons expressed more frequently TrkA (17/18, $p < 0.01$ vs. nodose) and GFRalpha3 (11/18, $p < 0.01$), slightly less frequently TrkB (10/18, $p < 0.05$) and similarly GFRalpha1 (11/18). Gastric DRG neurons occasionally expressed TrkC (5/18), but almost never GFRalpha2 (1/18). In TRPV1-negative populations the receptors for neurotrophins and neurotrophic factors were poorly expressed in gastric nodose TRPV1- neurons (only TrkB and GFRalpha2 were occasionally detected), but the expression of TrkA, TrkB and GFRalpha1 in gastric DRG TRPV1- neurons was largely similar to that in gastric DRG TRPV1+ neurons.
Conclusion: The vagal nodose and spinal DRG neurons innervating the rat stomach differentially express mRNA for multiple receptors for neurotrophins and neurotrophic factors. Gastric nodose and DRG TRPV1-positive neurons differ in the expression profile of neurotrophins and neurotrophic factors. While the majority of gastric nodose neurons will be influenced by BDNF through TrkB, the majority of gastric DRG neurons will be influenced by NGF through TrkA. A proportion of both gastric nodose and DRG neurons will be influenced by GDNF through GFRalpha1, but only the gastric DRG neurons will be influenced by artemin through GFRalpha3.

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Disclosure of Interest: None declared

OP128 ACTIVATION OF GASTRIC BITTER TASTE RECEPTOR BY QUININE HYDROCHLORIDE EFFECTS ON INTRAGASTRIC PRESSURE PROFILES AND NUTRIENT TOLERANCE IN HEALTHY VOLUNTEERS

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Introduction: Bitter taste receptors are expressed in the stomach and the duodenum but their function is unclear.
Aims & Methods: We conducted a single-blind crossover trial in healthy volunteers (HVs) who were administered 10 μmol/kg QHCl or placebo intragastrically 30 min before the experimental protocol started.
Drinking test (DT): 10 HVs (age 28 ± 3; BMI 22 ± 1) were asked to drink a nutrient drink (ND; 30% fat, 42% carbohydrate, 28% protein) (15mL/min) until maximum satiation. Satiation was scored every 5 minutes on a 0-5 scale.
Intragastric pressure (IGP) and nutrient tolerance: A high-resolution manometry (HRM) probe was placed via the nose till the duodenum in 12 HVs (age 34 ± 1; BMI 22 ± 2; protocol 1). ND was intragastrically infused (60mL/min) until maximum satiation, when it was stopped. Satiation score was scored every minute. Thereafter, IGP was measured for 4 hours.
Gut peptides: To analyze plasma levels of gut peptides, blood samples were collected before treatment, before the ND infusion, every 15 min for the first hour after the ND and then every 30 min till the end.
IGP was measured as average pressure over 5 channels in the fundus; 5 minutes before ND start was taken as baseline. All data are expressed as mean ± SEM. Outcomes were compared with paired t-test (ND tolerance, total area above the curve (AAC) and max IGP drop during ND infusion), or mix-model analysis (hormones).
Results: *DT*: The amount of ND tolerated was significantly inhibited by QHCl (721.5 ± 93.4 ml) compared to placebo (846 ± 88.5 ml) (p = 0.04). Satiation scores after QHCl tended to be higher (p = 0.09).
IGP and nutrient tolerance: During the intragastric ND infusion, the IGP decreased initially and gradually increased thereafter both after placebo and QHCl. After QHCL, the max IGP drop (7 ± 1 mmHg vs. 3 ± 1 mmHg p = 0.03) and the AAC of the IGP drop (64 ± 12 mmHg*min vs 11 ± 1 mmHg*min, p = 0.01) were significantly suppressed, consistent with inhibition of gastric accommodation. Post-prandial IGP profiles did not differ between the two treatments. Satiation scores tended to be higher after QHCl (p = 0.06), and the volume of ND ingested at maximum satiation was significantly lower after QHCl (805 ± 82 vs 660 ± 56 ml, p = 0.05).
Gut peptides: Both GLP-1 and motilin plasma levels did not differ between both conditions.
Conclusion: Intragastric administration of QHCl inhibits gastric accommodation and decreases nutrient volume tolerance. These effects do not seem to be mediated by altered GLP-1 or motilin release. The mechanism involved in this action, and its application in the treatment of obesity, warrant further study.
Disclosure of Interest: None declared

OP129 NA+/CA2+ EXCHANGER 2-HETEROZYGOTE KNOCKOUT MICE DISPLAY INCREASED RELAXATION IN GASTRIC FUNDUS

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Introduction: The movements of the contents of the gastrointestinal tract rely on the coordinated contractions and relaxations of the smooth muscles that surround each specialised region. For contraction and relaxation to occur, the intracellular Ca^{2+} concentration must be altered upward and downward. The Na^{+}/Ca^{2+} exchanger (NCX) is a plasma membrane transporter involved in regulating intracellular Ca^{2+} concentrations.
Aims & Methods: We focused on Ca^{2+} movement through NCX, especially NCX2, on gastrointestinal tract motility because Ca^{2+} homeostasis is central to the regulation of smooth muscle function. To obtain further insight in the physiological roles of NCX2 in gastrointestinal motility, we used an organ tissue bath system to characterize motor function of circular smooth muscle segments from the gastric fundus.
Results: We initially investigated the expression and localization of NCX2 in the gastric fundus of WT using immunofluorescent staining. Strong immunoreactivity of NCX2 was observed within the myenteric plexus layers. Immunoreactivity of NCX2 was observed in the longitudinal and circular muscle layers as well as in the myenteric plexus layers. Electrical field stimulation (EFS) induced a rapid relaxation that showed during the stimulus, and a sustained relaxation, that persisted after the end of the stimulus. We found that the amplitudes of EFS-induced rapid relaxation and sustained relaxation after EFS were greater in NCX2 heterozygote mice (NCX2 HET) than in wild-type mice (WT). In the experiments in which inhibitor of nitric oxide synthase was added following the EFS, NCX2 HET exhibited no EFS-induced rapid relaxation similar to those of WT. In the experiments in which PACAP antagonist was added following the EFS, furthermore, sustained relaxation after EFS in NCX2 HET was similar in amplitude to that of WT. Because there is expression of NCX2 in circular smooth muscles as well as in neurons of the myenteric plexus layers, we determined whether NCX2 deficiency affects relaxation in response to NO and PACAP in smooth muscle cells. NCX2 HET demonstrated magnitudes of NOR-1-induced and PACAP-induced relaxations were similar to those of WT. Therefore, we can exclude the possibility that the NCX2 deficiency of smooth muscle cells enhances their sensitivity to NO and PACAP.
Conclusion: In this study, we demonstrate that NCX2 expressed in the neurons regulates the motility in gastric fundus.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 15:45–17:15
ENDOSCOPIC SUBMUCOSAL DISSECTION IN THE UPPER GI TRACT – ROOM B3

OP130 EFFICACY OF ENDOSCOPIC SUBMUCOSAL DISSECTION WITH DENTAL FLOSS CLIP TRACTION FOR GASTRIC EPITHELIAL NEOPLASIA: A PILOT STUDY

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Introduction: Providing appropriate tension to the lesion and securing a stable view of the submucosal layer are important to accomplish a successful endoscopic submucosal dissection (ESD). Dental floss clip traction (DFC), a new traction method, is expected to reduce the difficulty of ESD [1].
Aims & Methods: The objective of this pilot study was to investigate the efficacy of DFC for gastric ESD.
From August to November 2014, a total of 95 patients with 104 gastric epithelial neoplasms underwent DFC ESD (DFC group) at a cancer referral center. Historical controls treated by conventional ESD (control group) were individually matched to cases with a 1:1 ratio by the location of the lesion, the presence of ulcer findings, the resected specimen size, and the proficiency of the operator (trainee / expert). The outcomes of the procedure in two groups were then compared.
DFC was performed as follows: after circumferential mucosal incision, the clip tied with a dental floss was applied to the edge of the lesion. The anchored dental floss was continuously pulled per-orally with a gentle manual traction.
Results: The mean (SD) procedure time was 43 ± 24 minutes in the DFC group and 52 ± 30 minutes in the control group (P < 0.01). Fewer lesions in the DFC group needed more than 80 minutes compared with the control group (3 cases vs 16 cases, P = 0.01). There were no significant differences in adverse events between the groups. Perforation and delayed bleeding occurred in 1 lesion (1%) and 4 (4%) in the DFC group, and 3 (3%) and 9 (9%) in the control group, respectively. En bloc resection was achieved in all cases. No significant difference was found in regard to the curability of ESD between the groups.

Table: Results of DFC ESD

	DFC (n = 104)	Controls (n = 104)	P value
Procedure time, mean ± SD, min	43 ± 24	52 ± 30	< 0.01
Procedure time ≥ 80min, n	3	16	0.01
Adverse events, n			
Perforation	1	3	0.31
Delayed bleeding	4	9	0.36
Damage of specimen, n	0	0	-
En bloc resection, n	104	104	-
HM+	0	0	-
VM+	3	4	0.17
Curability, n			0.84
Curative resection	88	87	
Noncurative resection	16	17	

HM, horizontal margin involvement; VM, vertical margin involvement

Conclusion: DFC efficiently reduced the procedure time of ESD without increasing adverse events. DFC is helpful for a quick and safe ESD.

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Disclosure of Interest: None declared

OP131 COMPARISON OF O-TYPE HYBRIDKNIFE TO CONVENTIONAL KNIFE IN ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC MUCOSAL LESIONS: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic submucosal dissection (ESD) has been accepted as a minimal invasive alternative to surgery for localized superficial gastrointestinal neoplasms recently. However, the procedure remains to be technically challenging and time consuming. A new dissecting knife with partially insulated tip has been recently developed with built-in injection capability.
Aims & Methods: The purpose of this study was to investigate whether the efficiency of ESD procedure could be improved with this new device. A total of 78 patients, who underwent ESD with gastric mucosal lesions including flat type polyps, adenoma or early gastric cancer, were randomly assigned to either ESD with O-type HybridKnife or conventional ESD knives without waterjet. Procedure time and related factors of ESD were analyzed.
Results: ESD procedure time was 43.0 (Interquartile range, IQR 27.0 - 60.0) minutes in HybridKnife group compared to 60.5 (IQR 44.0 - 86.3) minutes in the control group ($P = .001$). There was no difference in the clinical outcome and the adverse event rate. The former demonstrated more favorable results in lesions ≤ 4 cm of specimen size ($P \leq .0001$) and when located in the distal stomach ($P = .001$), also in lesions with fibrosis ($P = .008$). Multivariate regression analysis showed that O-type Knife ($P \leq .0001$), specimen size ($P \leq .0001$) and fibrosis ($P \leq .0001$) were independent predictors of procedure time.
Conclusion: The O-type HybridKnife yields faster procedure time compared to the conventional knives in gastric ESD with a similar safety profile.

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Disclosure of Interest: None declared

OP132 FURTHER EXPANDED INDICATIONS OF ENDOSCOPIC RESECTION FOR EARLY GASTRIC CANCER IN ELDERLY PATIENTS

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Introduction: Early gastric cancers (EGCs) are increasingly encountered in elderly patients, and endoscopic resection (ER) is expected to cover a larger part of the treatment of EGCs in the elderly as it is a less invasive procedure than surgery. However, the widely accepted ER indications stated in the Japanese gastric cancer treatment guidelines, in which ER is indicated only for EGCs with nominal risk of lymph node metastasis (LNM), may be too strict for elderly patients. Management of elderly EGC patients, including the selection of ER or surgery, should be done taking their life expectancy into consideration; this way of thinking could lead to more expanded ER indications for them.
Aims & Methods: The aim of this study was to examine further expanded ER indications in elderly EGC patients (aged $\geq$80 years) based on the data on the risk of LNM in EGC and the overall survival in the elderly. We obtained the LNM risk data from our large retrospective study of 3,131 EGCs undergoing gastrectomy with lymphadenectomy at our institution between 1997 and 2013. These cases were analyzed for the percentage of positive LNM according to the conditions of tumor size, depth, histological type, ulcerative finding (UL), and lymphovascular involvement (LVI). The overall survival rates of the elderly were calculated at the Division of Surveillance, Center for Cancer Control and Information Services at our institution on the basis of the abridged life tables for Japan in 2013.
Results: The percentage of positive LNM in each EGC subgroup in the 3,131 cases, stratified by tumor size, depth, histological type, UL, and LVI, varied considerably from 0% to >50%, even among the noncurative subgroups according to the current guidelines. The 5-year overall survival rates of 80-, 85-, and 90-year-old Japanese were as follows: male, 69.5, 53.1, 34.9%; female 83.7, 69.4, 49.3%, respectively. Several EGC subgroups, for which the upper limit of 95% confidence interval (CI) of the percentage of positive LNM was lower than the 5-year total mortality of 80-year-old females (16.3%), were extracted as follows in addition to the current guidelines' curative subgroups: a) size >3 cm, UL (+), pure differentiated type, depth: mucosa, LVI (−) (positive LNM percentage with 95% CI: 0%, 0–2.9), b) size $\leq$2 cm, UL (+), pure undifferentiated type, depth: mucosa, LVI (−) (4.8%, 3.2–7.0), c) size >2 cm, pure undifferentiated type, depth: mucosa, LVI (−) (5.4%, 3.5–7.8), d) size >3 cm, pure differentiated type, depth: submucosa <500 μm, LVI (−) (1.6%, 0–8.7), e) size $\leq$3 cm, pure differentiated type, depth: submucosa $\geq$500 μm, LVI (−) (5.7%, 2.3–11.5). For elderly populations of older age and/or different sex, more subgroups were extracted in which the upper limit of 95% CI of the positive LNM percentage was lower than the 5-year total mortality.
Conclusion: Considering the extensive variation in LNM risk in EGC according to the lesion characteristics and the overall survival rates of the elderly, it is postulated that ER can be performed as a first-line treatment for more EGC subgroups than are stated in the current guidelines in elderly patients. In addition, after ER, the necessity of surgery can be more properly judged on the basis of the pathological results of the ER specimen and our detailed LNM risk data.
Disclosure of Interest: None declared

OP133 A COMBINATION METHOD OF SUBMUCOSAL TUNNELING ENDOSCOPIC RESECTION AND ENDOSCOPIC FULL-THICKNESS RESECTION FOR THE TREATMENT OF LARGE UPPER GASTROINTESTINAL SUBMUCOSAL TUMORS ORIGINATING FROM THE MUSCULARIS PROPRIA LAYER

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Introduction: Endoscopic full-thickness resection (EFR) can be adequately adopted as an effective treatment for upper gastrointestinal (GI) subumucosal tumors (SMTs) originating from the muscularis propria (MP) layer. However, the skills are more demanding for the endoscopist to seal the wall defect and the risks of GI tract leakage and/or secondary infection further limit the application of EFR. A new procedure, submucosal tunneling endoscopic resection (STER), has been developed to overcome these potential risks via the maintenance of GI tract mucosal integrity. However, the resectable lesion size of STER is limited by the relatively narrow space of the submucosal tunnel. Herein, we used a combination method of STER and EFR for the treatment of large upper GI SMTs originating from the MP layer.
Aims & Methods: Five patients with large upper GI SMTs from the MP layer were included. A submucosal tunnel was created to expose the large tumor as much as possible. EFR was further performed to completely remove the large tumor. Although mucosal perforation was unavoidable due to the large tumor

Abstract number: OP131 Table Univariate analysis of factor related with procedure time

	IT knife	HybridKnife	P value*
Specimen size, Median (mm) (IQR)	40.0 (31.5-50.0)	35.0(30.0-48.0)	*0.866*
Overall median procedure time (min) (IQR)	60.5(44.0-86.3)	43.0(27.0-60.0)	*0.001*
Median procedure time according to locations (min) (IQR)			0.3690.0540.012
U	60.0(33.0-128.5)	43.5(27.5-75.8)	
M	54.0(45.5-95.3)	43.0(27.0-60.0)	
L	64.0(47.5-87.5)	33.0(21.3-43.0)	
Median procedure time according to specimen sizes (min) (IQR)			<0.00010.455
≤40mm	60.0(41.0-84.0)	29.0(21.3-43.0)	
> 40mm	66.0(51.0-99.0)	62.0(43.0-82.0)	
Median procedure time according to fibrosis (min) (IQR)			0.0170.008
No	55.0(38.5-77.5)	37.0(26.5-56.0)	
Yes	63.0(75.0-207.0)	57.5(41.5-66.3)	
Median procedure time according to histology of lesion (min) (IQR)			0.1190.006
Non-Ca	53.0(29.0-79.0)	36.0(23.0-43.0)	
Ca	66.0(47.0-93.0)	43.5(27.8-66.5)	
Median submucosal dissection time (min) (IQR)	34.0(21.0-53.3)	24.0(12.0-38.0)	0.003
Median non-submucosal dissection time (min) (IQR)	26.0(18.0-36.0)	16.0(12.0-27.0)	0.005

U, lower third; M, middle third; U, upper third; Ca, cancerous lesion; Non-Ca, Non-cancerous lesion; IQR, interquartile range.*Due to deviation from normal distribution indicated by Shapiro-Wilk test, Mann-Whitney's U statistic was used to compare medians.

and limited submucosal space, most part of the normal mucosa covering the tumor was protected and the mucosal integrity was easily repaired with several hemostatic clips.
Results: Of the five lesions, 2 were located in the esophagus, 2 in the cardia, and 1 in the gastric antrum. The mean tumor size was 6.6 cm (range 5.0-10.0 cm). The combination procedure was successfully performed in all patients with piecemeal resection of tumors. The operation time ranged from 70 to 180 min (mean, 133.3 min). Mucosal perforations occurred in all cases and were clipped successfully. All complications related to the procedure were successfully managed with conservative treatments. Local recurrence or distant metastasis did not occur during follow-up.
Conclusion: The combination of STER and EFTR is a safe and effective therapeutic strategy for large upper GI SMTs originating from the MP layer. This method can maintain the mucosal integrity as much as possible while achieving completely full-thickness resection of the large tumor.

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Disclosure of Interest: None declared

OP134 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR GASTRIC CANCER INVADED TO THE SUBMUCOSA: A RESULT OF A PROSPECTIVE STUDY OF THE EXPANDED INDICATION OF ESD

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Introduction: ESD is a promising endoscopic treatment for early gastric cancer (EGC) without lymph node metastasis, and an expanded indication of ESD for EGC is proposed including some submucosal cancers (Soetikno R., et al. J Clin Oncol. 23:4490-98, 2005). However, it is not fully reported about long-term outcomes of ESD for them. The aim of this study was to evaluate short-term and long-term outcomes of ESD for submucosal gastric cancers which were recruited in a prospective study regarding the expanded indication of ESD.
Aims & Methods: We previously designed a prospective study in which ESD was applied in patients with differentiated-type EGC up to 30 mm in diameter regardless of ulceration or above 30 mm without ulceration, but definite signs of submucosal invasion. As for cancers invaded to the submucosa diagnosed after ESD, ones less than 500um in depth (SM1) and less than 30mm in size were followed up, and otherwise were advised to be operated on additionally. We assessed short-term and long-term outcomes of ESD for them. Followed-up endoscopic examinations were performed 6 months later, and then every 6 months.
Results: We finally performed ESD in 81 patients with submucosal cancers (SM1; 32, SM2 (deeper invasion than SM1); 49 cases) from April 2006 to March 2013. Cancers were resected en bloc in all patients, and R0 resection were achieved in 72 (89%) patients. The rest, who had all SM2 cancers (range 800-3500μm in depth), had positive vertical margin. In the SM1 cancers, 23 were less than 30mm in size and the patients were followed up. Two of the rest of 9 SM1 patients received surgery. In the 49 patients with SM2, 38 received surgery and the rest refused it. In totally 40 (49%) patients who received surgery, lymph node metastasis were found in 3 patients (7%; all were SM2 cancers more than 2000μm in depth), and the residual cancer were found in 3 patients. In 41 followed-up patients, local recurrence was detected in one (2%) patient, and the subsequent cancer was detected in 8 (20%) patients (median follow-up period 49 months (range 3-106 months)). None of these patients died from gastric cancer, and 7 patients died from other disease.
Conclusion: The short-term and long-term outcomes of ESD for those patients would be preferable. ESD could not only bring accurate diagnosis by en bloc resection, but produce local control of the EGC even in patients with SM2 cancers.
Disclosure of Interest: None declared

OP135 PREVENTION OF BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC NEOPLASMS USING POLYGLYCOLIC ACID SHEETS AND FIBRIN GLUE

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Introduction: For bleeding after endoscopic submucosal dissection (ESD) for gastric neoplasms, no preventive method has been established other than preventive coagulation of visible vessels on the artificial ulcer after ESD or the usage of proton pump inhibitors. We have reported that the endoscopic tissue shielding method with polyglycolic acid (PGA) sheets and fibrin glue can reduce the risk of post-ESD bleeding.
Aims & Methods: The aim of this study is to evaluate the efficacy of PGA sheets and fibrin glue for preventing bleeding after gastric ESD after accumulating more cases. This is a non-randomized historical controlled study. We defined high-risk patients for post-ESD bleeding as follows: 1) those who took antithrombotic drugs regularly; or 2) those expected to undergo large mucosal resection ($\geq$ 40mm). We enrolled patients scheduled to undergo gastric ESD and had above-mentioned risk factors from July 2013 as the study group (Group A). Immediately after ESD we placed PGA sheets on the mucosal defect and fixed them with fibrin glue in the study group. We extracted high-risk patients from those who had undergone gastric ESD at our institution before the enrollment of the first study patient, and defined the group as the historical control group (Group B). The post-ESD bleeding rate was the primary endpoint in comparative analysis.
Results: From July 2013 to October 2014, 98 ESD-induced ulcers in 91 high-risk patients were enrolled in Group A. In Group B, 91 ESD-induced ulcers in 84 consecutive patients were extracted between January 2012 and July 2013. There was a significant difference in antithrombotic drugs use (A: 62 lesions, 63.3%, B: 44, 48.4%; $P = 0.039$), but the other baseline characteristics were not significantly different between the two groups: sex (A: male 86/female 12, B: male 73/female 18; $P = 0.156$); age (A: 71.8 ± 8.2 yrs, B: 73.3 ± 7.9 yrs; $P = 0.229$); Heparin bridging therapy (A: 18 lesions, 18.4%, B: 10, 11.0%; $P = 0.151$); and the diameter of resected specimens (A: 43.7 ± 16.1 mm, B: 48.1 ± 19.7 mm; $P = 0.094$). Perforation did not occur in either group. Post-ESD bleeding occurred in 7.1% of the study group (7 lesions), and 17.6% of the historical control group (16 lesions). There was a significant difference in the post-ESD bleeding rate between the two groups ($P = 0.027$). Multivariate logistic regression analysis also confirmed that applying PGA sheets and fibrin glue was an independent significant factor for decreasing the risk of post-ESD bleeding (Odds Ratio, 0.33; 95% CI: 0.11-0.89, $P = 0.029$). The mean procedural time for applying PGA sheets and fibrin glue was 20.0 ± 9.1 min.
Conclusion: Even after accumulating more cases, this study all the same implied that the endoscopic tissue shielding method with PGA sheets and fibrin glue might be promising for the prevention of post-ESD bleeding.
Disclosure of Interest: Y. Tsuji Lecture fee(s): Olympus Medical Systems, HOYA Pentax, Eisai, GUNZE, CSL Behring, M. Fujishiro Financial support for research: Astellas Pharmaceutical, Takeda Pharmaceutical, Zeria Pharmaceutical, Otsuka Pharmaceutical, Astrazeneca Pharmaceutical, Dainihon-Sumitomo Pharmaceutical, Taiho Pharmaceutical, Ajinomoto Pharmaceutical, and Eisai for his department outside the submitted work, Lecture fee(s): Olympus Medical Systems, HOYA Pentax, Eisai, MSD, Daiichi-Sankyo Pharmaceutical, Astrazeneca Pharmaceutical, Aska Pharmaceutical, Taisho-Toyama Pharmaceutical, Otsuka Pharmaceutical, Zeria Pharmaceutical, Takeda Pharmaceutical, Astellas Pharmaceutical, Seikagaku Corp., Johnson & Johnson, Ajinomoto Pharmaceutical, Amco, Novartis Pharmaceutical, Boston Scientific, and, Boehringer-Ingelheim outside the submitted work, Conflict with: non-financial support from HOYA Pentax, Olympus Medical Systems, and, Fujifilm for his department outside the submitted work, Y. Kataoka Conflict with: None, I. Saito Conflict with: None, S. Shichijo Conflict with: None, Y. Sakaguchi Conflict with: None, D. Yamaguchi Conflict with: None, K. Niimi Conflict with: None, S. Ono Conflict with: None, S. Kodashima Conflict with: None, N. Yamamichi Conflict with: None, K. Koike Conflict with: None

MONDAY, OCTOBER 26, 2015 15:45–17:15
ABSTRACTS ON FIRE: HOT TOPICS IN HEPATOLOGY AND PANCREATOLOGY – HOTSPOT

OP136 HEPATIC ARTERY RECONSTRUCTION IS UNNECESSARY AFTER CELIAC ARTERY RESECTION FOR ANY TYPE OF CELIACO – MESENTERIAL ANATOMY

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Introduction: Distal pancreatectomy with celiac artery resection (DPCAR) is widely used for borderline-resectable pancreatic cancer. It is believed that considerable reduction of the liver arterial supply after DPCAR may cause severe liver dysfunction and/or gallbladder necrosis. The necessity of arterial reconstruction is still debated.
Aims & Methods: To study liver collateral arterial supply after temporary occlusion of the common (CHA) and accessory/replaced left hepatic arteries (a/rLHA). Arterial anatomy, diameters of CHA, proper hepatic (PHA), gastroduodenal arteries (GDA) and pancreatoduodenal arcades (PDA) were registered before surgery in 107 consecutive patients with pancreatic body/tail cancer (n32), gastric cancer with pancreatic involvement (n30) and liver tumors (n45) by CT. For DPCAR (n16) these data were obtained after surgery as well. Diameters of peripancreatic arteries and mean systolic blood velocity in hepatic arteries before and after CHA clamping were measured intraoperatively by Doppler ultrasound.
Results: Classical arterial anatomy was identified in 72% and replaced right hepatic artery (rRHA) from the SMA in 12.2% of cases. PDA were not identified before surgery in 20% of cases. Pulse had disappeared in 18 (17%) cases after clamping of CHA and aLHA/rLPA. Collateral arterial blood flow in the liver parenchyma was revealed in all cases. DPCAR led to 1.increase of GDA and rRHA diameters in 1.2-1.5 times; 2. visualization of PDA in all cases as main vessels, whereas they were invisible for CT in 50% before DPCAR.

Conclusion: Hepatic artery reconstruction is unnecessary after DPCAR for any type of arterial anatomy; Doppler ultrasound is the best modality for intraoperative assessment of liver arterial blood supply after DPCAR.
Disclosure of Interest: None declared

OP137 PANCREATIC CYSTIC LESIONS IN LIVER TRANSPLANT RECIPIENTS: PREVALENCE AND OUTCOME

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Introduction: Pancreatic cystic lesions (PCL) are common in the general population and their prevalence increases with age. Pancreatic cystic neoplasia account for more than half of pancreatic cysts. Some of them have malignant potential. Solid organ transplant recipients have an elevated cancer risk due to immunosuppression.
Aims & Methods: The purpose of this study was to investigate the prevalence and course of incidental PCL in liver transplant recipients. We performed a retrospective analysis of imaging findings and medical records of all adult patients who underwent liver transplantation in our center between September 1996 and November 2014.
Results: Nine hundred and sixty-seven orthotopic liver transplantations were performed in 578 males and 389 females (mean age 51 years, range 18-74). PCL were found in 60 patients (6.2%; 26 males, 34 females; mean age 61, range 31-74), with 29 of them diagnosed pre-transplant. The mean size of detected PCLs was 14 mm (range 5-85mm). PCLs were located in the head (35%), body (33%) and tail (15%) of the pancreas, 17% of patients had multifocal PCL. More than 2 PCLs were present in 20 patients (33%). Mean follow-up duration was 51 months. In 10 patients (17%), the size of lesion increased (mean +4mm), however in none of them the progression was clinically relevant. No patient developed symptoms or died from PCL during follow-up. Patients with PLCs were significantly older ($p < 0.001$), more likely to be women ($p < 0.05$) and were more often transplanted for primary biliary cirrhosis ($p < 0.01$) and Alpha1-Antitrypsin Deficiency ($p < 0.001$).
IPMN was suspected in 9 patients (15%, all branch-type). One multifocal IPMN exhibited worrisome features at the time of diagnosis and total pancreatectomy was performed in early post-transplant period.
Conclusion: PCLs are equally frequent in liver transplant recipients compared to general population. Their presence was associated with higher age, female sex, type of liver disease and did not influence patients survival.
Disclosure of Interest: None declared

OP138 LAVAGE VERSUS NO LAVAGE THROUGH PERCUTANEOUS CATHETER DRAINS IN SEVERE ACUTE PANCREATITIS: A RANDOMIZED CONTROL TRIAL

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Introduction: Lavage through peri-pancreatic drains placed after laparotomy has been the standard treatment for patients undergoing surgical necrosectomy in severe acute pancreatitis (SAP). However, it is not known whether large volume lavage given through percutaneous drains (PCDs), placed under radiological guidance, provides further benefits when compared to simple percutaneous drainage only in patients with SAP.
Aims & Methods: Sixty patients of SAP who required placement of PCDs were randomised into 2 groups: group A included 28 patients given high-volume saline lavage through PCD while group B included 32 patients who were managed by PCD drainage alone. Patients in group B who did not improve with drainage alone were transferred to group A and analysed as per protocol. The end-points were improvement of APACHE-II score, reversal of pre-existing organ failure (OF), development of new onset OF, need for surgery and mortality.
Results: The mean duration of PCD placement in group A and B were 24.82 ± 9.62 and 20.00 ± 11.17 days ($p = 0.08$). The mean improvement in APACHE-II scores with intervention was significantly more in group A as compared to group B (3.50 ± 3.40 vs 1.16 ± 3.81, $p = 0.012$). 24/28 (85.7%) patients showed reversal of persistent OF in the irrigation group compared to only 20/32 patients (62.5%) in the control group ($p = 0.023$). There was no statistically significant difference in the development of new onset OF (25% vs 37.5%, $p = 0.299$) and in number of patients requiring surgery (17.8% vs 15.6%, $p = 0.737$) in the two groups. The mortality was less in the lavage group and this difference trended towards significance (18.8% vs 28.8%, $p = 0.37$).
Conclusion: The study showed significant reduction in APACHE-II score and reversal of persistent OF in patients receiving irrigation with PCD as compared to PCD drainage alone. It also showed improvement in survival rates in the irrigation group trending towards significance.
Disclosure of Interest: None declared

OP139 IS RIBAVIRIN ACTUALLY USEFUL FOR GENOTYPE 1 (G1) CIRRHOTIC PATIENTS WHO RECEIVE DAAS COMBINATION? A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS (RCTS)

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Introduction: The use of ribavirin has been suggested to increase SVR12 rates and allow short treatment durations in G1 cirrhotic patients receiving DAAs, especially G1 treatment-experienced (TE) cirrhotic patients. The aim of this meta-analysis was to address this issue and to investigate whether the use of RBV allows 12 weeks duration regimens in TE G1 cirrhotic patients without impairing SVR rates.
Aims & Methods: All phase II and phase III RCTs published or communicated to date which included GI naïve (TN) or TE cirrhotics and contained arms with or without ribavirin and/or compared 12 weeks vs. extended (i.e., 18 or 24 weeks) treatment durations were included. All DAAs regimen were analyzed together. For TN and TE patients, 2 analyses evaluated the ribavirin use (regardless of the treatment duration and for a fixed 12 weeks treatment duration) and 3 analyses evaluated the treatment duration (regardless of, with, or without ribavirin). Another analysis compared 12 wks with RBV vs. 24 wks without RBV. Meta-analyses were performed according to the Der Simonian and Laird method and reported weight-adjusted SVR12 gains.
Results: 10 RCTs including 1307 G1 cirrhotic patients (573 TN, 734 TE) were selected for this meta-analysis. The distribution of DAA combinations was as follows: SIM + SOF (COSMOS, N = 168), 3D Abbvie (TURQUOISE II, N = 380), DCV-TRIO BMS (UNITY 2, N = 202), GPV + EBV (C-WORTHY, N = 253), and LDV + SOF (6 RCTs, N = 496). In G1 TN cirrhotic patients, the use of ribavirin (ΔSVR = +2.45%; 95%CI: -1.27 to +6.16%, NS, N = 411) or an extended duration (ΔSVR = +0.64%; 95%CI :-3.03 to +4.32%, NS, N = 434) did not increase SVR12. In G1 TE cirrhotic patients, the use of ribavirin did not increase SVR12 (ΔSVR = +0.23%; 95%CI :-3.54 to +4.01%, NS, N = 494), even in analyses restricted to 12wks treatment duration (ΔSVR = +1.85%; 95%CI :-3.75 to +7.44%, NS, N = 267). Conversely, extended duration was associated with higher SVR rates (ΔSVR = +6.35%; 95%CI: +1.49 to +11.20%, p = 0.018, N = 532), even with ribavirin use (ΔSVR = +8.26%; 95%CI: +2.29 to +14.23%, p = 0.028, N = 278). The magnitude of SVR gain was similar between the different DAA regimen suggesting that a 18 wks extended duration (as performed in the C-WORTHY study) would be sufficient for other combos. Only four studies (229 patients) compared 12wks + RBV vs. 24wks w/o RBV. Extended duration was associated with a 5.09% SVR gain that did not reach significance, probably because of a type II error and the overweight of the SIRIUS study.
Conclusion: In G1-naïve patients with compensated cirrhosis, ribavirin as well as extending treatment duration are useless. In G1 treatment-experienced patients with compensated cirrhosis, ribavirin does not increase SVR rates but extending treatment duration (18 or 24 wks) significantly increases SVR rates.
Disclosure of Interest: None declared

OP140 2D-SHEAR WAVE ELASTOGRAPHY AS A NON-INVASIVE METHOD FOR PREDICTION OF ESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: 2D-SWE might be a valuable, easy to use method for the non-invasive quantification of portal hypertension in patients with liver cirrhosis.
Aims & Methods: The aim of this study was to evaluate the feasibility of 2D-SWE in cirrhotic patients with esophageal varices and the performance of 2D-SWE for predicting the presence of esophageal varices.
The study group included 141 subjects diagnosed with cirrhosis by clinical, biological, ultrasound and/or endoscopic criteria. All subjects underwent 2D-SWE with an AixplorerTM ultrasound system (SuperSonic Imagine S.A., Aix-en-Provence, France). In each patient we performed three liver stiffness measurements in a homogenous color-coded box placed 1-2 cm under the liver capsule, with the patient in supine position, with a mean value expressed in kiloPascals (kPa), as a reliability criteria it was used the standard deviation (SD)/median ratio ≤ 0.10 (1).
Results: The ethiology of the liver cirrhosis was: HCV-38.2%, HBV- 31.5%, HCV and HBV-3.5%, ethanol-21.4% and other ethiologies-5.4%. Esophageal varices were present in 46.8% of cases and significant esophageal varices (grade II and III) in 32.4%. 2D-SWE had similar feasibility in patients with and without esophageal varices: 89.2.7% vs. 92.1%, ($p = 0.54$). The mean 2D-SWE values (kPa) were similar when no reability criteria were used in patients with esophageal varices (grade II and III) vs. those without or grade I esophageal varices: 31 ± 10.6 vs. 27.8 ± 13.8, ($p = 0.24$). After applying the reliability criteria ((SD)/median ratio ≤ 0.10), the mean 2D-SWE values (kPa) were significantly higher in patients with esophageal varices (grade II and III) vs. those without or grade I esophageal varices: 34 ± 12 vs. 23 ± 12.7, ($p = 0.03$). The best

cut-off value for the prediction of significant esophageal varices was 25.7 kPa (AUROC = 0.636, p = 0.03, Se 92.1%, Sp = 44.2%).
Conclusion: 2D-SWE is a feasible method in patients with cirrhosis and esophageal varices and seems to be able to predict the presence of esophageal varices when reliability criteria are used.

Reference

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Disclosure of Interest: None declared

OP141 MORTALITY AND DISEASE PROGRESSION AMONG CYSTIC FIBROSIS PATIENTS WITH NON-SPECIFIC LIVER ABNORMALITIES

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Introduction: CF liver disease (CFLD) is associated with a worse CF phenotype and reduces life expectancy. While less than 10% of patients develop CFLD, up to 30% have non-specific abnormalities on liver biochemistry and imaging (non-specific liver disease - NSCFLD) and little is known of the natural history of disease in this group.
Aims & Methods: The aim of this study was to prospectively determine the outcome of NSCFLD in a national cohort.
All children under 18 years old with CF in the Republic of Ireland were invited to participate and underwent in-depth clinical and nutritional assessments in 2007 and 2012. Liver disease status was classified using North American Cystic Fibrosis Foundation (NACFF) criteria as: No evidence of liver disease (NoLD), Non-specific liver disease (NSCFLD) and clinically significant liver disease (CFLD).
Results: 521 children were enrolled in 2007; mean age 9.04 SD4.9, 52% Male, mean follow-up 4.01 years SD1.05. In 2007 119 (22.8%) children were classified having NSCFLD, 35 (6.7%) as CFLD, and 367 (70.4) as NoLD. In 2012 all children underwent in-depth clinical re-evaluation. In 2012 10 (8.4%) children with NSCFLD had died (compared with 7 (1.9%) of those with NoLD and 11 (31.4%) of those with CFLD, P = 0.00). Of the children alive with NSCFLD in 2012, 3 (2.52%) were lost to follow-up, 13 (10.9%) progressed to CFLD, 41 (34.4%) remained unchanged and 50 (42%) had no evidence of liver disease (normal clinical biochemical and radiological parameters). Of the 13 who progressed to clinically significant liver disease, 8 (61.5%) were less than 10 years of age while 38.5% were over 10 years of age (P = NS). Of the 50 participants reclassified as NoLD in 2012, 44 had had liver ultrasound abnormalities and 6 liver biochemistry abnormalities in 2007. No child with both liver imaging and biochemical abnormalities at enrolment reverted to NoLD in follow up. However of the 5 participants with ultrasound and biochemical abnormalities, 4 have progressed to CFLD and the 5th still has NSCFLD.
Conclusion: While most children with CF and evidence of biochemical or ultrasonographic liver abnormalities alone will not develop more severe liver abnormalities in the medium term, a substantial minority progress to CFLD/cirrhosis – especially if they have both ultrasound abnormalities and laboratory derangements. Furthermore, mortality among children with NSCFLD is substantially higher than in CF children with normal livers.
Disclosure of Interest: None declared

OP142 LONG TERM CHANGE IN AETIOLOGY OF CIRRHOSIS AND HEPATOCELLULAR CARCINOMA IN CRETE,GREECE: A 25 YEAR STUDY

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Introduction: Over the last years Non Alcoholic Fatty Liver Disease (NAFLD) has emerged as a major aetiological factor in Cirrhosis and HCC. No sequential long term data exist for Greece.
Aims & Methods: We studied therefore the aetiological evolution of cirrhosis and HCC over a period of 25 years in the genetically homogeneous population of the island of Crete .We used the Data Base of our Unit which is the Reference Center for Liver Disease of the Island. A total of 820 cases of cirrhosis (561 male, median age 69 years) and 321 cases of HCC (234 male median age 70 years) were recorded and classified in 5 year periods according to aetiology (HBV, HCV, Alcohol, Alcohol plus viral and NAFLD). Primary Biliary Cirrhosis was not included
Results: Cirrhosis: There was a relative uniformity in absolute numbers over the years. However there was a significant change in aetiologies. Thus, while the association with HBV remained constant , there was a reduction of association with HCV (1990-1994:45%, 2010-2014: 12%) with a parallel increase of Alcoholic (1990-1994: 36%, 2010-2014:59%) and NAFLD associated cirrhosis (!990-1994: 2%, 2010-2014:16%). In HCC there was also a decrease in the association with HCV (90-94: 50%, 10-14: 21%) and a very significant increase in the association with NAFLD (90-94: 1%, 10-14:23%). HBV and alcohol were unchanged
Conclusion: 1) Aetiology of cirrhosis and HCC have considerably changed over the past 25 years in Crete. 2) The initial high HCV association has significantly decreased 3) Alcohol is now the main aetiological factor in cirrhosis 4) NAFLD has emerged as a continually increasing association with both cirrhosis and HCC.
Disclosure of Interest: None declared

OP143 THE IMPACT OF CLINICAL PORTAL HYPERTENSION ON THE PROGNOSIS OF PATIENTS WITH HEPATOCELLULAR CARCINOMA AFTER RADIOFREQUENCY ABLATION

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Introduction: Portal hypertension is an important prognostic factor for patients with advanced liver disease, but whether it could also determine the outcomes of patients with hepatocellular carcinoma (HCC) after radiofrequency ablation (RFA) is still obscure.
Aims & Methods: To assess the impact of clinical portal hypertension on the prognosis of patients with HCC undergoing percutaneous RFA. We enrolled 280 treatment-naïve HCC patients who also received upper gastrointestinal endoscopy examination at the time of HCC diagnosis. Clinical portal hypertension was defined as (1) platelet count < 100,000/mm^3 associated with splenomegaly, or (2) presence of esophageal/gastric varices by endoscopy.
Results: A total of 192 (68.6%) patients had clinical portal hypertension at the time of receiving RFA. Among them, 154 patients had splenomegly and blood platelet count < 100,000/mm^3 at the same time, 140 patients had esophageal varices and 25 patients had gastric varices. Patients with portal hypertension were younger in age, with low serum albumin and cholesterol levels, higher bilirubin, alanine aminotransferase levels, lower platelet count, lower hepatitis B virus carriers and higher rate of positive antibody against hepatitis C virus than their counterpart. After a median follow-up of 23.5 months (25-75 percentiles 13.1-43.6 months), 76 patients died. The cumulative five-year survival rates were 50.6% and 76.7% in patients with and in those without portal hypertension, respectively ($p = 0.016$). By multivariate analysis, age > 65 years hazard ratio (HR) 1.661, 95% confidence interval CI 1.028-2.684, $p = 0.038$), serum albumin levels ≤ 4.0 g/dL (HR 3.472, 95% CI 1.715-6.993, p = 0.001), multiple tumor (HR 1.753, 95% CI 1.059-2.903, p = 0.029) and serum alpha-fetoprotein level > 20 ng/mL (HR 1.831, 95% CI 1.134-2.957, p = 0.013) were independent risk factors associated with poor overall survival after RFA.
Conclusion: HCC patients with clinical portal hypertension had relatively poorer liver functional reserve than those without portal hypertension. However, portal hypertension was not an independent risk factor predicting overall survival for patients with small HCC undergoing RFA by multivariate analysis. Therefore, portal hypertension or EV is not the contraindication for RFA.
Disclosure of Interest: None declared

OP144 CLINICAL SIGNIFICANCE AND RISK FACTORS OF RECURRENCE BEYOND MILAN CRITERIA WITHIN 2 YEARS AFTER RADIOFREQUENCY ABLATION IN PATIENTS WITH SINGLE SMALL HCC

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Introduction: Radiofrequency ablation (RFA) is one of most commonly applied curative treatment modalities in patients with small hepatocellular carcinoma (HCC). However, clinical significance and risk factors of recurrence beyond Milan criteria within 2 years after RFA, a dreadful event excluding the possibility of further curative treatment, has not been fully evaluated.
Aims & Methods: Among 477 patients with single HCC < 3 cm undergoing percutaneous RFA as initial treatment modality at our institution from 2006 to 2009, 438 patients showing complete ablation were included in this study. Baseline patient characteristics including age, sex, etiology of the liver disease, Child-Pugh class, Eastern Cooperative Oncology Group performance status, and tumor characteristics including alpha-fetoprotein levels, tumor size, number, conspicuity, and proximity to the surface of the liver, colon, diaphragm and vascular structures were reviewed. Clinical outcomes of the whole patients and incidence, impact on overall survival, and risk factors of recurrence beyond Milan criteria within 2 years after RFA were also investigated.
Results: During the median follow-up period of 68.4 months (range: 1.0-117.1), recurrent HCC was noted in 302 patients (68.9%). Median time to recurrence was 19.7 months (range: 1.0-110.2). Recurrence beyond Milan criteria within 2 years after RFA was noted in 27 patients (8.0%) with the following reasons: detection of tumor(s) with size and/or numbers beyond Milan criteria (n = 11, 2.5%), vascular invasion (n = 3, 0.7%), and extrahepatic metastasis (n = 13, 2.9%). While 1-, 3-, and 5-year overall survival rates were 98.1%, 86.3%, and

72.8%, respectively in the whole patients, those were 92.6%, 46.5%, and 0.05% in patients with recurrence beyond Milan criteria within 2 years. Multivariable analysis identified older age (OR = 1.04; 95% CI 1.02-1.05; p < 0.001), albumin (OR = 0.53; 95% CI 0.39-0.71; p < 0.001), recurrence beyond Milan criteria within 2 years (OR = 7.72; 95% CI 4.91-12.13; p < 0.001) as the independent risk factors predictive of poor overall survival. Initial tumor size ≥ 20 mm (OR = 2.30; 95% CI 1.02-5.16; p = 0.044) and tumor adjacent to the colon (OR = 4.64; 95% CI 1.75-12.31; p = 0.002) were identified as independent risk factors predictive of recurrence beyond Milan criteria within 2 years.
Conclusion: Recurrence beyond Milan criteria within 2 years after RFA is independently predictive of poor overall survival and associated with size ≥ 2 cm in size and proximity to colon of tumor in patients with single small HCC.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30
THERAPY UPDATE: EOSINOPHILIC OESOPHAGITIS – ROOM F2

OP145 FAMILIAL EOSINOPHILIC ESOPHAGITIS (EOE) UNCOVERS A NEW EOE-LIKE SYNDROME WITHOUT TISSUE EOSINOPHILIA

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Introduction: Eosinophilic esophagitis (EoE) is a chronic-inflammatory disease of the esophagus defined clinically by symptoms of esophageal dysfunction and pathologically by an eosinophil-predominant infiltration. EoE has a strong genetic component. We identified in four EoE-families totally five members with an EoE-like syndrome, presenting with typical symptoms of EoE responding promptly to treatment with topical corticosteroids, but without tissue eosinophilia. The purpose of this study was to investigate this intriguing syndrome of "EoE without eosinophilia", in order to improve the understanding of this inflammatory condition.
Aims & Methods: The five patients suffering from EoE-like syndrome were evaluated by laboratory analyses, endoscopy, histologic and quantitative immuno-histologic examinations and genome-wide association analyses. In addition, we searched in all 46 members of these EoE-families for EoE-associated molecular abnormalities.
Results: Using immunohistochemistry we detected in the esophagus of patients with EoE-like syndrome a chronic, Th2 type inflammation, but definitely a lack of eosinophils. In addition, we found the EoE-risk allele *TSLP rs3806932* in their genome. First generation offspring of EoE-like syndrome patients had on average a 40% risk of being affected by conventional EoE.
Conclusion: These five members of EoE families suffering from "EoE without eosinophilia" do formally not fulfill the diagnostic criteria of EoE. However, clinical manifestation, the finding of a Th2 type inflammation, the bequeath of conventional EoE to their offspring and the detection of the EoE-risk allele *TSLP rs3806932* in their genome strongly suggests a uniform underlying pathogenesis. Conventional EoE with the predominant eosinophilia might therefore be only one phenotype of this dysphagia syndrome. The role of the eosinophils and the disease-definition must therefore be reconsidered. Moreover, as these patients have endoscopically and histologically only discreet abnormalities, this syndrome might so far often be misdiagnosed as functional dysphagia.
Disclosure of Interest: None declared

OP146 LONG-TERM LOSS OF RESPONSE IN PROTON PUMP INHIBITOR-RESPONSIVE ESOPHAGEAL EOSINOPHILIA IS UNCOMMON AND INFLUENCED BY CYP2C19*2 GENOTYPE AND RHINOCONJUNCTIVITIS

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Introduction: Proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE) is diagnosed in at least a third of patients with suspected eosinophilic esophagitis (EoE). However, the durability and factors influencing the long-term efficacy of PPI therapy remain unknown.
Aims & Methods: We aimed to evaluate the durability and factors influencing long-term efficacy of PPI therapy. Retrospective multicenter cohort study of patients with PPI-REE who had at least 12 months of follow-up. PPI therapy was tapered to the lowest dose which maintained clinical remission. Primary outcomes were the proportion of patients with loss of histological response (< 15 eos/HPF) and predictors of loss of response. *CYP2C19* polymorphisms were determined from blood samples in a subset of patients.
Results: Seventy five PPI-REE patients were included [mean follow 26 months (12-85)], of whom fifty five (73%) had sustained histological remission on low-dose PPI therapy. Loss of response was significantly higher in those patients with a *CYP2C19*2* rapid metabolizer genotype (36% *vs.* 6%, p 0.01) and with rhinoconjuctivitis (40% *vs.* 13%, p 0.007). On multivariate analysis, a *CYP2C19*2* rapid metabolizer genotype (odds ratio (OR) 12.5; 95%CI:1.3-115.9) and rhinoconjunctivitis (OR 8.6; 95%CI:1.5-48.7) were independent predictors of loss of response. Among relapsing patients, eosinophilia was limited to the distal esophagus in 14/20 (70%). Nine of ten relapsers, with distal eosinophilia, all showing a *CYP2C19*2* rapid metabolizer genotype, regained histological remission after PPI dose intensification.
Conclusion: Most PPI-REE patients remain in long-term remission on low-dose PPI therapy. A CYP2C19*2 rapid metabolizer genotype and rhinoconjunctivitis were independent predictors of loss of response to PPI, but patients frequently responded to PPI therapy intensification.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30
RATIONAL DIAGNOSTIC APPROACH TO BARRETT'S OESOPHAGUS – ROOM A2

OP147 IDENTIFICATION OF CLINICAL AND ENDOSCOPIC PREDICTORS FOR NEOPLASTIC PROGRESSION IN BARRETT'S ESOPHAGUS USING A PROSPECTIVE MULTI-CENTER COMMUNITY-BASED COHORT OF 1003 PATIENTS

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Introduction: The absolute risk to develop esophageal adenocarcinoma (EAC) from Barrett's esophagus (BE) is low, however, once diagnosed it is an aggressive and often fatal disease. Aim of this study was to assess the risk of neoplastic progression in BE and identify endoscopic and clinical predictors for neoplastic progression, to enable risk-stratification in BE patients and improve current surveillance strategies.
Aims & Methods: In 2003 a prospective surveillance study was initiated in 6 community-based hospitals in the Netherlands, coordinated by a tertiary BE referral center. Patients with known BE identified using the Dutch pathology registry (PALGA) and patients newly diagnosed with BE were asked consent to enter a prospective surveillance program. Exclusion criteria were no intestinal metaplasia, history of esophageal carcinoma and prevalent high-grade dysplasia (HGD) or EAC (defined as diagnosed at index endoscopy or within 6 months thereafter). All surveillance endoscopies were scheduled and performed according to international guidelines, using Seattle protocol biopsies. In each center, all endoscopies were performed by a single endoscopist. Two research nurses coordinated the surveillance program and attended all procedures for optimal data registration. Questionnaires to collect demographic and clinical information were completed at each endoscopy. Endoscopic and histological data from gastroscopies prior to inclusion were collected retrospectively. Endpoint of the study was progression to HGD/EAC during endoscopic follow-up. Univariate logistic regression was used to identify predictors of progression.
Results: 1003 patients were included: 726 (72%) men, mean age at diagnosis 55 ± 12 years, median BE length 3 cm (IQR 1-5), median surveillance time 7.1 years (IQR 3.4-11.1). A total of 52/1003 patients (5%) developed HGD (24/52) or EAC (28/52); median time to progression was 7.9 years (IQR 3.9-11.6). Annual risk of neoplastic progression was 0.64% per patient year. Presence of low-grade dysplasia (LGD) (OR 2.47, 95% CI 1.01-5.85)), age at baseline endoscopy (OR 1.03, 95% CI 1.00-1.05) and length of BE (OR 1.22 per cm, 95% CI 1.13-1.31) were predictive for neoplastic progression (table 1).

Table 1: Odds ratios

	OR	95% CI	p-value
Age at baseline endoscopy (years)	1.03	1.00-1.05	0.029
Male	1.29	0.67-2.49	0.453
BMI	1.05	0.99-1.10	0.096
PPI use	0.67	0.38-1.17	0.157
Total surveillance time (years)	1.04	0.97-1.06	0.559
BE length (per cm)	1.22	1.13-1.31	<0.001
LGD at baseline	2.47	1.05-5.81	0.038

Conclusion: This large prospective BE surveillance cohort is unique for its community based setting (avoiding referral bias) and long-term optimal surveillance circumstances. We found an annual risk of progression to HGD or EAC of 0.64% per patient year. BE segment length, presence of LGD and age at diagnosis were predictive for neoplastic progression and may therefore be used to tailor surveillance in BE patients.
Disclosure of Interest: A. Bureo Gonzalez: None declared, L. Duits: None declared, R. Mallant-Hent: None declared, J. Bergman Financial support for research: Boston Scientific, Olympus Endoscopy, Cook Medical, Boston Scientific, Covidien/Medtronics, Erbe, Ninepoint Medical, Consultancy: Cook Medical, Boston Scientific, Covidien/Medtronics, R. Pouw: None declared

OP148 PROSPECTIVE COMPARISON OF EMR VS ESD IN BARRETT'S NEOPLASIA: ARE WE TOO AFRAID OF KNIVES IN THE OESOPHAGUS?

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Introduction: Use of ESD in the Western setting is limited to a few centres with limited numbers of cases, due to concerns regarding complication rates and no established training pathway. The risks of ESD in the oesophagus are perceived to be high and the consequences disastrous. For this reason, endoscopic mucosal resection (EMR) is the most common technique used to resect early Barrett's cancer. The drawback of EMR is piecemeal resection and poor interpretation of histology.
Aims & Methods: We report our experience of oesophageal ESD in 51 cases and compare our data for EMR over the same period.
Results: 51 ESD resections for Barrett's neoplasia were performed between 2006 and 2014. 140 EMR's were performed in the same period. Mean age 71 years for ESD group and 75 for EMR group. All procedures were undertaken by a single expert endoscopist (PB).

Table 1: Lesion Characteristics & Post-resection Histology

	Mean Follow Up(Yrs)	Paris IIa (nodular)	Intra-mucosal (IMC)	Submucosal (SM1+)	Indeterminate Histology
ESD groupn = 51	4.2	92%	62%	32%	0%
EMR groupn = 140	5.7	10%	43%	15%	5%

The endoscopic cure rate in the ESD group was 83% and the EMR group was 82%. In the ESD group there was a recurrence rate of 3%, in the EMR group 16%. Additional radiofrequency ablation was required in 17% of patients in the ESD group and 34% of patients in the EMR group. There were no significant complications in the ESD group, there were 4 cases of bleeding and 4 cases of stricturing in the EMR group.
Conclusion: ESD for Barrett's neoplasia is feasible, safe and effective in Western hands. Our lesion selection data shows that ESD is being used mainly for nodular lesions and cancerous lesions as compared to EMR for flat and non-cancerous lesions. Neoplasia recurrence is higher in EMR vs ESD. The complication rates are similar. This calls for a randomised controlled trial comparing EMR vs ESD for the resection of nodular lesions in Barrett's neoplasia.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30
THE DIFFICULT CIRRHOTIC PATIENT – ROOM A1

OP149 VALIDATION OF THE CLIF-ACLF SCORE IN PREDICTING MORTALITY IN ACUTE-ON-CHRONIC LIVER FAILURE PATIENTS IN A WARD

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Introduction: Admission of cirrhotic patients to intensive care unites is limited by high mortality, high costs and scarcity of intensive care beds.
Aims & Methods: We sought to validate the Chronic Liver Failure - Acute-on-Chronic Liver Failure (CLIF-ACLF) score[1] in patients with acute-on-chronic liver failure (ACLF) admitted in a Gastroenterology ward and compare it with the existing scoring systems Model for End-Stage Liver Disease (MELD), MELD-Sodium and Child-Turcotte-Pugh (CTP). Retrospective analysis of demographic, clinical and laboratorial data of patients admitted for acute cirrhosis decompensation between January 2013 and September 2014. Twenty eight (M28) and 90-day (M90) mortality were evaluated. Patients with and without ACLF were compared. CLIF-ACLF performance was compared with MELD, MELD-Sodium and CTP.
Results: 179 patients were included (male sex:73.7%, mean age:61 ± 11 years). 82.6% had alcoholic cirrhosis (with or without viral infection) and previous episodes of acute decompensation were absent in 24.6%. At admission 20.7% fulfilled criteria for ACLF and 7.8% developed ACLF during hospitalization (overall prevalence 28.5% - Grade 1:15.6%, Grade 2:12.3%, Grade 3:0.6%) . M28 e M90 were, respectively, 7.8% and 21.9% in patients without ACLF and 51.0% and 66.7% in patients with ACLF ($p < 0.001$). The AUROC of CLIF-SOFA in predicting M28 and M90 was respectively 0.809 ± 0.071 and 0.852 ± 0.054, and was superior to MELD (0.694 ± 0.076 and 0.689 ± 0.081), MELD-Sodium (0.715 ± 0.077 and 0.697 ± 0.081) and CTP (0.647 ± 0.08 e 0.684 ± 0.085); $p < 0.01$.
Conclusion: The application of ACLF criteria in the ward identifies patients with high mortality. The new CLIF-ACLF score accurately predicts short-term mortality of patients with ACLF hospitalized in a ward and is superior to MELD, MELD-Sodium and CTP.

Reference

1. Jalan R, Saliba F and Pavesi M, et al. Development and validation of a prognostic score to predict mortality in patients with acute-on-chronic liver failure. *J Hepatol* 2014; Nov; 61(5): 1038–47.

Disclosure of Interest: None declared

OP150 ULTRA-THIN DISPOSABLE GASTROSCOPE IS SAFE, FEASIBLE AND HIGHLY ACCURATE FOR SCREENING AND SURVEILLANCE OF GASTRO-OESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS: A PROSPECTIVE STUDY

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Introduction: Variceal haemorrhage is a serious consequence of portal hypertension. It is recommended that all patients with liver cirrhosis undergo endoscopic screening and surveillance for gastro-oesophageal varices. Upper gastrointestinal endoscopy is the gold standard technique, but can be costly and requires sedation.
Aims & Methods: The aim of this study is to evaluate and compare the role of an unsedated, disposable ultra-thin gastroscope against conventional upper gastrointestinal endoscopy in screening and surveillance of gastro-oesophageal varices in patients with liver cirrhosis. Forty six patients (56.4 ± 1.4 years; 35M:11F) with liver cirrhosis who were referred to the Gastrointestinal Investigation Unit at the Royal Adelaide Hospital for screening or surveillance of gastro-oesophageal varices were prospectively enrolled. In all subjects, unsedated gastroscopy was initially performed with a thin disposable endoscopy (E.G. Scan, South Korea) with lignocaine gargle, followed by the conventional upper endoscopy (Olympus QF 180, Japan) with conscious sedation. The 2 gastroscopies were performed by different gastroenterologists who were blinded to the results of the previous examination. Videos of all procedures were recorded for subsequent validation by an independent investigator in a random, blinded fashion, and determination of the presence of varices, variceal size and high risk stigmata. Patient tolerability was assessed by pain visual analogue scale (VAS: 0-10).
Results: Upper endoscopy was performed for variceal screening in 11 patients, primary surveillance in 30 patients, and secondary surveillance in 5 patients. All unsedated disposable endoscope were well tolerated, with a mean pain VAS score of 1.87 ± 0.33 (equivalent to "annoying") and no adverse events. Of the 25 patients who had oesophageal varices on the gold-standard conventional gastroscopy, varices were confirmed in 24 (96%) patients on disposable gastroscopy. Similarly, 18/21 (86%) patients who had no varices on conventional gastroscopy was confirmed on disposable scope, giving the overall accuracy of 91%. For the detection of varices, disposable endoscope had 96% sensitivity, 86% specificity, 89% positive predictive value, and 95% negative predictive value. The diagnostic accuracy increased to 96% (kappa score of 0.87) for high-risk varices characterised by large varices or high-risk stigmata. Compared to conventional sedated upper gastroscopy, the use of clinic-based unsedated disposable gastroscopy resulted in an estimated cost saving of $AUD 250 per case.
Conclusion: Unsedated disposable endoscopy with local anaesthetic gargle is well tolerated, safe and has excellent diagnostic accuracy for the detection of gastro-oesophageal varices. Together with the cost saving, the use of clinic-based disposable gastroscopy is a very attractive approach for variceal screening and surveillance program in large liver clinics as the gastroscopy results allow immediate determination of follow-up plan.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30
SCREENING FOR COLORECTAL CANCER – ROOM A3

OP151 COST-EFFECTIVENESS ANALYSIS ON SURVEILLANCE FOLLOWING NEGATIVE COLONOSCOPY IN POPULATION-BASED COLORECTAL CANCER SCREENING

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Introduction: Population-based colorectal cancer (CRC) screening using the fecal immunochemical test (FIT) as a primary screening tool, with total colonoscopy (TCS) being performed for positive-FIT individuals, has been conducted in Japan as in several European countries. The cost-effectiveness of FIT-based screening has been reported in several studies including our recent study (Sekiguchi M, et al. *DDW* 2015). However, in screening program, no consensus has been reached on which should be used as a surveillance tool after negative TCS in terms of cost-effectiveness, FIT or TCS.
Aims & Methods: The aim of this study was to clarify which was a more cost-effective tool for surveillance following negative TCS in FIT-based screening, FIT or TCS. A Markov model was developed simulating the clinical course of CRC as a transition from normal epithelium, low-risk adenomatous polyps sized 1–4 mm and 5–9 mm, high-risk adenomatous polyps, and CRC to death from CRC. The initial population comprised 100,000 average-risk individuals aged 40 years. Transition probabilities, costs, and test characteristics were mostly based

on Japanese data, including data from the Japan polyp study (Matsuda T, et al. *UEGW* 2014); FIT and TCS cost $13.30 and $128.87, respectively. Two types of FIT-based screening strategies, one using FIT (strategy 1) and the other using TCS (strategy 2) as a surveillance tool after negative TCS, were evaluated for costs (US$), gained quality-adjusted life-years (QALYs), and the number of TCS procedures. In both strategies, those with positive FIT were invited to undergo TCS; polyps found were removed and surveillance TCS was repeated every 3 years until no more polyps were found. In the case of normal results on TCS, FIT was resumed 5 years after TCS in strategy 1, whereas TCS was repeated 10 years after in strategy 2. Screening compliance rates were set at 60% in the base-case analysis, and scenario analyses were performed on the compliance rates (10%–100%) and starting age of screening (50 years).

Results: QALYs and costs per person in strategy 1, 2, and no screening were as follows: strategy1, 23.000 QALYS and $787.65; strategy 2, 23.007 QALYs and $823.41; no screening, 22.799 QALYs and $1298.09. Both strategy 1 and 2 yielded higher QALYs with lower costs than no screening. Compared with strategy 1, strategy 2 increased QALYs with more costs. The incremental cost per QALYs gained for strategy 2 against strategy 1 was $5,108.57, which was much lower than the known upper limit of willingness-to-pay values ($50,000). However, the number of required TCS procedures (/100,000 persons) in strategy 2 was 202,988, which was twice as many as with strategy 1 requiring 100,740 TCS procedures. In the scenario analyses, the incremental cost per QALYs gained for strategy 2 against strategy 1 remained less than $50,000.

Conclusion: Whether FIT or TCS is used for surveillance following negative TCS, FIT-based CRC screening is more cost-effective than no screening. In the screening system, TCS can be used as a more cost-effective tool than FIT for surveillance following negative TCS; however, considering the increased number of TCS procedures, the choice should be determined according to the nationwide availability of TCS resources.

Disclosure of Interest: None declared

OP152 CORRELATION BETWEEN ADENOMA DETECTION RATE (ADR) IN DIRECT COLONOSCOPY BASED COLORECTAL CANCER (CRC) SCREENING AND ADR IN COLONOSCOPY IN THE FIRST ROUND OF FECAL IMMUNOCHEMICAL TEST (FIT) BASED CRC SCREENING

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Introduction: Adenoma detection rate (ADR) is the main quality indicator in CRC screening colonoscopy. An ADR <20% is associated with an increased risk of interval CRC after screening colonoscopy. However, there is no information on the recommended ADR in the work-up colonoscopy of FIT-based CRC screening programs

Aims & Methods: Our analysis evaluated if there was a correlation between the ADR in primary colonoscopy of a colonoscopy-based program and the corresponding figure in the work-up colonoscopy of a FIT-based program. We designed a post-hoc analysis within the first round of the COLONPREV study, a randomized controlled trial comparing the efficacy of biennial FIT and one-time colonoscopy for reducing CRC-related mortality. The study included asymptomatic people between 50-69 years from 15 hospitals in 8 Spanish regions. Colonoscopies were performed by the same endoscopists in each hospital. We evaluated the ADR by age group (50-59, 60-69), sex and region, and calculated the Pearson's correlation coefficient. Moreover, we developed a predictive model based on a multivariable lineal regression analysis including the confounding variables (i.e. age, sex, and region). Finally, we determined the ADR in work-up colonoscopy of a FIT-based program equivalent to the well-defined and accepted ADR of 20% in a colonoscopy-based program.

Results: Colonoscopy was performed in 5722 subjects (5059 primary colonoscopy, 663 after a positive FIT). The median ADR was 31% (range, 14-51%) in colonoscopy group and 55% (range, 21-83%) in FIT group. In the colonoscopy group, median ADR distribution was as follows: male, 37% (22-51%); female, 23% (14-51%); 50-59 years, 28% (14-47%); and 60-69 years, 36% (16-51%). In the FIT group, median ADR distribution was as follows: male, 67% (26-78%); female, 45% (21-83%); 50-59 years, 53% (21-78%); and 60-69 years, 56% (38-83%). There was a positive correlation in the ADR between primary colonoscopy and work-up colonoscopy (Pearson's coefficient 0.716; $p < 0.001$). The coefficient of multiple correlation of the predictive multivariable lineal regression model was 0.68. In this model, ADR in the FIT group was independently related to ADR in the colonoscopy group: regression coefficient for colonoscopy ADR, 0.71 ($p = 0.009$); sex, 0.09 ($p = 0.09$); age, 0.3 ($p = 0.5$); and region 0.00 ($p = 0.9$). Estimated ADR in work-up colonoscopy equivalent to the 20% ADR in primary colonoscopy was 45% (95% confidence interval, 34-57%)

Conclusion: ADR in primary and work-up colonoscopy of a FIT-positive result are positively and significantly correlated. According to this correlation, ADR should be set at 45% as quality indicator in FIT-based CRC screening programs.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30

EPIDEMIOLOGY OF IBD – ROOM 7.1

OP153 HIGHLIGHTING OF EPIDEMIC AREAS OF CROHN'S DISEASE IN A POPULATION-BASED REGISTRY OVER 22 YEARS: GENETIC OR ENVIRONMENTAL CAUSE?

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Introduction: Our previous studies detected a spatial heterogeneity in standardized incidence ratios of Crohn's disease (CD), through a population-based IBD registry over a 17-year period, pointing the existence of clusters with low and high incidence

Aims & Methods: The first aim of the present study was to determine the origin of these clusters according with CD family history (CD-FH) or not over a 22-year period (1990-2011). The second aim of this study was to compare the clinical phenotype at CD diagnosis between clusters with high and low CD incidence. From 1990 to 2011, the Epimad population-based registry recorded 8,970 incident CD cases distributed in 273 administrative areas of Northern France. Isotonic scan statistics allowed the detection of clusters and their epicenter. Several data were collected at time of diagnosis including: gender, age, CD-FH, smoking status, phenotype (location, behavior and anoperineal lesion) according to Montreal classification and diagnosis management.

Results: Seven clusters including all patients ($n = 8,970$) have been identified in both analyses; 4 with high incidence (2,163 CD cases; RR from 1.27 to 1.46; $p < 10^{-3}$) and 3 with low incidence (861 CD cases; RR from 0.69 to 0.71; $p < 10^{-2}$). After exclusion of patients with CD-FH ($n = 1,086$) prone to have a genetic burden, the size of cluster with high incidence in the southeastern part of the area was greatly reduced.

Concerning clinical parameters; gender, median age at diagnosis, smoking status and CD phenotype were not different between clusters with high and low incidences.

Conclusion: Four clusters of epidemic CD areas have been identified in our population-based study over a 22-year period. Only one cluster was reduced in size when excluding CD-FH patients. These results assumed for a high impact of environmental risk factors in the origin of these clusters. It is now our challenge to highlight them.

Disclosure of Interest: M. Genin: None declared, C. Vignal: None declared, F. Vasseur: None declared, M. Fumery: None declared, G. Savoye: None declared, M. Body-Malapel: None declared, C. Préda: None declared, H. Sarter: None declared, L. Peyrin-biroulet: None declared, P. Desreumaux: None declared, C. Gower-Rousseau Financial support for research: MSD & Ferring companies for Grants for Registry, Lecture fee(s): MSD, Ferring, Janssen, Abbvie

OP154 SHORT-TERM AND LONG-TERM DURABILITY IN THE RISE OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE INCIDENCE IN SCOTLAND BETWEEN 1969-2013: A NATIONAL COHORT STUDY

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Introduction: Scotland has one of the highest rates of paediatric inflammatory bowel disease (PIBD) worldwide, with previously demonstrated medium-term increases in PIBD incidence between 1990-2008(1). However, it is not yet clear if this rise has been sustained over a more prolonged time-frame and if this increasing incidence has been preserved in recent years.

Aims & Methods: We aimed to evaluate the long-term temporal trends in PIBD incidence in Scotland over a 45 year period. National data from previously published incident cases of PIBD in Scotland during the periods 1969-1995 and 2003-2008 were examined; prospectively collected incident cases from 2009-2013 were also included. Incidence rates were calculated using publicly available population data from the Scottish government and trends across

cohorts calculated using Poisson regression analysis. Rates were standardised to the 2001 census population for comparison.
Results: There was a moderate, but significant, increase in PIBD incidence from 2.3/100,000/yr (95%CI 2.0-2.6) to 4.5/100,000/yr (95%CI 3.9-5.0) between the 1969-1974 and 1990-1995 epochs respectively ($p < 0.001$). A more dramatic rise was evident in the most recent cohort (2009-2013) with a rate of 10.4/100,000/yr (95%CI 9.6-11.5), showing a sustained increased from the 2003-2008 cohort (7.8/100,000/yr [95%CI 7.1-8.6]; $p < 0.001$). For Crohn's disease (CD) a more linear trend was observed with rates increasing steadily from 0.9/100,000/yr (95%CI 0.7-1.1) during 1969-1974, to 2.2/100,000/yr (95%CI 1.8-2.7) during 1986-1989 and 6.3/100,000/yr (95%CI 5.6-7.0) in the 2009-2013 cohort ($p < 0.001$). Between the 1969-1974 and 2009-2013 cohorts the incidence rate ratio (IRR) for PIBD and CD were 4.6 (95%CI 3.7-5.7) and 7.4 (95%CI 5.5-10.0) respectively; a 33% rise was also apparent between the two most recent cohorts (IRR 1.3 [95%CI 1.2-1.5]). The ratio of non-Crohn's colitis (ulcerative colitis and IBD unclassified combined) to CD has reversed from 2:1 to 4:6 over the 45-year period.
Conclusion: Using historical and contemporaneous data over a 45-year period in a well-defined and stable population we have demonstrated a sustained incidence rise which is durable in both the short- and long-term, with a 4.6-fold increase in PIBD and a 7.4-fold increase in CD across the study period. Despite no discernible changes in population structure, genetic susceptibility or diagnostic evaluation over the past 12 years we also show a sustained short-term increase in incidence suggesting that aetiological factors continue to exert their effects on at-risk individuals.

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Disclosure of Interest: None declared

OP155 FREQUENT RAPID CLINICAL PROGRESSION OF NEWLY DIAGNOSED CROHN'S DISEASE: RESULTS OF A PROSPECTIVE INCEPTION COHORT

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Introduction: Population-based studies have shown that structural and functional bowel damage of Crohn's disease (CD) is a dynamic, progressive process. However, timing and degree of progression are unpredictable.
Aims & Methods: We aimed to investigate the time course to progression in newly diagnosed CD, and to identify risk factors. This is a longitudinal, prospective, observational follow up study, of an inception cohort, in a tertiary referral center. Adults (≥18 y-o), suspected of CD or diagnosed with CD during the preceding six months prior to enrollment, were recruited. Enrollees were prospectively followed at 6 months intervals. Progression to complicated disease, CD-related hospitalizations or surgeries, was documented.
Results: A total of 161 patients were enrolled between 05/2013-04/2015. Of these, 119 fulfilled inclusion criteria and 79 attained a definite diagnosis of CD. Male/female ratio was 32/47, mean age at diagnosis was 34.1 ± 16 years, average BMI was 21.8 ± 5 kg/m^2, positive family history of IBD was detected in 20.3%. Mean CDAI at enrollment was 173 ± 91 (19-359), mean CRP 19.1 ± 32 gr%, and mean fecal calprotectin 1162 ± 1808 mg/gr stool. Mean time between commencement of symptoms and diagnosis was 9.3 ± 16.1 months. L1, L2, and L3 phenotypes were detected in 45.65%, 24.1%, and 24.1%of patients, respectively. Stricturing and penetrating disease were detected in 5.1% and 15.2% respectively, and perianal disease in 16.5%. Six and 12 months after diagnosis 19 and 20 patients (24% and 25.3%, respectively) experienced disease complications. Stricturing (B1) phenotype significantly differentiated complicators and non-complicators: 18.8% vs. 1.8%, respectively ($p = 0.034$). Drug exposure rates within 6 months from diagnosis in complicators and non-complicators were: corticosteroids 44.4% vs. 6.9% ($p = 0.001$), immunmodulators 27.8% vs.6.9% ($p = 0.03$), and biologics 16.7% vs. 8.8% ($p =$ NS). Multivariate analysis demonstrated that demographics, Montreal criteria, and inflammatory markers at diagnosis were not associated with rapid complication. The model revealed that stricturing phenotype (OR 21.8, 95% CI 1.766-269.7), exposure to steroids (OR 9.8, 95% CI 2.04-47.6) or immunmodulators (OR 6.79, 95% CI 1.26-36.5) during the first 6 months since diagnosis were associated with rapid disease progression. Interestingly, exposure to biologics during the first 6 months of diagnosis was not associated with complication risk.
Conclusion: Early complications occurring within the first six months from diagnosis manifest in a quarter of newly diagnosed CD patients. These rapidly complicated CD patients are treated with significantly more steroids and immumodulators compared to non-rapidly complicated patients, but not with biologics. As complications emerge early and clinical and laboratory predictors for progression are unreliable, intensive follow-up for newly diagnosed patients and consideration of very early introduction of biologics to suspected complicators are warranted. More accurate molecular and serological characteristics are required to better phenotype these patients.
Disclosure of Interest: None declared

OP156 PHARMACOLOGICAL TREATMENT OF CROHN'S DISEASE CAN CHANGE THE COURSE DURING THE FIRST FIVE YEARS AFTER DIAGNOSIS. RESULTS FROM A SWEDISH PROSPECTIVE POPULATION-BASED COHORT

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Introduction: Although the pharmacological treatment of Crohn's disease has been intensified during later years with an increased use of immunomodulating drugs as well as the introduction of biologics, controversy still exists regarding the fundamental question whether the disease course can be changed with pharmacological treatment. We have previously reported that long symptom duration before diagnosis of Crohn's disease was associated with the prevalence of intestinal damage (1). Even if the patients received modern pharmacological treatment to a high extent, the bowel resection rate after one year was comparable with the IBSEN study (2) from the pre-biological era (12.5% vs 13.6%). We now report the five years result of the ICURE study (IBD Cohort Uppsala Region).
Aims & Methods: The aim of the study was to evaluate the frequency of intestinal resections in patients with Crohn's disease during the first 5 years after diagnosis. Within the Uppsala health care region of Sweden (population 642,000) all patients in all age groups with newly diagnosed Crohn's disease were included prospectively during the years 2005-2009 (n = 268). The average incidence was 9.9/100 000/year. After 5 years follow-up all journal records were analysed for surgery, medication and mortality.
Results: During follow-up 17 patients died (6.3%), whereof three cases related to the Crohn's disease (dehydration due to high ileostomy output, small bowel carcinoma and small bowel obstruction with sepsis). 226 of the surviving patients had a complete 5-year follow-up (90%). After 1 year the bowel resection rate was 12.4% and after 5 years it was 14.9% using Kaplan-Meier survival function. Patients < 17 years had a 5 years resection rate of 6.1%. 57% of the patients were treated with antimetabolites and 21% were treated with anti-TNF-alpha antibodies. Stricturing and penetrating behaviour were independent risk factors for bowel resection in a multivariate analysis.
Conclusion: The number of patients with Crohn's disease in need for intestinal resection within 5 years after diagnosis was only 15%, to be compared with a recent meta-analysis estimating the surgery rate to 24% for patients diagnosed 2000-2011 (3). Only 2.5% of the patients were subjected to surgery after the first year. 61% had been treated with either antimetabolites or anti-TNF-alpha antibodies, or a combination of these two. The disease-specific mortality after 5 years was 1.1%.

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Disclosure of Interest: None declared

OP157 CHOLANGIOGRAPHIC EVIDENCE OF SCLEROSING CHOLANGITIS AFTER TWO DECADES OF INFLAMMATORY BOWEL DISEASE: MRI SCREENING IN A POPULATION-BASED COHORT

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Introduction: The prevalence of primary sclerosing cholangitis (PSC) has been reported in the range of 2.4-7.5% in ulcerative colitis (UC) and 1.2-6.4% in Crohn's disease (CD). However, PSC may have a mild disease course and preliminary data have suggested that the true prevalence in inflammatory bowel disease (IBD) could be significantly higher (>10%). In the present study we aimed to determine the prevalence of PSC in longstanding IBD by performing magnetic resonance cholangiography (MRC) screening in a population-based cohort.
Aims & Methods: A standardized MRC protocol was included as part of the 20 years follow-up of the IBSEN (*IBD South-East Norway*) inception cohort. Out of 756 patients included at baseline with a definite diagnosis of IBD, 587 were alive at the time of 20 year follow-up. N = 470 (80.0%) attended and were offered MRC. Two experienced abdominal MRI readers blinded for clinical history and

previous imaging scored independently for radiological presence of PSC-like changes by using a previously validated classification system. Final diagnosis was made by reader consensus.
Results: MRC was successfully performed in 322 patients (68.5% of the attending), comprising 153 (47.5%) women with a median age 51.4 years (range 28.8-84.4) and median IBD duration of 20.1 years (17.9-23.8). N = 222 (68.9%) of the patients were classified as UC and 100 (31.1%) as CD. The MRC-examined subgroup of the cohort was comparable to the total alive population at the time of follow-up regarding age, gender, IBD type, extension and behaviour of the disease. MRC screening identified 24 (7.4%) with definite or probable large duct PSC, out of which 9 (2.7%) were previously known. The prevalence of PSC-like changes varied by gender (5.9% in men and 9.2% in women), and IBD type (9.0% in CD and 6.8% in UC patients), but these differences were not statistically significant. Extensive colitis was observed in 12 (80.0%) of the UC patients with PSC-like changes compared to 88 (45.1%) without PSC (p = 0.014). Disease distribution for CD patients with PSC-like changes was colonic (4), ileocolonic (4) and ileal (1). In patients with PSC-like changes, a chronic persistent IBD activity was more common, than in patients without PSC (p = 0.025).
Conclusion: Two decades after the diagnosis of IBD, cholangiographic evidence of large duct PSC was observed in 7.4% of the patients, more than twice the number of clinically recognized cases. Surprisingly, the prevalence did not vary significantly with gender or IBD type. Consistent with previous reports, colitis and persistent low-grade disease activity seems to be characteristic of PSC-IBD.
Disclosure of Interest: None declared

OP158 DO PATIENTS WITH LONGSTANDING INFLAMMATORY BOWEL DISEASE (IBD) HAVE A HIGHER CANCER RISK THAN CONTROLS? RESULTS FROM THE IBSEN (INFLAMMATORY BOWEL SOUTH-EASTERN NORWAY) STUDY

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Introduction: Inflammatory bowel disease (IBD) has been associated with a broad specter of both intestinal and extraintestinal malignancies.
Aims & Methods: Our aims were twofold - to determine cancer prevalence in an unselected population-based cohort of IBD patients 20 years after diagnosis and to assess if IBD patients had an increased cancer-specific risk compared with the normal age- and gender- matched population. The IBSEN (Inflammatory Bowel South-Eastern Norway) study prospectively followed all patients (n = 756) diagnosed with IBD from January 1, 1990, to December 31, 1993, in four geographically well-defined areas in southeastern Norway. This well characterized population-based cohort was prospectively followed for 20 years. Each IBD patient was matched with up to 25 controls (matching variables: age, sex, and county). Data on all cancer cases were collected from the Cancer Registry of Norway. Cox regression model was fitted to calculate cancer-specific (all cancers and gastrointestinal cancers only) risks for patients compared with their matched controls.
Results: In total, we analyzed 519 UC (51.4% males) and 237 CD (50.2% males) patients and 18825 controls. The median age at diagnosis was 37 years in the UC group and 28 in the CD group. There were 105 cancers (13.9%) in the IBD group and 1830 (9.7%) in the controls. Overall, IBD patients had 1.5 times higher risk of cancer development than their matched controls (HR = 1.52, 95% CI 1.26-1.83, p < 0.001). Males with IBD had a significantly increased risk of CRC (colo-rectal cancer) compared to controls (HR = 2.54, 95% CI 1.40-4.63, p = 0.002).The cancer-specific risk was slightly higher in UC than in CD patients compared to the normal population (HR = 1.79, 95%CI 1.42-2.23, p < 0.001) and (HR = 1.51, 95%CI 0.98-2.31, p = 0.056); for UC and CD respectively.
Conclusion: During 20 years' disease course IBD patients had about 50% increased cancer risk compared to matched controls. Most of the excess risk is comprised by increased risk for CRC in male IBD patients.
Disclosure of Interest: None declared

OP159 CANCER AND INFLAMMATORY BOWEL DISEASE PHENOTYPE: A PROSPECTIVE MULTICENTER NESTED CASE-CONTROL IG-IBD STUDY

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Introduction: Concern exists about the cancer risk using thiopurines (IS) and/or anti-TNFs in Inflammatory Bowel Disease (IBD), while the role of IBD phenotype in determining this risk is undefined.
Aims & Methods: In prospective, multicenter, nested case-control study at 3 years, we aimed to characterize incident cases of cancer in IBD. The role of IBD phenotype *vs* IS and/or anti-TNFs use in determining the incidence of cancer was investigated. From January 2012 to December 2014, all incident cases of cancer in IBD patients referring to 16 Units (≥2 visits/year) were recorded. Each IBD patient with cancer (IBD-K) was matched with 2 IBD patients with no cancer (IBD-C) for: IBD type (Crohn's Disase, CD vs Ulcerative Colitis, UC), gender, age (±5 years). Statistical analysis: data expressed as median (range), Wilcoxon test, Chi-squared test, multivariate logistic regression analysis.
Results: During the 3 years' follow up, 44,619 IBD patients (21,953 CD, 22,666 UC) were considered. Incident cancer occurred in 174. IBD patients (IBD-K): 99 CD (CD-K) and 75 UC (UC-K). Cancer incidence was 3.9/1000 IBD patients (174/44,619), being higher in CD (4.5/1000 [99/21,953]) than in UC (3.3/1000 [75/22,666]; p = 0.042). Cancers included or involved: digestive system (39.1%; n = 68), skin (13.2%; n = 23: 9 NMSC, 11 melanoma, 3 others), urinary tract (11.5%; n = 20), lung (9.2%; n = 16), breast (7.5%; n = 13), genital tract (6.3%; n = 11), thyroid (n = 8; 4.6%), lymphoma (3.5%, n = 6 CD: 3 NHL[IS 1;IS + anti-TNFs 1]), others (5.1%; n = 9). Cancers of the digestive system included (n = 68): 48 (71%) colorectal (CRC), 8 ileal (12% all CD), 12 (17%) others. Cancer sites and CRC incidence were comparable in CD vs UC (n = 24/99; 35.2% vs n = 24/75; 32%). The percentage of patients with perforating CD was higher in CD-K vs CD-C (26% (26/99 vs 15%; 30/198; p = 0.02). The percentage of patients with extensive UC was higher in UC-K vs UC-C (55%; 41/75 vs 34%; 51/159; p = 0.03). Risk factors for any cancer included perforating CD (OR 2.33; 95% CI 1.01-5.47) and IS + anti-TNFs use in CD (OR 1.94, 95% CI 1.1-3.5), pancolitis (OR 2.95; 95% CI 1.35-6.71) and surgery in UC (OR ; 5.09: 95%CI: 1.73-17.15). When excluding CRC from the analysis, perforating CD, pancolitis and surgery in UC, but not IS + anti-TNFs in CD, were risk factor for cancer in IBD.
Conclusion: In a prospective, multicenter, nested-case control study, CD phenotype, penetrating CD and extensive UC represented risk factors for any cancer in IBD.
Disclosure of Interest: L. Biancone Lecture fee(s): MSD, Takeda, Abbvie, Zambon, A. Armuzzi Lecture fee(s): Abbvie, Astra Zeneca, Chiesi, Ferring, MSD, Otsuka, Takeda, Zambon, Consultancy: Abbvie, Hospira, Lilly, MSD, Sofar, M. L. Scribano Lecture fee(s): Zambon, Consultancy: Biogen Idec, Takeda, Mundipharma, R. D'Inca' Lecture fee(s): Hospira, Abbvie, MSD, Cadigroup, C. Papi Consultancy: Takeda, Abbvie,MSD, sofar, Chiesi, L. Spina: None declared, E. Angelucci: None declared, C. Petruzziello: None declared, L. Guidi: None declared, A. Kohn: None declared, F. Mocciaro: None declared, P. Alvisi: None declared, A. Ruffa: None declared, R. Monterubbianesi: None declared, W. Fries Lecture fee(s): Abbvie, MSD, Hospira, Ferring, G. Riegler Lecture fee(s): Takeda, MSD, M. Daperno Financial support for research: MSD, Lecture fee(s): Abbvie, MSD, Hospira, Mundipharma, Takeda, Sofar, Chiesi, Ferring, F. Castiglione Lecture fee(s): Takeda, Chiesi, MSD, Abbvie, Sofar, G. Condino: None declared, S. Renna: None declared, E. Calabrese Lecture fee(s): Abbvie. MSD, R. Di Mitri: None declared, G. Meucci: None declared, F. Rogai: None declared, S. Ardizzone Lecture fee(s): MSD, abbvie, A. Rossi: None declared, A. Orlando: None declared, F. Pallone Lecture fee(s): Zambon, Takeda

OP160 EXTRACOLONIC NEOPLASIAS IN INFLAMMATORY BOWEL DISEASE PATIENTS: DATA FROM THE GETECCU ENEIDA REGISTRY

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Aims & Methods: a) To know the prevalence and distribution of ECNs in IBD patients; b) To estimate the incidence rate of ECNs; c) To evaluate the association between ECNs and the treatment with IMMs and anti-TNF agents
Inclusion criteria: IBD patients included in ENEIDA Project from GETECCU. To estimate the incidence rate of ECNs, only patients diagnosed with IBD after the implementation of ENEIDA in each center (2007 in most of them) were considered (inception cohort).
Results: 11,047 patients met the inclusion criteria with a median follow-up of 98 months. 48% of patients had been exposed to IMMs or anti-TNFs. The prevalence of ECNs was 3.6%. In the multivariate analysis, age (OR = 1.03, 95%CI = 1.03-1.04) and to have been ever smoker (OR = 1.2, 95%CI = 1.04-1.6) were the only variables associated with a higher risk of ECN. 3,485 patients

comprised the inception cohort, with a median follow-up of 27 months. 45% of patients had been exposed to IMMs or anti-TNFs at any time during follow-up (42% thiopurines, 3.5% methotrexate, 20% anti-TNFs). 38 patients developed ECNs (1.1%). In the multivariate analysis, age was the only variable associated with a higher risk of ECN (HR = 1.04, 95%CI = 1.02-1.07). The treatment with IMMs or anti-TNFs was not associated with a higher risk of ECN. The relative risks (RR) of melanoma and bladder, lip and oral cavity, and lung cancer were increased compared with the background population. The RR of lip and oral cavity, melanoma, thyroid and breast cancer in ulcerative colitis, and the RR of bladder cancer and non-Hodgkin lymphoma were increased in Crohn's disease patients.

Conclusion: Older age and smoking habit were associated with a higher prevalence ECNs. Older age was associated with a higher incidence of cancer. Neither thiopurines/methotrexate nor anti-TNF drugs seem to increase the risk of ECNs. The RR of melanoma and tobacco-related cancers were increased in IBD patients.

Disclosure of Interest: None declared

OP161 UNCHANGED SURGERY AND HOSPITALIZATION RATES IN AN EAST-WEST EUROPEAN INCEPTION COHORT DESPITE DIFFERENCES IN USE OF BIOLOGICALS – 3-YEAR FOLLOW-UP OF THE ECCO-EPICOM COHORT

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Introduction: The EpiCom-cohort is a European prospective population-based cohort of unselected, uniformly diagnosed patients with inflammatory bowel disease (IBD) in 2010 from Western and Eastern European countries. The cohort aims at describing differences in occurrence, treatment strategies, and disease course within Europe.

Aims & Methods: Patients were followed prospectively from the time of diagnosis. Clinical data on surgery, hospitalization and medical treatment were captured throughout the follow-up period. The aim of the study was to investigate differences in treatment strategy and disease outcome between Eastern and Western Europe during the first 3 years of follow-up.

Results: A total of 934 patients aged ≥15 years from 21 centres (13 Western, 8 Eastern European) were eligible for follow-up of whom 501 (54%) had ulcerative colitis (UC), 335 (36%) had Crohn's disease (CD), and 98 (10%) had IBD unclassified (IBDU). At 3-years follow up 80 patients had undergone 1st surgery (resections or colectomy) (17 from Eastern Europe, 63 from Western Europe), 120 had received biological therapy (12 from Eastern Europe, 108 from Western Europe) and 180 were hospitalized (35 from Eastern Europe, 145 from Western Europe). Crude annual rates for surgery, biological treatment and hospitalization are shown in Table 1. The cumulative probability of CD patients receiving treatment with 5-ASA within the three first years of disease was 90% in Eastern Europe and 55% in Western Europe ($p < 0.05$), 69% and 64% for prednisolone, 49% and 61% for immunomodulators, respectively. For UC patients the cumulative probability of receiving 5-ASA was 100% in Eastern Europe and 86% in Western Europe ($p < 0.05$), 40% and 47% for prednisolone, 20% and 26% for immunomodulators, respectively. Cox regression analysis revealed that hospitalization, surgery, and need for higher treatment steps was associated with stricturing or penetrating disease in CD and extensive disease in UC.

Conclusion: In an era of early and aggressive immunological therapy, surgery and hospitalization rates were similar in Eastern and Western Europe and comparable to population-based cohorts from the pre-biological era. This similar disease course was in spite of more early and aggressive treatment with biologics, with significantly more patients in Western Europe receiving biologics. The use of 5-ASA for CD is frequent and differs between Eastern and Western Europe.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30

NEW PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENT ALTERNATIVES FOR IBS – ROOM E1

OP162 BIFIDOBACTERIUM LONGUM NCC3001 IMPROVES DEPRESSION AND REDUCES BRAIN EMOTIONAL REACTIVITY IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS): A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

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Introduction: Specific probiotic bacteria can improve gut symptoms of IBS[1], however, their efficacy in treating co-morbid anxiety or depression in this population is unknown. We have previously shown that the probiotic *B. longum NCC3001* normalizes anxiety-like behaviour and hippocampal neurotrophin levels in murine models of low-grade gut inflammation[2].

Aims & Methods: To evaluate the effects of *B. longum NCC3001* on anxiety and depression in patients with IBS and to study the underlying mechanisms. We conducted a randomized, double-blind, placebo-controlled, single center study in adult patients with IBS with diarrhea or mixed stool pattern (Rome III criteria) and mild to moderate anxiety and/or depression. *B. longum* or placebo (maltodextrin) was administered daily for 6 weeks. Validated questionnaires were used to assess anxiety and depression (HAD score, STAI), IBS symptoms (adequate relief question, IBS Birmingham and Bristol scale), quality of life (SF-36) and somatization (PHQ-15) before, at the end and 1 month after the treatment (follow-up). We assessed brain activation patterns using the backward masked fear paradigm (fMRI), cognitive function (memory and concentration), serum BDNF and inflammatory markers, and gut microbiota profiles (16S rRNA Illumina).

Results: We randomized 44 patients, 38 of them (*B. longum* = 18, placebo = 20) completed the study. At six weeks, depression scores improved in patients treated with *B. longum* compared with placebo (RR 2.94, 95% CI 1.05-8.23, $p = 0.01$) and this was maintained at follow-up. More patients treated with *B. longum* than placebo reported adequate relief of overall IBS symptoms (RR 2.1, 95% CI 1.15-3.83, $p = 0.02$) but no statistically significant changes were found in the IBS Birmingham scores. The physical subdomain of quality of life improved in *B. longum* treated group compared with placebo ($p = 0.03$, Mann–Whitney $U = 228.5$), with trends for improvement in the mental subdomains of vitality and emotional role functioning. Functional MRI revealed significant reductions from baseline in response to negative emotional stimuli in multiple brain areas involved in emotion processing, including amygdala, frontal and temporal brain regions ($p < 0.001$), in *B. longum* treated patients compared with placebo. No statistically significant differences were observed in anxiety, cognitive function, inflammatory markers, serum BDNF levels or gut microbiota profiles in *B. longum*-treated patients compared to placebo.

Conclusion: Our results demonstrate that six-week treatment with *B. longum NCC3001* improves comorbid depression, overall gastrointestinal symptoms and quality of life in patients with IBS. This is associated with changes in the brain activation patterns in the amygdala and fronto–limbic regions, suggesting that reduction in limbic reactivity may underlie the beneficial effect of this probiotic.

References

1. Ford et al. *Am J Gastroenterol* 2014.
2. Bercik et al. *Gastroenterology* 2010.

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Disclosure of Interest: M. Pinto-Sanchez: None declared, G. Hall: None declared, K. Ghajar: None declared, A. Nardelli: None declared, C. Bolino: None declared, C. Welsh: None declared, A. Rieder: None declared, J. Traynor: None declared, C. Gregory: None declared, J. Lau: None declared, A. Ford: None declared, G. Bergonzelli Shareholder: Nestle Research Center, M. Surette: None declared, S. Collins: None declared, P. Moayyedi: None declared, P. Bercik Financial support for research: Study supported by a grant from Nestle Switzerland

Abstract number: OP161 Table 1: Crude rates for surgery, biological therapy and hospitalization (*$p < 0.05$)

		Biological treatment		Surgery		Hospitalization	
		1 year	3 years	1 year	3 years	1 year	3 years
Crohn'sdisease	Eastern Europe	4 (5%)	7 (8%)	10 (12%)	14 (17%)	16 (19%)	20 (24%)
Western Europe	50 (20%)*	67 (27%)*	26 (10%)	40 (16%)	46 (18%)	63 (25%)	
Ulcerative colitis	Eastern Europe	1 (1%)	5 (4%)	2 (2%)	3 (2%)	8 (6%)	15 (12%)
Western Europe	18 (5%)*	32 (9%)*	9 (2%)	18 (5%)	47(13%)	68 (18%)	

OP163 THE IMPACT OF LOW FODMAP DIETARY ADVICE AND PROBIOTICS ON SYMPTOMS IN IRRITABLE BOWEL SYNDROME: A RANDOMISED, PLACEBO-CONTROLLED, 2X2 FACTORIAL TRIAL

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Introduction: Controlled trials using complete feeding diets have demonstrated that dietary restriction of fermentable carbohydrates (low FODMAP diet, LFD) reduces symptoms in patients with irritable bowel syndrome (IBS). However, a randomised, placebo controlled dietary advice trial has not been performed. Also, LFD has a negative impact on the gastrointestinal microbiota and the benefit of combining LFD with probiotics is unknown.

Aims & Methods: This randomised controlled trial aimed to investigate the effect of LFD dietary advice with a probiotic on symptom response compared with a sham diet in patients with IBS. Adults with IBS referred to a secondary care dietetic service were screened for inclusion (n = 162). Eligible patients were randomised to LFD or sham (placebo) dietary advice and to the multi-strain probiotic VSL#3 or placebo for 4 weeks in a 2x2 factorial design. The sham (placebo) diet was designed to be equivalent in nutrients and FODMAP content to habitual diet. Outcome measures included the global symptom question ('did you have adequate relief of your IBS symptoms over the last 7 days?') and the validated IBS symptom severity scale (IBS-SSS, maximum score 500) at baseline and follow up. Statistical analysis was performed using logistic and linear regression.

Results: A total of 104 patients were recruited and 95 completed the study (63 females, 66%). There were 8 withdrawals (4 LFD, 4 sham) and 1 loss to follow up (sham). There was no significant interaction between diet (LFD/sham) and probiotic (VSL#3/placebo) for adequate relief or IBS-SSS. In the intention-to-treat analysis, a higher proportion of patients reported adequate relief at follow up in LFD (57%) versus sham (38%, p = 0.05; RR 1.51, 95% CI 0.99, 2.29) and for probiotic (57%) versus placebo (37%, p = 0.05, RR 1.52, 95% CI 0.99, 2.33). Mean IBS-SSS scores were significantly lower following the LFD versus sham (165.5 vs 231.8, $p < 0.001$) but not different for probiotic versus placebo (196.9 vs 201.7, p = 0.75), after adjusting for baseline values. Subscores for IBS-SSS were significantly lower after LFD versus sham for days of pain (28.6 vs 44.7, $p < 0.001$), distension (27.3 vs 41.6, p = 0.001) and satisfaction with bowel habit (40.7 vs 54.5, $p < 0.001$).

Conclusion: This is the first randomised placebo-controlled trial evaluating the effect of LFD advice which demonstrates greater effectiveness compared with sham advice for IBS symptoms. The effectiveness of this probiotic is equivocal. Whether concomitant probiotic treatment is able to prevent the impact of LFD on the microbiota will be investigated.

Disclosure of Interest: None declared

OP164 THE EFFECT OF DIETARY GUIDANCE ON THE DUODENAL ENDOCRINE CELLS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Altered neuroendocrine system is one of the pathophysiological factors in irritable bowel syndrome (IBS). The densities of the gut endocrine cells are found abnormal in IBS patients. Dietary guidance with low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet has improved the symptoms and quality of life of IBS patients (1) and normalized the densities of several endocrine cell types in the stomach (2) and the colon (3).

Aims & Methods: The aim of the current study is to investigate the effect of dietary guidance on the duodenal endocrine cells in the same cohort of patients with IBS. The study included 14 IBS patients (9 females and 5 males, age range 20-45 years) and 14 control subjects (9 females and 5 males, age range 26-70 years). The patients received three 45-min sessions of individualized dietary guidance. The patients and controls underwent gastroscopies at baseline and again for the patients at 3–9 (median 4) months after receiving the last session of dietary guidance. Biopsy samples were taken from pars descendens of the duodenum and were immunostained by Avidin-biotin-Complex method for all types of endocrine cells. The endocrine cells were quantified using computerized image analysis.

Results: The daily total consumption (mean ± SEM values) of fruits and vegetables high in FODMAPs decreased significantly from 16.2 ± 5.3 g before receiving dietary guidance to 9.2 ± 3.2 g after receiving dietary guidance ($P = 0.02$). The densities of the duodenal endocrine cells before and 3–9 (median 4) months after receiving dietary guidance are presented in Table 1.

Table 1: Densities of immunoreactive endocrine cells in the duodenum of control subjects and of IBS patients before and after receiving dietary guidance

	Endocrine cell densities (cells/mm2)			
Hormone	Control	Before guidance	After guidance	*P*-value
Chromogranin A	235.9 ± 31.9	36.9 ± 9.8	103.7 ± 16.9	0.007[b]
Serotonin	76.1 ± 11.9	6.8 ± 1.8	20.6 ± 6.0	0.03[a]
Somatostatin	43.1 ± 5.2	10.7 ± 1.5	24.4 ± 2.4	< 0.0001[c]
Cholecystokinin	80.7 ± 4.0	64.1 ± 4.2	77.8 ± 8.2	0.21
Secretin	76.9 ± 3.8	54.4 ± 2.1	61.1 ± 3.4	0.05
Gastric inhibitory peptide	54.3 ± 4.9	39.3 ± 2.9	45.9 ± 4.3	0.096

Data are presented as the mean ± SEM. a: P < 0.05, b: P < 0.01, c: P < 0.0001

Conclusion: The main triggers of the gut endocrine cells are the luminal contents of the gut, especially nutrients. This study is the first to show that the interaction between the ingested food and the endocrine cells is reflected by a change in the densities of the duodenal endocrine cells in IBS patients towards the values of healthy controls after receiving dietary guidance. The positive effects of dietary guidance may be attributed to changes in the gut endocrine cells densities, thus improving the symptoms of IBS.

References

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Disclosure of Interest: None declared

OP165 A REASON WHY LACTOSE-FREE DIET CAN BE CLINICALLY INEFFECTIVE IN LACTOSE INTOLERANCE PATIENTS

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Introduction: Lactose intolerance is highly prevalent in Mediterranean area. A substantial proportion of patients remain symptomatic notwithstanding lactose-free diet.

Aims & Methods: Assess in a series of IBS consecutive patients: 1) the prevalence of lactose intolerance (LI); 2) the frequency of association of lactose intolerance with small intestinal bacterial overgrowth (SIBO); 3) the possibility of SIBO as a cause of symptom persistence in patients with lactose intolerance on lactose-free diet. Patients were recruited from November 2011 to July 2012 at the Gastroenterology Unit of Mauriziano Hospital U. I[st,] Turin, Italy. Lactose malabsorption was assessed by means of Lactose Hydrogen Breath Test (LHBT) and SIBO by means of Glucose Hydrogen Breath Test (GHBT), using Breath Tracker digital microlyzer, on 500 IBS patients (360 F; mean age 45 ± 23 SD years) and 50 controls (30 F mean age 43 ± 24 SD age). Lactose intolerance patients with SIBO were treated either with rifaximin 1200 mg a day for 2 weeks plus exclusion diet, or only with exclusion diet, randomly, on 1 to 1 basis, for 6 months. Symptoms frequency and intensity (abdominal pain, bloating, diarrhea) were recorded by means of a visual analogue scale. Statistical analysis were carried out by SPSS software.

Results: Prevalence of lactose intolerance resulted to be 59% in IBS patients and 6% in controls, with a statistically significant difference ($p < .001$). SIBO was present in 72% of patients with lactose intolerance in IBS group, ad in none of the subjects with lactose malabsorption (3) from the control group. No significant difference was registered in gender and age between the 2 groups. After 6 months, 105 out of 106 patients affected by LI + SIBO treated with rifaximin + lactose free diet (99%), and 34 out of 107 patients affected by LI + SIBO treated only with lactose free diet (32%) resulted completely asymptomatic, with statistically significant difference ($p < 0.001$).

Conclusion: Lactose intolerance is a common condition in patients with IBS in Northwest Italy (59%), very frequently associated with SIBO (72%). This association turned out to be a major cause of symptom persistence in patients on lactose-free diet until successful eradication of SIBO was achieved.

Disclosure of Interest: None declared

OP166 ELUXADOLINE DEMONSTRATES SUSTAINED EFFICACY FOR THE TREATMENT OF IRRITABLE BOWEL SYNDROME WITH DIARRHOEA IN PHASE 3 CLINICAL TRIALS

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Introduction: Eluxadoline (ELX), is a locally active, mixed mu-opioid receptor agonist and delta-opioid receptor antagonist being developed to treat irritable bowel syndrome with diarrhoea (IBS-D).

Aims & Methods: To assess the efficacy of ELX in two double-blind, placebo (PBO)-controlled Phase 3 trials (IBS-3001, IBS-3002). Patients (pts) meeting Rome III criteria for IBSD were randomised to twice-daily ELX (75 or 100 mg) or PBO. Efficacy was evaluated through 26 weeks (wks). Efficacy was assessed via a composite response endpoint, requiring simultaneous improvement in abdominal pain and stool consistency. Pts who met both daily pain responder (≥30% improvement in abdominal pain) AND daily stool consistency responder (Bristol Stool Scale score of <5) criteria for ≥50% of days were considered responders. To assess both onset and sustainability of response, responder analyses included monthly, 3-month and 6month assessments of the composite endpoint. For the monthly or 3-month intervals pts had to record ≥72% daily diary entries of symptoms to be assessed for response on the composite endpoint, whereas for the 6-month interval ≥60% daily diary entries were required.

Results: A total of 2428 IBS-D pts were enrolled across both trials. Significantly more pts ($p \leq 0.017$) receiving ELX 100 mg were composite responders than pts receiving PBO over every time interval examined using the Cochran–Mantel–Haenszel (CMH) analysis (Table 1). Longitudinal analyses (LA) at specific time points supported the CMH results. No age or gender differences were detected in the composite response rates. The proportions of pts with adverse events (AEs) were similar across the ELX 75 mg (60.2%), ELX 100 mg (58.2%) and PBO (55.7%) groups; this was also true for serious AEs (4.2%, 4.8% and 3.0%, respectively). The most common AEs were in the gastrointestinal system: 30.0%, 27.7% and 19.4% for ELX 75 mg, ELX 100 mg and PBO, respectively.

Conclusion: Phase 3 trial results demonstrated that ELX was an effective treatment for IBS-D, exhibiting rapid onset of action and sustained efficacy over 6 months.

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OP167 EFFECT OF ELUXADOLINE ON HEALTH-RELATED QUALITY OF LIFE IN ADULTS WITH IRRITABLE BOWEL SYNDROME WITH DIARRHOEA: RESULTS FROM TWO RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 TRIALS

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Introduction: Eluxadoline, a locally active, mixed mu-opioid receptor agonist and delta-opioid receptor antagonist, significantly improved both abdominal pain and diarrhoea in two Phase 3 trials (IBS-3001 and IBS-3002) in patients with irritable bowel syndrome with diarrhoea (IBSD). The objective of this analysis was to evaluate the impact of eluxadoline treatment on health-related quality of life (HRQoL) in patients with IBS-D based on data from IBS-3001 and IBS-3002.

Aims & Methods: Adults meeting Rome III criteria for IBS-D were randomised to twicedaily oral eluxadoline (75 or 100 mg) or placebo for 26 weeks in IBS-3002 and 52 weeks in IBS-3001. The Irritable Bowel Syndrome Quality of Life questionnaire (IBS-QOL), consisting of 34 items, each with a 5-point response scale (1 = "not at all", 5 = "extremely"/"a great deal"), was completed at baseline and Weeks 4, 8, 12, 18 and 26 in both trials and at Week 30 in IBS-3002 and Weeks 36, 44 and 52 in IBS-3001. Mean IBS-QOL total scores were evaluated for trends by treatment groups by employing a longitudinal mixed-effects polynomial model fitted to pooled data to estimate treatment effects of eluxadoline. Cumulative distribution functions for changes from baseline to Weeks 12, 26 and 52 in IBS-QOL total scores were plotted.

Results: Of the 2428 patients in the two Phase 3 trials, 2404 (99%) had baseline IBS-QOL scores (n = 1270, IBS-3001; n = 1134, IBS-3002). The mean age was 45.4 years; 66.1% of patients were female. Patients treated with eluxadoline 75 and 100 mg had consistently higher IBSQOL total scores over 52 weeks of treatment compared with patients who received placebo (Table). The longitudinal mixed-effects model showed a significant treatment effect for both the eluxadoline 75 mg ($t = 4.34$; $p < 0.0001$) and 100 mg groups ($t = 4.45$; $p < 0.0001$). Cumulative distribution function plots of change from baseline scores confirmed that patients treated with eluxadoline 75 and 100 mg showed consistently higher increases in IBS-QOL total scores compared with patients who received placebo over a range of improvement levels for Weeks 12, 26 and 52.

Table: Post-baseline model estimates for IBS-QOL total scores for the pooled analysis cohort: Weeks 4, 12, 26 and 52

	Placebo (n = 807)	Eluxadoline 75 mg (n = 797)	Eluxadoline 100 mg (n = 800)
Week 4, mean (SE)	55.6 (0.71)	61.0 (0.67)	60.5 (0.67)
Week 12, mean (SE)	64.8 (0.76)	71.4 (0.71)	70.8 (0.71)
Week 26, mean (SE)	66.1 (0.87)	73.0 (0.80)	72.2 (0.82)
Week 52, mean (SE)	66.2 (1.04)	73.6 (0.94)	78.7 (1.03)

SE, standard error

Conclusion: Compared with placebo, twice-daily eluxadoline treatment significantly improved overall HRQoL among patients with IBS-D over the course of the treatment periods in two Phase 3 trials as measured by the IBS-QOL, with patients treated with eluxadoline 100 mg showing particularly strong effects.

Disclosure of Interest: J. Buono Financial support for research: Actavis, Shareholder: Actavis, D. Andrae Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), P. Covington Consultancy: Actavis, Shareholder: Furiex Pharmaceuticals (subsidiary)

OP168 CONSISTENCY IN EFFICACY OUTCOMES OF ELUXADOLINE-TREATED PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH DIARRHOEA USING RECENT AND TRADITIONAL ENDPOINTS

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Introduction: Eluxadoline (ELX), a locally active, mixed mu-opioid receptor agonist and delta-opioid receptor antagonist, demonstrated improvements in the symptoms of irritable bowel syndrome with diarrhoea (IBS-D) based on a composite endpoint of improved stool consistency and reduced abdominal pain.

Aims & Methods: To further examine the consistency of ELX efficacy outcomes in two double-blind, placebo (PBO)-controlled Phase 3 trials (IBS-3001, IBS-3002), results of the daily composite response endpoint were compared with Global Symptom Score (GSS) and the patient (pt)-friendly, traditional adequate

Abstract number: OP166 Table 1: Composite response rate at varying intervals

CMH composite response rate (%) [p values of ELX vs PBO]

		Wks 1–4	p	Wks 5–8	p	Wks 9–12	p	Wks 13–16	p	Wks 17–20	p	Wks 21–24	p	Wks 1–12	p	Wks 1–26	p
IBS-3001	PBO	12.9		19.9		21.8		21.1		21.8		20.4		17.1		19.0	
	ELX 75 mg	20.6	0.003	26.5	0.023	23.7	0.514	22.7	0.563	27.6	0.047	27.4	0.016	23.9	0.014	23.4	0.112
	ELX 100 mg	22.5	<0.001	28.9	0.002	30.3	0.005	29.1	0.007	28.9	0.017	28.2	0.008	25.1	0.004	29.3	<0.001
IBS-3002	PBO	12.0		19.9		22.0		20.9		22.5		19.9		16.2		20.2	
	ELX 75 mg	25.2	<0.001	31.5	<0.001	32.3	0.001	30.7	0.002	31.2	0.007	28.9	0.004	28.9	<0.001	30.4	0.001
	ELX 100 mg	26.7	<0.001	33.5	<0.001	31.9	0.002	33.8	<0.001	31.2	0.007	32.5	<0.001	29.6	<0.001	32.7	<0.001

LA composite response rates (odds ratios and p values of ELX vs PBO)

		Wk 4	p	Wk 8	p	Wk 12	p	Wk 16	p	Wk 20	p	Wk 24	p	Wk 26	p
IBS-3001	ELX 75 mg	1.51	0.025	1.50	0.026	1.50	0.027	1.49	0.029	1.49	0.031	1.48	0.034	1.48	0.036
	ELX 100 mg	1.76	0.002	1.75	0.002	1.73	0.003	1.72	0.003	1.71	0.004	1.69	0.005	1.69	0.005
IBS-3002	ELX 75 mg	2.64	<0.001	2.60	<0.001	2.55	<0.001	2.50	<0.001	2.46	<0.001	2.41	<0.001	2.39	<0.001
	ELX 100 mg	2.71	<0.001	2.74	<0.001	2.77	<0.001	2.80	<0.001	2.83	<0.001	2.86	<0.001	2.88	<0.001

Abstract number: OP168 Table 1: Efficacy outcomes

		IBS-3001			IBS-3002		
Responders (%)*p value vs PBO*		**PBO**	**ELX 75 mg**	**ELX 100 mg**	**PBO**	**ELX 75 mg**	**ELX 100 mg**
Daily composite endpoint	Wks 1–12	17.1	23.9*0.014*	25.1*0.004*	16.2	28.9 < *0.001*	29.6 < *0.001*
	Wks 1–26	19.0	23.4*0.112*	29.3 < *0.001*	20.2	30.4*0.001*	32.7 < *0.001*
GSS	Wks 1–12	28.8	35.1*0.048*	34.7*0.063*	29.6	43.6 < *0.001*	42.4 < *0.001*
	Wks 1–26	32.3	36.3*0.221*	37.1*0.144*	34.3	45.1*0.002*	43.2*0.012*
AR	Wks 1–12	43.8	52.9*0.008*	54.2*0.002*	49.2	60.1*0.003*	58.4*0.011*
	Wks 1–26	40.0	45.7*0.097*	49.5*0.005*	43.7	52.8*0.013*	53.7*0.006*

relief (AR) endpoint. Pts meeting Rome III criteria for IBS-D were randomised to twice-daily ELX (75 or 100 mg) or PBO. Efficacy was evaluated through 26 weeks (wks). The primary endpoint was composite response (based on simultaneous improvement in daily worst abdominal pain [0–10 scale] and stool consistency [Bristol Stool Scale 1–7] with ≥50% of days demonstrating a response) evaluated over Wks 1–12 and 1–26 (with ≥60/84 or ≥110/182 days of diary compliance, respectively). Pts indicated whether they had AR from IBS symptoms over the past wk and rated their daily IBS symptoms over the past 24 h (0 = none, 4 = very severe). Efficacy assessments included Cochran–Mantel–Haenszel (CMH) analysis requiring AR response of ≥6/12 or ≥13/26 wks and, for assessment of GSS, CMH analysis of ≥50% of days with either daily GSS < 2 or GSS improved by ≥2 compared with the baseline average. Pooled data using analysis of covariance (ANCOVA) assessed change from baseline (CFB) in GSS.

Results: A total of 2428 pts with IBS-D were enrolled across both trials. Average GSS scores decreased in all groups and in both studies from baseline through Wk 26. Table 1 shows responder outcomes for the composite, GSS and AR endpoints. A significantly greater proportion of pts receiving ELX were composite responders compared with pts receiving PBO ($p \leq 0.014$), with the exception of pts receiving ELX 75 mg in IBS-3001 over Wks 1–26. Comparable results were seen for GSS and AR endpoints with ELX 75 and 100 mg. Efficacy in the ELX 100 mg group was more robust than in the 75 mg group in both trials, and results from IBS-3002 were generally more robust than those from IBS-3001. Pooled data for ANCOVA CFB for GSS also demonstrated superiority over PBO at Wks 12 and 26 ($p \leq 0.008$).

Conclusion: Individual studies and pooled data demonstrated that ELX was superior to PBO in relieving IBS-D symptoms. Efficacy outcomes for the GSS endpoint and the more pt-friendly, traditional AR endpoint were consistent with the primary efficacy composite endpoint over 12 and 26 wks.

Disclosure of Interest: M. Zuckerman Consultancy: Actavis, Inc. and has taken part in Actavis, Inc. advisory boards, L. Dove Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), D. Andrae Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), J. M. Davenport Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), L. Turner Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), R. Lopez Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), P. Covington Consultancy: Actavis, Shareholder: Furiex Pharmaceuticals (subsidiary)

OP169 THE RESTORE-4 STUDY: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, PARALLEL-GROUP PHASE II STUDY ASSESSING THE EFFICACY AND SAFETY OF ONO-2952, A NOVEL AND SELECTIVE ANTAGONIST OF TRANSLOCATOR PROTEIN

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Introduction: Translocator protein (TSPO) is mainly located in the outer mitochondrial membrane of steroid-producing cells, including brain glial cells, and transports cholesterol from intracellular sources into the mitochondria, a rate limiting step of neurosteroidogenesis. TSPO ligands have been suggested to regulate levels of neurosteroids which are known to act as allosteric modulators of both excitatory and inhibitory neurotransmission. We have demonstrated that ONO-2952, a novel and selective TSPO antagonist, inhibits stressinduced defecation and visceral hyperalgesia in rat stress models, suggesting a therapeutic potential in the treatment of stress-related disorders such as irritable bowel syndrome (IBS). We evaluated the efficacy and safety of ONO-2952 in a Phase 2 study in patients with diarrhea-predominant IBS (IBS-D).

Aims & Methods: A randomised, double-blind, placebo-controlled study was conducted at 49 centres in the United States and recruited 200 female patients (aged 18-65 years) with IBS-D according to Rome III criteria. Patients were randomly assigned to receive either 20 or 60 mg ONO-2952 or placebo (1:1:1 ratio) orally once-daily for 4 weeks. Patients recorded their IBS symptoms on a daily basis in an e-diary during a 2-week baseline, the 4-week treatment period and for 4 weeks post-treatment. Safety monitoring was performed throughout the study. The co-primary endpoints were change from baseline to week 4 in stool consistency, stool frequency and abdominal pain. Secondary endpoints included FDA responder analyses. Patients were considered responders if they met the FDA daily responder criteria for at least 50% of time over the interval from weeks 1-4.

Results: Demographics and baseline characteristics were comparable for the 3 treatment arms. Per protocol set analyses demostrated improvements over placebo in the number of days per week with at least one stool having a BSS classification of 6 or 7 and mean weekly score of the worst abdominal pain experienced during the past 24 hours were observed with 60 mg ONO-2952 over the 4-week treatment period but did not achieve significance at a 5% level ($P < 0.10$).

A statistically significant difference in the odds ratio for the percentage of responders was observed following ONO-2952 60mg compared with placebo for the change from baseline of 40% (odds ratio: 2.44; 95% CI: 0.95, 6.23; $p < 0.10$) and 50% in abdominal pain (odds ratio: 2.89; 95% CI: 1.04, 8.00; $p < 0.05$).

ONO-2952 was well-tolerated and had a favourable safety profile. The majority of AEs were mild in intensity and unrelated to study drug. A similar pattern of central nervous system (CNS) AEs was observed across all treatment groups and there were no clinically significant AEs related to the CNS.

Conclusion: ONO-2952 demonstrated a greater potential to impact clinical symptoms compared to placebo in female patients with IBS-D. Those given ONO-2952 60mg were more likely to be clinical responders on both abdominal pain and stool consistency, in addition to a composite of these endpoints. Further examination of ONO-2952 is warranted to assess its potential as a treatment for IBS.

Disclosure of Interest: W. Whitehead Consultancy: Received consultancy fees from Ono Pharmaceuticals, T. Nabata Conflict with: Employee of Ono Pharma UK Ltd., K. Duffy Conflict with: Employee of Ono Pharma UK Ltd., J. Sharpe Conflict with: Employee of Ono Pharma UK Ltd., M. Bruce Conflict with: Employee of Ono Pharma UK Ltd.

OP170 EFFICACY OF ORAL IBODUTANT IN IBS-D FEMALE PATIENTS MEASURED BY URGENCY SCORE: AN IRIS-2 EXPLORATORY ANALYSIS

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Introduction: Irritable bowel syndrome with diarrhoea (IBS-D) is particularly debilitating due to urgency and episodic incontinence. Ibodutant, a selective potent antagonist of neurokinin-2 receptor is in Phase III development for IBS-D. A phase II (IRIS-2) study tested the efficacy of 3 oral doses of ibodutant (1 mg, 3 mg, 10 mg) vs placebo in 559 IBS-D patients (333 females) defined by Rome III criteria, over a daily 8-week oral treatment, followed by 2-weeks treatment withdrawal resulting in a total of 10 weeks of daily and weekly measurements of symptoms. Based on the combined response of satisfactory relief of IBS symptoms and abdominal pain/discomfort according to the 75% rule, a statistically and clinically relevant efficacy was demonstrated in the female subgroup (n = 333) at the 10 mg dose with 46.84% of responders vs 24.36% in placebo ($p = 0.0034$).

Aims & Methods: To evaluate the benefit of ibodutant in a female IBS-D population exposed to oral daily ibodutant doses of 1, 3 and 10 mg over 8 weeks of treatment and 2 weeks of treatment withdrawal in terms of the mean stool urgency score changes versus baseline.

Among data collected through the IVRS/IWRS diary to characterize the efficacy profile of ibodutant, stool urgency was assessed as measure of IBS-D severity. Mean change after 4 weeks, 8 weeks of treatment and after 2 weeks of treatment withdrawal vs baseline (Visit 2-randomisation) (daily IVRS/IWRS diary records) were recorded according to a 5-point scale ranging from 0 = no symptoms, 1 = mild, 2 = moderate, 3 = severe to 4 = very severe. Urgency (5-point scales) response was defined as intensity reduction of ≥ 1 score point compared to baseline. This was a pre-specified analysis of variance (ANOVA) by gender.

Results: At baseline, female patients (59.57% of total patients) reported a moderate urgency intensity with a mean score value of 2.4 (±0.7), without relevant differences between the treatment groups. In this population, ibodutant confirmed the high clinically and statistically significant superiority over placebo in terms of improving stool urgency scores measured after the treatment (Least Square Means: -33.71 in placebo, -34.86 in 1 mg, -38.34 in 3 mg, -38.17 in 10 mg treatment arm), with a mean estimated score reduction of -4.47 ($P = 0.007$) in the 10 mg treatment arm vs baseline and 2 weeks after treatment withdrawal. A mean score reduction of -4.63 ($P = 0.004$) was also shown in females at 3 mg dose, whereas in males there was no statistically significant change.

Table: Stool Urgency Score Mean change during the Treatment and Withdrawal Period in IBS-D female population (n = 333)

Treatment	Estimated mean change vs placebo (SE)	P-value	CI 95%
Ibodutant 1 mg	-1,15 (1,617)	0.475	-4,32; 2,01
Ibodutant 3 mg	-4,63 (1,623)	0.004	-7,81; -1,45
Ibodutant 10 mg	-4,47 (1,655)	0.007	-7,71; -1,22

SE= Standard Error CI=Confidence Interval

Conclusion: Ibodutant doses of 10 mg and 3 mg given once daily over 8 weeks of treatment significantly improved mean stool urgency scores in female IBS-D patients. This decrease of stool urgency scores was maintained also over the ensuing 2-week treatment-free withdrawal phase.

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Disclosure of Interest: J. Tack Consultancy: Menarini Ricerche Spa, K. Schumacher Financial support for research: Menarini Ricerche Spa, S. Scartoni Financial support for research: Menarini Ricerche Spa, G. Tonini Financial support for research: Menarini Ricerche Spa, K. Ott Financial support for research: Menarini Ricerche Spa, I. Koch Financial support for research: Menarini Ricerche Spa, I. Otranto Financial support for research: Menarini Ricerche Spa, F. Masciopinto Financial support for research: Menarini Ricerche Spa, M. Bertolotti Financial support for research: Menarini Ricerche Spa, A. Capriati Financial support for research: Menarini Ricerche Spa, C. Maggi Financial support for research: Menarini Ricerche Spa

TUESDAY, OCTOBER 27, 2015 08:30–10:30

OBESITY AND CANCER: IS THERE A LINK? – ROOM E4

OP171 A CCRK INFLAMMATORY CIRCUITRY DRIVES OBESITY-ASSOCIATED HEPATOCARCINOGENESIS THROUGH CONCORDANT ACTIVATION OF MULTIPLE ONCOGENIC CASCADES

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Introduction: Recent large-scale prospective and population-based studies have underscored obesity as an important cause of certain cancers including hepatocellular carcinoma (HCC). In two cohorts of more than 900,000 United States and 5 million United Kingdom adults, overweight and obese men were shown to have much higher risks of HCC mortality and incidence when compared to women. Given the prevalence of obesity in developed countries and its rapid increase in developing countries, there is a compelling need to understand the molecular pathways that promote hepatocarcinogenesis in obese individuals. Accumulating evidence has unmasked the molecular linkage between androgen receptor (AR) signaling and gender disparity in HCC. Our previous genome-wide location and functional analysis has pinpointed cell cycle-related kinase (CCRK) as a critical mediator of AR oncogenic activity in hepatitis B virus-related HCC through glycogen synthase kinase-3β (GSK-3β)/β-catenin/enhancer zeste of homolog 2 (EZH2) signaling (1-3).
Aims & Methods: Here we investigated whether CCRK plays an oncogenic role in obesity-related hepatocarcinogenesis.
Results: Using a murine dietary obesity-promoted HCC model, we showed that lentiviral-mediated knockdown of *Ccrk* dramatically reduced hepatic lipid accumulation, inflammation and tumorigenicity. An obesity-induced pro-inflammatory cytokine, interleukin-6 (IL-6), was found to trigger signal transducer and activator of transcription 3 (STAT3) signaling to up-regulate *CCRK* expression in human hepatic cells, which in turn stimulated a positive feedback circuit involving EZH2 and nuclear factor-κB (NF-κB). In addition, both *in vitro* and *in vivo* data suggested that CCRK simultaneously activated the mechanistic target of rapamycin complex 1 (mTORC1) and β-catenin pathways crucial for many cellular processes including lipogenesis, survival and proliferation. Importantly, CCRK and its signaling components were significantly and concordantly over-expressed in human HCCs associated with nonalcoholic fatty liver disease.
Conclusion: Our findings delineate a tumor-initiating circuitry in which obesity-mediated chronic inflammation induces an IL-6-STAT3-CCRK-EZH2-NF-κB loop to drive lipogenesis and hepatocarcinogenesis through concordant mTORC1 and β-catenin activation. This study unveils the central role of CCRK in regulating multiple oncogenic cascades, thus providing a therapeutic target to combat this unrelentingly-increasing dreadful disease.

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Disclosure of Interest: None declared

OP172 ESOPHAGEAL ADENOCARCINOMA FOLLOWING OBESITY SURGERY IN A POPULATION-BASED COHORT STUDY

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Introduction: Obesity is strongly associated with EAC. Yet, whether weight loss reduces the risk of EAC is unclear.
Aims & Methods: To test the hypothesis that the risk of esophageal adenocarcinoma (EAC) decreases following weight reduction achieved by obesity surgery. This population-based cohort study included a majority of individuals who underwent obesity surgery in Sweden in 1980-2012. The incidence of EAC following obesity surgery was compared to the incidence in the corresponding background population by means of calculation of standardized incidence ratios (SIRs) with 95% confidence intervals (CIs). The risk of EAC after obesity surgery was also compared with the risk in non-operated obese individuals by means of multivariable Cox regression, providing hazard ratios (HRs) with 95% CIs, adjusted for potential confounders.
Results: Among 34,437 study participants undergoing obesity surgery and 239,775 person-years of follow-up, 8 cases of EAC occurred (SIR of 1.6, 95% CI 0.7-3.2). No clear trend of decreased SIRs was seen in relation to increased follow-up time after surgery. The SIR of EACs (n = 53) among 123,695 non-operated obese individuals (673,238 person-years) was increased to a similar extent as in the obesity surgery cohort (SIR = 1.9, 95% CI 1.4-2.5). Cox regression showed no difference in risk of EAC between operated and non-operated participants (adjusted HR = 0.9, 95% CI 0.4-1.9).
Conclusion: The risk of EAC might not decrease following obesity surgery, but even larger studies with longer follow-up are needed to establish this association.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30

FROM OMICS TO BETTER UNDERSTANDING OF PATHOGENESIS – ROOM E2

OP173 COMPARATIVE GENOMIC ANALYSIS OF HPV POSITIVE VERSUS HPV NEGATIVE OESOPHAGEAL ADENOCARCINOMA IDENTIFIES A DIFFERENTIAL MUTATIONAL LANDSCAPE

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Introduction: High-risk human papillomavirus (hr-HPV) has been implicated in a subset of patients with oesophageal adenocarcinoma (OAC) [1-3]. We therefore hypothesized that HPV associated OAC may have a distinct distribution of molecular aberrations and genomic abnormalities compared with HPV negative oesophageal cancer.
Aims & Methods: As such, whole exome sequencing (WES) was performed to explore the genomic landscape and potential molecular signature of HPV positive versus viral negative OAC.
Four hr-HPV-positive and 8 HPV-negative treatment naive fresh-frozen OAC tissue specimens were analysed to identify somatic genomic mutations. Seventy-eight recurrent and pathway related mutations were validated by Sanger sequencing and mutation specific PCR. Data was subjected to cancer driver gene identification and pathway analysis. The off-target reads were utilized for viral integration studies.
Results: The HPV-positive OAC group was younger ($p = 0.015$) and harboured approximately 50% less non-silent somatic mutations than the HPV-negative esophageal cancer patients (1.31 mutations/Mb versus 2.56 mutations/Mb, $p = 0.026$). TP53 aberrations were absent in the HPV-positive EAC group whereas 50% of the HPV-negative OAC patients exhibited TP53 mutations. Apart from TP53, genes previously described as mutated significantly in EAC i.e. SYNE1, LRP1B, CSMD3 were repeatedly detected in our cohort. HPV negative cancers were enriched with cancer driver gene mutations, but not HPV-positive tumours. Viral integration analysis identified sub-fragments of hr-HPV sequences at low frequency. Enriched A > C transversions at AA dinucleotide was observed in 5/7 Siewert class I OAC samples but none (0/5) in Siewert class II tumours ($p = 0.027$).
Conclusion: These findings demonstrate distinct genomic differences between HPV-positive and HPV-negative OAC suggesting different biological mechanisms of tumour formation.

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Disclosure of Interest: None declared

OP174 MOLECULAR BASIS OF COLORECTAL TUMORS DEVELOPED THROUGH SERRATED PATHWAY

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Introduction: Recent genomic research has revealed that CRC can develop through various pathways, resulting in tumors with distinct molecular characteristics. Serrated pathway has been considered as an alternative pathway of colorectal cancer (CRC) distinct from the adenoma-carcinoma sequence. To clarify involvement of molecular alterations in serrated pathway, we performed epigenetic and genetic analyses.

Aims & Methods: A total of 45 sessile serrated adenoma/polyp (SSA/P) and 14 traditional serrated adenoma (TSA) samples were obtained from patients who underwent endoscopic submucosal dissection. Samples of 17 high-methylation CRCs, which seemed to be developed through serrated pathway, were also included. To epigenotype serrated lesions and high-methylation CRCs, the methylation levels of six Group-1 and 14 Group-2 markers, established in our previous study, were analyzed quantitatively by pyrosequencing. Subsequently, we performed target exon sequencing analysis of 126 candidate CRC driver genes, using HaloPlex target enrichment system, and evaluate how carcinogenic pathways, e.g. RTK/RAS, PI3K, WNT, TGF-ß, BMP and TP53 signaling, are associated with CRC development through serrated pathway.

Results: SSA/P showed high methylation of both Group-1 and Group-2 markers, thus high-methylation epigenotype, and frequent *BRAF* mutation (36/45 cases, 80%), which were characteristics of high-methylation CRC. Traditional serrated adenoma (TSA) showed high methylation of Group-2 markers but low methylation of Group-1 markers, thus intermediate-methylation epigenotype, and less frequent BRAF mutation (43%, $P = 0.02$) but significantly frequent *KRAS* mutation (50%, $P = 0.003$). High-methylation CRC showed even higher methylation of genes e.g. *MLH1* than SSA/P, suggesting that methylation of genes could increase during development from adenoma to cancer in the serrated pathway. Significantly frequent somatic mutations in non-synonymous mutations ($P < 0.0001$) and indels ($P = 0.002$) were identified in high-methylation CRC. Mutation frequencies, however, were not different between *MLH1*-methylayed and *MLH1*-unmethylated SSA/P samples. Significantly mutated genes in cancer included mismatch repair genes e.g. *MSH3* and *MSH6*, and those involved in PI3K, WNT, TGF-β, and BMP signaling, but not in TP53 signaling.

Conclusion: For serrated pathway, SSA/P, but not TSA, is considered to be precursor lesions of high-methylation CRC with *BRAF* mutation. Further DNA methylation accumulation occurs, including *MLH1*, during development from adenoma to cancer in serrated pathway. While abrogation of mismatch repair genes was suggested to be important, *MLH1* methylation might be insufficient, and additional abrogation by mutation of genes e.g. *MSH3* and *MSH6* might be necessary to develop cancer with hypermutation phenotype, involving abrogation of PI3K, WNT, TGF-β, and BMP signaling.

Disclosure of Interest: None declared

OP175 WHOLE METHYLOME ANALYSIS OF COLORECTAL TISSUE SAMPLES USING METHYL CAPTURE SEQUENCING REVEALED EPIGENETIC ALTERATIONS OF FREQUENTLY MUTATED GENES DURING NORMAL-ADENOMA-CARCINOMA SEQUENCE PROGRESSION

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Introduction: During colorectal carcinogenesis, accumulation of genetic and epigenetic alterations leads to adenoma-carcinoma transition in colon. The colorectal carcinoma (CRC), which is a rather heterogeneous malignant disease, can develop through various different molecular ways, therefore the mutations of key tumor suppressor and/or oncogenes cannot provide complete explanation in several cases.

Aims & Methods: In this study, parallel analysis of genetic and epigenetic alterations was performed during the colorectal normal-adenoma-carcinoma sequence progression focusing on the role and possible epigenetic regulation of genes frequently mutated in CRC.

Mutations of 12 CRC oncodiagnostic panel genes (APC, BRAF, CTNNB1, EGFR, FBXW7, KRAS, MSH6, NRAS, PIK3CA, SMAD2, SMAD4, TP53) were analyzed by 454 sequencing on GS Junior platform on 54 colorectal tissue samples (9 normal, 25 AD, 20 CRC). Whole methylome analysis was performed from 30 colorectal tissue samples (9 colorectal carcinoma (CRC), 15 adenoma (AD) and 6 normal adjacent tissue (NAT) samples) by next generation sequencing (Illumina) after enrichment of methylated DNA using MethylCap kit (Diagenode). Methylation alterations were determined on the whole sequence of the selected oncodiagnostic panel genes including promoter regions, gene body regions and mutation hot spots. Promoter regions were determined according to the 'Integrative annotation of chromatin elements from ENCODE data'. For validation, Illumina BeadChip450K methylation data of Luo et al. (GSE48684) were also involved.

Results: In CRC samples the most frequently mutated genes were TP53, KRAS and APC with 40%, 30% and 25% frequencies. APC mutation could be detected in 32% of adenoma samples, KRAS was found to be mutated in 24% of adenomas, while none of the adenoma samples carried TP53 mutation. Parallel mutation-methylation data were available from 26 samples (4 NAT, 15 AD, 7 CRC). In adenoma compared to NAT samples, aberrant methylation was detected in gene body regions of APC, CTNNB1, TP53 and SMAD4 genes and in promoter regions of APC (hypermethylation), FBXW7 and SMAD4 genes (hypomethylation). In CRC compared to NAT samples, gene body hypermethylation was found in APC, and promoter hypomethylation was determined in CTNNB1, SMAD2, SMAD4 and NRAS genes. The results of the GSE48684 methylation analysis also confirmed the APC hypermethylation and CTNNB1, SMAD2 promoter hypomethylation in CRC. Between adenoma and CRC samples the most significant methylation differences were observed in APC, CTNNB1, TP53 and MSH6 genes ($p < 0.01$).

Conclusion: DNA methylation alterations, partly in the promoter regions of the frequently mutated genes, can also contribute to functional disturbance of the CRC-related genes during the colorectal cancer development and progression. Beside the frequent APC, KRAS and TP53 mutations, aberrant promoter methylation of key genes such as APC and beta-catenin suggests the essential role of epigenetic regulation from early stage of colorectal carcinogenesis.

Disclosure of Interest: None declared

OP176 PROFILING AND MODULATION OF SKELETAL MUSCLE MICRORNAS IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS AND IN INSULIN-RESISTANT C2C12 MUSCLE CELLS

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Introduction: Intramyocellular lipid deposition associates with mitochondrial dysfunction and insulin resistance (IR), constituting a key pathophysiological event in human non-alcoholic fatty liver disease. Further, recent evidences support a functional role for microRNAs (miRNA/miRs) in regulating muscle IR. Finally, tauroursodeoxycholic acid (TUDCA) is a cytoprotective bile acid in both liver and muscle cells, in part, by acting as a molecular chaperone and stabilizing mitochondria.

Aims & Methods: Our aims were to profile global muscle miRNA expression in human patients at different NAFLD stages and evaluate their potential functional role, as well as modulation by TUDCA, in insulin-resistant C2C12 cells. Skeletal muscle biopsies were obtained from morbid obese NAFLD patients undergoing bariatric surgery. Muscle RNA was run in TaqMan MicroRNA arrays. qPCR array data was analyzed using the HTqPCR package in Bioconductor. Differential expression analysis was performed with interquantile range values > 1.5 using the lmfit function of the Limma package and the Benjamini-Hochberg conditional hypergeometric test algorithm. C2C12 cells were incubated with or without palmitic acid (PA), in the presence or absence of 100 μM of TUDCA, for evaluation of the insulin-signaling pathway, mitochondrial function and overall cellular toxicity.

Results: Six muscle miRNAs were found to progressively and significantly increase from steatosis to more severe NASH (at least $p < 0.05$). These included miR-339-3p, a regulator of glucose synthesis, and miR-361, previously found to be increased in the serum of type II diabetes (T2D) patients. Inversely, eight miRNAs were decreased, including miR-20b, down-regulated in T2D patients plasma.

Incubation of C2C12 cells with PA increased mitochondrial dysfunction and apoptosis (at least $p < 0.05$) while decreasing mitochondrial ATP production ($p < 0.05$), all of which were prevented by co-incubation of cells with TUDCA ($p < 0.05$).

Of note, miR-339-3p was also increased by PA and inhibited by TUDCA ($p < 0.05$). Inversely, MAPK phosphatase-7 (MKP-7), a negative regulator of JNK and a target of miR-339-3p was decreased in cells incubated with PA and rescued by TUDCA co-incubation (at least $p < 0.05$). In fact, C2C12 cells exposed to PA displayed JNK phosphorylation and activation, with concomitant downstream deregulation of the insulin-signaling pathway (at least $p < 0.05$). Remarkably, these events were prevented by co-incubation of cells with TUDCA ($p < 0.05$).

Conclusion: Collectively, T2D-associated miRNAs are differently modulated with NAFLD severity in the skeletal muscle, with miR-339-3p arising as a likely mechanistic target contributing for IR. In addition, TUDCA attenuates

muscle cell IR and lipoapoptosis and may ameliorate NAFLD-associated muscle dysfunction. (PTDC/BIM-MEC/0873/2012, SFRH/BD/104160/2014, FCT, Portugal).
Disclosure of Interest: None declared

OP177 IMMUNE AND METABOLIC DISORDERS IN OBESE PATIENTS WITH HEPATIC STEATOSIS AND HYPERTENSION ASSOCIATE WITH PPAR-GAMMA2 PRO12ALA AND ACE I/D GENES' POLYMORPHISMS

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Introduction: Hepatic steatosis (HS) and arterial hypertension (AH) have multiple common mechanisms of development involving metabolic and immune changes. Among them, impairment or inhibition of receptor molecules controlling enzymes responsible for oxidation and fatty acids synthesis, appear to contribute to fat accumulation. However, HS is to some extend still accepted as a non-systemic pathology, rather than systemic disease, not limited to liver but involving interaction between genetically determined mechanisms of metabolism regulation and vascular inflammation.
Aims & Methods: The aim of study was to investigate the influence of Pro12Ala polymorphism of Peroxisome proliferator Activated Receptor Gamma (PPAR-γ2) gene and Insertion/Deletion (I/D) polymorphism of Angiotensin Converting Enzyme (ACE) gene on metabolic profile and cytokines in obese patients with common combination of HS and AH.
Study included 154 HS patients with AH (87 male, 67 female, age 50.06 ± 7.34). Duration of HS: 1-5 years, AH 3-21 years. NAFLD/NASH diagnosis based on EASL (2009) and AGA/AASLD/ACG (2012) recommendations. Metabolic disorders were defined with body mass index (BMI), glycemia, immunoreactive insulin (IRI), total cholesterol (TC), low and high density cholesterol (LDL-C, HDL-C), triglycerides (TG), C-peptide (CP) levels and HOMA-IR index. TNF-α and leptin plasma levels were assessed by ELISA. Genes' polymorphism of PPAR-γ2 (Pro12Ala), and ACE (I/D) alone or in combination was studied with PCR.
Results: Differences of BMI, plasma glucose, IRI, HOMA-IR, CP and leptin are independent from ACE gene genotypes ($p > 0.05$). Pro-allele carriers of PPAR-γ2 gene have higher BMI than AlaAla carriers (32.7 ± 2.1 and 27.9 ± 1.1 kg/m^2 vs 25.6 ± 0.8 kg/m^2, accordingly ($p < 0.05$); leptin level – 14.3 ± 0.41 and 8.6 ± 0.25 ng/ml vs 3.7 ± 0.22 ng/ml, ($p < 0.001$), glucose level – to 10.2% and 10.9% accordingly ($p < 0.05$); CP level was higher in ProPro-genotype than in Ala-allele carriers to 15.7% ($p < 0.05$). Risk group for dyslipidaemia are ProPro-genotype carriers of PPAR-γ2 gene with higher level of TC, TG and LDL-C by 16.4%, 17.3% and 27.9% ($p < 0.05$) and lower level of HDL-C in women by 25.6% ($p = 0.038$). Lipids levels are independent on ACE I/D polymorphism. Baseline TNF-α plasma levels did not significantly deviate between genotypes of PPAR-γ2 gene, but D-allele carriers (I/D + DD) of ACE gene had higher baseline TNF-a plasma levels (91.61 pg/ml and 109.11 pg/ml, accordingly, $p < 0.01$).
Conclusion: Metabolic disorders in HS hypertensive patients are associated with PPAR-γ2 Pro-allele (carbohydrates) and ProPro-genotype (lipids). Presence of D-allele of ACE gene is associated with reliably higher TNF-α plasma levels.
Disclosure of Interest: None declared

OP178 RECONSTRUCTING THE EVOLUTIONARY HISTORY OF METASTATIC OESOPHAGEAL ADENOCARCINOMA USING WHOLE GENOME SEQUENCING

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Introduction: Metastases are responsible for greater than 90% of all cancer deaths, yes little is known about the governing principles that guide disease progression. This holds particularly true for metastatic oesophageal adenocarcinoma (OAC). It remains unclear whether metastases have the ability to continually evolve, and acquire subclones that breed a competitive survival advantage or whether heterogeneity in metastases is a reflection of the architecture of the primary tumour, hence supporting the bulk of tumour evolution to be an early event.
Aims & Methods: Whole-genome sequencing (WGS) was performed across multiple primary and metastatic samples obtained from a rapid autopsy programme with the aim of delineating the clonal ordering of metastatic events in OAC. 10 rapid autopsies have been completed to date, within 6 hours of death and 5 cases have been analysed. WGS was performed on 41 fresh frozen samples from the primary and multiple nodal and distant organ metastases (liver, pancreas, adrenal). Subclonal copy number analysis was performed using the ASCAT/Battenberg algorithm and single nucleotide variants (SNVs) were clustered based on their allele frequency using a Bayesian Dirichlet process. Phylogenetic trees were annotated with copy number and point mutation events in order to identify potential drivers of progression.
Results: The ancestral clone contained a median of 24% and up to 90% of the total number of SNVs (range 8238-29883 SNVs). TP53 coding mutations and amplifications in MYC, GATA4, CCND1, KRAS and CDK6 were early events in the evolutionary tree. Both patterns of branching and linear evolution were observed. Metastases in solid organs (pancreas, liver) and lymph nodes could be traced back to spatially distinct areas of the primary tumour. Interestingly, solid organ metastases occurred at similar instances and in some cases preceded local nodal metastases.
Conclusion: Through the development of the first rapid autopsy programme in this cancer, we have begun to reconstruct the evolution of metastatic OAC. We demonstrate that distant organ seeding may occur prior to local nodal involvement hence challenging our traditional clinical staging algorithms. Further cases and samples are being analysed to support our findings.
Disclosure of Interest: None declared

OP179 EFFECT OF CO-MORBIDITIES ON URINARY METABOLIC PROFILING IN THE CHARACTERISATION OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Several studies have successfully used metabolic profiling (metabonomics) of urine to distinguish patients with IBD from healthy controls (1); many discriminatory metabolites identified relate to microbial or host-microbial cometabolism, supporting the concept of gut dysbiosis in IBD pathogenesis. An individual's metabolic phenotype may be influenced by factors including comorbidities such as diabetes mellitus, and previous studies have been restricted to IBD patients with no significant comorbidities which does not accurately reflect clinical practice. In order to assess the potential of metabonomics in a clinically relevant population, this study analysed urinary metabolic profiles of IBD patients with and without comorbidities.
Aims & Methods: Nuclear magnetic resonance spectroscopy was used to acquire urinary metabolic data from 51 IBD patients with at least one significant comorbidity (including diabetes mellitus, asthma and ischaemic heart disease), 46 patients with IBD alone, and 54 healthy controls. Groups were matched for age, sex, race, BMI and IBD diagnosis. As a preliminary analysis, resonances specific for metabolites influenced by gut microbes based on prior observations were integrated and analysed using appropriate univariate statistics.
Results: Univariate analysis showed that hippurate excretion was significantly lower in patients with IBD and comorbidities compared to healthy controls ($p = 0.01$), as well as patients with IBD alone ($p = 0.04$) confirming results of other published studies. In addition, trimethylamine (TMA) levels were relatively increased in patients with IBD and comorbidities ($p = 0.03$) and IBD alone ($p = 0.07$) compared to healthy controls, although trimethylamine-N-oxide (TMAO) levels showed no significant difference due to IBD or comorbid status.
Conclusion: In this study urinary hippurate was significantly lower in IBD patients, regardless of other comorbid diagnoses or treatments, which is consistent with previous studies. Hippurate is not a specific marker for IBD but rather related to gut microbiome metabolic dysfunction as it has also been observed when comparing the urine metabolic profile of lean and obese people and in intestinal parasitic infections. The relative increase in TMA has not been previously reported in humans, but correlates with a study that shows increasing TMA with progression of IBD in the IL10 knock-out mouse model (2). Future work will include multivariate analysis of this dataset to elucidate metabolic phenotypes associated with complex comorbidities in IBD.

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Disclosure of Interest: None declared

OP180 HISTONE H3K27 TRIMETHYLATION IN NORMAL COLON IS ASSOCIATED WITH THE DEVELOPMENT OF COLORECTAL TUMORS WITH CPG ISLAND METHYLATOR PHENOTYPE

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Introduction: Epigenetic alterations, including DNA methylation and histone modifications, play critical roles in the development of colorectal cancer (CRC). These epigenetic alterations are thought to be the main driving force in CRCs derived from sessile serrated adenomas (SSAs) exhibiting concurrent hypermethylation of multiple loci, which is termed as CpG island methylator phenotype (CIMP). Recent studies have shown that SSAs are associated with an increased risk of synchronous CRC. These findings are indicative of the epigenetic field effect in the normal-appearing colonic mucosa of SSA patients. In addition, recent studies suggest a tight association between bivalent chromatin domain in embryonic stem cells (ESCs) and aberrant DNA methylation in cancer cells. However, the chromatin signature in adult normal colon is not well characterized.
Aims & Methods: We aimed to clarify the chromatin signature in background normal colonic mucosa of CRCs with or without CIMP, and its association with aberrant DNA methylation in matched CRCs. Histone modifications (H3K4me3 and H3K27me3) in crypts isolated from surgically resected colonic tissues were

analyzed by performing chromatin immunoprecipitation (ChIP)-sequencing. Genome-wide DNA methylation was assessed by using the Infinium HumanMethylation450 BeadChip. Histone modifications of selected genes were analyzed by ChIP-PCR.
Results: We found that genes marked by bivalent chromatin domain in ESCs are significantly associated with H3K27me3 in noncancerous colonic mucosa of patients with CIMP-positive tumors. Moreover, a large number of genes marked by H3K27me3 in noncancerous colonic mucosa were specifically methylated in CIMP-positive CRCs. In contrast, such enrichment of H3K27me3 was not observed in colonic mucosa of patients with CIMP-negative tumors. We identified a series of genes which were marked by H3K27me3 in the background colonic mucosa of CIMP-positive CRCs and were aberrantly methylated in CIMP-positive CRCs. To evaluate the clinical implication of the histone marks in colonic mucosa, we next assessed histone marks of selected genes in a large number of fresh frozen noncancerous colonic mucosa specimens.
Conclusion: Our results are indicative of a tight association between H3K27me3 mark in adult normal colon, bivalent chromatin domain in ESCs and aberrant DNA methylation in cancer cells. Our results suggest that H3K27me3 may act as a pre-mark in the noncancerous colon mucosa of patients at a high risk of CIMP-positive cancer and that histone marks in colonic mucosa may be a predictive biomarker of the CRC risk.
Disclosure of Interest: None declared

OP181 LABEL FREE PROTEOMICS IDENTIFIES OLFACTOMEDIN-4 AS A MARKER OF EPITHELIAL TRANSITION OF EARLY CRC STAGES

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Introduction: Colorectal cancer (CRC) is the third leading cause of cancer death worldwide. CRC prognosis being closely linked to staging at diagnosis, new early diagnostic tools are awaited. Formalin-Fixed Paraffin-Embedded (FFPE) tissues stored in hospital biobanks represent a valuable resource for retrospective analysis, as larger populations can be studied, increasing the possibility to identify significant and specific potential new diagnosis/ prognosis biomarkers.
Aims & Methods: To identify biomarker from early CRC stages patients, we performed a retrospective study on 36 CRC tissue samples ($pT_1N_0M_0$, $n=16$ and $pT_2N_0M_0$, $n=20$) compared together and with 40 control tissue samples (20 patients with diverticulitis, using paired inflamed (DI) and healthy tissue (DH)). Each tissue slice was macrodissected to enrich in epithelial cells. We used FFPE-FASP kit (Expedeon) for sample preparation and protein digests were analyzed using label free proteomics (using 2D-*nano*Aquity UPLC separation online with *Q*-Tof Synapt HDMS^{TM} G2, Waters). We performed protein identification and differential analysis using Progenesis QI for proteomics (Nonlinear Dynamics). The validation of Olfactomedin-4 (OLFM4) and 2 other potential markers was obtained by immunohistochemistry on a new and independent set of 40 patients with early CRC stages.
Results: We selected 149 proteins differentially distributed between T1 and T2 CRC stages which are not significantly distributed between CRC and DH or DI. Only 30 proteins were significantly more abundant in T1 *versus* T2 and 119 were distributed inversely (minimum fold ratio > 2). Among those, ATP synthase subunit beta, Aspartate-tRNA ligase, Haptoglobin and Kininogen were previously identified. We selected several potential markers for validation by immunohistochemistry. OLFM4 validated the difference observed by proteomics (pT1N0M0 < pT2N0M0). Validation was also performed on other protein like Kininogen as this protein was previously found in serum of early CRC.
Conclusion: This FFPE retrospective proteomic study done on very early CRC stage highlighted proteins previously identified as potential CRC, other cancers and new potential biomarkers. These might be involved in early CRC stages epithelium progression and might represent early CRC biomarkers. OLFM4 was validated by IHC on new patients and could be implicated in early tumour progression.
Disclosure of Interest: None declared

OP182 GUT MICROBIOTA MOLECULAR SPECTRUM IN HEALTHY CONTROLS, DIVERTICULAR DISEASE, IBS AND IBD PATIENTS: TIME FOR MICROBIAL MARKER OF GASTROINTESTINAL DISORDERS?

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Introduction: Increasing evidence has emerged on the analysis of bacterial species making up the gastrointestinal microbiota. However few data exist on differences in gut microbiota composition in GI diseases, such as IBD, IBS and diverticular disease compared to healthy controls.
Aims & Methods: Aim of our study was to evaluate the differences in gut microbiota composition between IBD, IBS and diverticular disease (DD) patients. 10 Crohn's Disease (CD), 5 Ulcerative Colitis (UC), 4 DD, 3 IBS patients, and 8 controls (CD) were enrolled and fecal samples collected from each. Microbiota composition was assessed by a metagenomic gene-targeted approach (16S rRNA) using the Roche 454 GS Junior, following DNA isolation from stool samples stored at –80°C. Data were analyzed in Qiime. Individual species richness was estimated using Chao1 alpha-diversity index. We also explored the differential relative abundance of several taxa of interest, selected according to literature.
Results: Bacteria amplicons were detected in all samples. Prevalent classes of bacteria were: Bacteroidia (min 13.06% - max 91.55%), Firmicutes (min 7.48% - max 86.10%) and Proteobacteria (min 0.48% - max 46.48%). Fusobacteria were found only in CD and DD patients (min 0.67% > max 50.71%). IBD microbiota composition differed significantly compared to all other. In particular, UC patients showed a reduced concentration in Bacteroidetes and an increased presence of Firmicutes vs. CT, DD and IBS. On the other side, Bacteroidetes and Firmicutes composition varied among CD patients, being increased or reduced when compared to the other groups. Proteobacteria were increased in all diseased group compared to CT, being more represented in CD and IBS-D. Moreover, Actinobacteria were increased in IBD and DD vs. IBS and CT. The most represented species in IBD and DD vs. other groups was Collinsella Aerofaciens. Rikenellaceae were suppressed in IBD patients, as well as Fecalibacterium Prausnitzii. Akkermansia Muciniphila was present only in IBS patients. Enterobacteriaceae were increased only in CD patients vs. other groups. Finally, while chao1 score was similar between CT, IBS and DD, it was deeply reduced in IBD patients.
Conclusion: These preliminary data show that starting from microbiota, GI disease can be a continuous pathological spectrum where IBD display one extreme in gut microbiota composition while controls display the other. Furthermore, GI diseases share some microbial patterns, sharing perhaps common pathophysiological pathways. New analyses are needed to confirm this hypothesis and evaluate therapeutical implications.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30
IMPROVING COLONOSCOPIC PATHOLOGY RECOGNITION – ROOM E3

OP183 NARROW BAND IMAGING OPTICAL DIAGNOSIS OF SMALL COLORECTAL POLYPS IN ROUTINE CLINICAL PRACTICE: THE DETECT INSPECT CHARACTERISE RESECT AND DISCARD (DISCARD 2) STUDY

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Introduction: Accurate optical characterisation and removal of small adenomas (<10mm) at colonoscopy would allow hyperplastic polyps to be left in situ and surveillance intervals to be determined without delay for histopathology. Although accurate in specialist practice, the performance of narrow band imaging (NBI) colonoscopy in routine clinical practice is poorly understood.
Aims & Methods: NBI assisted optical diagnosis was compared with reference standard histological diagnosis in a prospective, blinded calibration study. Adults undergoing routine colonoscopy in 6 general (community) hospitals in northeast England. Participating colonoscopists (N = 28) were trained using the NBI International Colorectal Endoscopic (NICE) classification. By comparing optical and histological findings in patients with only small polyps, test sensitivity was determined at two thresholds: presence of adenoma and need for surveillance. Accuracy of characterising adenomatous polyps <10mm was compared using hierarchical models, allowing determinants of accuracy to be explored.
Results: Of 1688 patients recruited, 723 (42.8%) had polyps <10mm with 567 (78.4%) having only polyps <10mm. Overall, the median patient age was 64.3 years (interquartile range 55.0 to 70.2) and 53.1% were male. Test sensitivity (presence of adenoma, N = 499 patients) by optical diagnosis was 83.4% (95%CI: 79.6% to 86.9%), significantly less than the required 95% sensitivity ($p < 0.001$). Test sensitivity (need for surveillance) was 73.0% (95%CI: 66.5% to 79.9%). Analysed at the polyp level, test sensitivity (chracterisation of an adenoma, N = 1620 polyps) was 76.1% (95%CI: 72.8% to 79.1%). In fully adjusted analyses, test sensitivity was 99.4% (95%CI: 98.2% to 99.8%) if two or more NICE adenoma characteristics were identified (relating to colour, vessel structure and surface pattern). Colonoscopist expertise and confidence in diagnosis did not independently improve test accuracy.
Test sensitivity at the four thresholds:
1.The presence of a histological confirmed adenoma: 83.4% (HR'+IR'+LRS'+LRNS'/HR + IR + LRS + LRNS = 297/356)
2.Identifying the need for surveillance (vs. no surveillance): 73.0% (HR'+IR'+LRS'/HR + IR + LRS = 119/163)
Conclusion: NBI assisted optical diagnosis cannot yet be recommended for application in routine clinical practice. Further work is required to evaluate

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		Histological Surveillance Interval					
		Adenoma				No adenoma	
		Surveillance			No Surveillance		
	NBI Surveillance Interval	HR	IR	LRS	LRNS	NANS	Total
Surveillance	High Risk' (HR')	***9***	4	0	3	2	18
	Intermediate Risk (IR')	3	***30***	12	10	2	57
	Low Risk Surveillance' (LRS')	2	13	***46***	52	13	126
No surveillance	Low Risk No Surveillance' (LRNS')	0	4	*9*	***100***	***19***	132
	No adenoma No surveillance' (NANS')	0	4	27	***28***	***107***	166
	Total	14	55	94	193	143	499

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	# of polyps	# of frames	# of frames with correct localization	# of frames per polyp	# of frames with correct localization per polyp	# of polyps with at least one frame with correct localization
<10mm	22	430	308 (71.6%)	19.5 ± 6.3 (2-25)	14 ± 6.8 (1-24)	22 (100%)
IIa + IIb	11	218	169 (77.5%)	19.8 ± 5.3 (6-25)	15.4 ± 7 (2-24)	11 (100%)
Is	9	162	105 (65%)	18 ± 7.6 (2-25)	11.7 ± 7.3 (1-22)	9 (100%)
Ip	2	50	34 (68%)	25 ± 0 (25-25)	17 ± 1.4 (16-18)	2 (100%)
≥10 mm	9	182	122 (67%)	20 ± 7.1 (5-25)	13.8 ± 8.3 (3-25)	9 (100%)
IIb	1	12	6 (50%)			1 (100%)
Is	2	46	31 (67.4%)	23 ± 2.8 (21-25)	15.5 ± 12 (7-24)	2 (100%)
Ip	6	124	85 (68.5%)	20.7 ± 7.8 (5-25)	14.5 ± 8.3 (3-25)	6 (100%)

whether variation in test accuracy is related to polyp characteristics or colonoscopist training.
Disclosure of Interest: None declared

OP184 COLONIC POLYPS ARE CORRECTLY IDENTIFIED BY A COMPUTER VISION METHOD USING WM-DOVA ENERGY MAPS

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Introduction: Polyp miss-rate is a drawback of colonoscopy that results in a lack of total effectiveness in preventing colorectal cancer. The miss-rate increases significantly in small polyps.
Aims & Methods: To evaluate the usefulness of a computer vision method for the identification of colonic polyps.
612 polyp images were used from a data base (CVC-ClinicDB) containing an average number of 20 frames (range 2-25) of 31 different polyps. Our method is based on a model of appearance for polyps which defines a polyp as a protrusion enclosed by valleys of different intensity image. Valley information allows the creation of energy maps (WM-DOVA) related with the likelihood of polyp presence in the image.
Results: 22 polyps were small (< 10 mm), representing a total of 430 frames of the database: 11 non-polypoid (IIa and IIb), 9 sessile (Is) and 2 pedunculated (Ip) with a total of 218, 162 and 50 frames, respectively. All polyps were correctly localized in at least one frame. The number of frames with correct localization was 308 (71.6%) in small polyps compared with 122/182 (67%) in polyps ≥10 mm ($p = 0.2$) (table). Small non-polypoid polyps were correctly localized in more frames than all the other types: 169/218 (77.5%) vs 261/394 (66.2%); $p = 0.003$. In the 182 frames without a correct polyp location, the possible causes of failure were: folds in 81 (43.8%), polyps in a lateral position in 57 (30.8%), blood vessels in 21 (11.3%), absence of valleys in 12 (6.5%), fecal content in 7 (3.8%) and others in 4 (2.1%).
Conclusion: Computer vision method WM-DOVA shows good performance for the identification of colonic polyps, particularly those small non-polypoid which are the most difficult to detect during colonoscopy. These results indicate a potential applicability in clinical practice and warrant further clinical studies.
Disclosure of Interest: None declared

OP185 COMPUTER AIDED DIAGNOSIS OF THE MICROVASCULATURE OBSERVED BY ENDOCYTOSCOPY PROVIDE FULLY AUTOMATED DIAGNOSIS OF COLORECTAL LESIONS

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Introduction: Endocytoscopy (EC) is the next generation of ultra-magnification endoscopy that allows visualization of the glandular structure and cellular atypia. EC in conjunction with NBI (EC-NBI) enable the ultra-magnified microvessels of the lesion to be observed without dye. We called these findings as endocytoscopic vascular pattern (EC-V). We reported that the EC-V diagnosis highly correlated with the histopathologic diagnosis. Furthermore EC-V simplifies the complicatedness of conventional EC observation. Because conventional EC classification (EC-C) which evaluate the cellular and glandular structure atypia requires dye staining, whereas EC-V requires no dye staining. [1] However, for accurate diagnosing by EC-V, it requires training and experiences. We have also reported that the efficacy of computer aided diagnosis for EC-C. [2]
Aims & Methods: The aim of this study is to construct automatic diagnostic system for EC-V (EC-NBICAD). The algorithm of this system was programmed based on 288 features of each image by texture analysis which can quantify the pattern of picture. Support vector machine was used for classifier and a total of 979 EC-NBI images (non-neoplastic; 381, neoplastic; 598) were used for machine learning. To validate the diagnostic ability of EC-NBICAD, the randomly selected 100 images (neoplastic; 50, non-neoplastic; 50) which were not used for machine learning, were evaluated by EC-NBICAD. The sensitivity, specificity and accuracy for distinguishing neoplastic lesions from non-neoplastic lesions were calculated.
Results: The EC-NBICAD calculated the probability of the output pathological prediction. We defined over 90% probability as "high confidence". High confidence pathological prediction was made in 67% (67/100) images of the subject images. The sensitivity, specificity and accuracy of EC-NBICAD output with high confidence were 97.8%, 92.9% and 95.9%, respectively. By contrast, the overall sensitivity, specificity and accuracy for the all the subject images were 98.0%, 82.0% and 90.0%, respectively.
Conclusion: The diagnostic ability of EC-NBICAD was substantially good, although it was tentative system. However, further training images should be collected, because they will increase the rate of high confidence histopathological prediction.
Acknowledgement: We express great gratitude to Prof. Kensaku Mori and Yukitaka Nimura (Nagoya University, Information and Communications Headquaters) for their invaluable support as co-researchers.

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Disclosure of Interest: None declared

OP186 IN VIVO REAL-TIME PREDICTION OF COLORECTAL POLYP HISTOLOGY USING AN OPTICAL BIOPSY FORCEPS SYSTEM BASED ON LASER-INDUCED FLUORESCENCE SPECTROSCOPY

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Introduction: In order to reduce procedural time, costs and potential risks associated with the resection of diminutive colorectal polyps, the ASGE recently proposed performance thresholds that a new technology should meet for the accurate real-time assessment of the histology. Within this study, we prospectively assessed whether the newly introduced WavSTAT 4 optical biopsy forceps system can accurately predict polyp histology according to the ASGE PIVI statement.

Aims & Methods: Consecutive patients undergoing screening or surveillance colonoscopy were included. Real-time histology of 142 diminutive colorectal polyps was evaluated using the WavSTAT 4 system and compared to the results of conventional histology. The accuracy of predicting histology with the optical biopsy system for colorectal polyps according to the ASGE PIVI statement was assessed.

Results: The overall accuracy of the WavSTAT 4 system for prediction of adenomatous polyp histology was 84.1% with a sensitivity, specificity, and negative predictive value of 81.5%, 85.2%, and 95.4%. When only distal colorectal diminutive polyps were considered, the negative prediction for excluding adenomatous histology was increased to 98% (accuracy: 81.7%, sensitivity: 88.9%, specificity: 80.6%). On site-surveillance intervals were correctly predicted with an accuracy of 89.6% with WavSTAT 4 when compared to recent histology based US guideline recommendations. In all patients in which histology and WavSTAT 4 based surveillance intervals differed, WavSTAT 4 predicted narrower surveillance intervals.

Conclusion: The WavSTAT 4 optical biopsy system is accurate enough to leave distal colorectal polyps in place without resection or to resect and discard them without pathologic assessment. The WavSTAT system therefore has the potential to reduce costs and risks associated with the redundant removal of diminutive colorectal polyps.

Disclosure of Interest: None declared

OP187 CLASSIFICATION OF CELL NUCLEI MORPHOLOGY OF EC3A FINDINGS IN COLORECTAL ENDOCYTOSCOPY

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Introduction: Endocytoscopy (EC) is a next-generation endoscopy that enables diagnostic imaging at 450× magnification. To date, excellent results have been achieved using EC classifications for qualitative diagnosis and assessment of depth of invasion of colorectal lesions (neoplasia/non-neoplasia accuracy: 96.5%; accuracy for carcinomas with massive submucosal invasion (SM-m): 96.3%).(1, 2)

Aims & Methods: In the EC classifications, lesions diagnosed as EC3a vary extensively from adenoma to SM-m, including some lesions that are unsuitable for endoscopic treatment. Therefore, to improve the accuracy of asssessing the depth of invasion based on the EC classification, we investigated the presence or absence of certain endoscopic factors in EC3a findings that could be indicators of SM-m. Among lesions that were observed by EC between May 2005 and January 2015, we retrospectively examined 277 lesions diagnosed as EC3a or EC3b, according to the EC classification. Patients with unclear glandular lumen were excluded. The presence or absence of four findings that are indicators of SM-m were examined by EC. The four factors were: 1) extremely enlarged nuclei (EEN), 2) stratified nuclei (SN), 3) marked vascular dilatation (MVD), and 4) fine granular structure (FGS). Based on the results, we thoroughly examined the diagnostic accuracy of EC3a findings in the diagnosis of depth of invasion.

Results: Based on the results of multiple logistic regression analysis, the factors useful for the diagnosis of SM-m were EEN ($p < 0.01$), SN ($p < 0.01$), and FGS ($p < 0.05$). Of these, EEN and SN had odds ratios > 10 and were considered important predictors of SM-m invasion. So we diagnosed the lesions which were positive for EEN and SN as EC3a-high grade, whereas lesions negative for such findings were diagnosed as EC3a-low grade. As a result, 32 of 119 lesions were diagnosed as EC3a-high grade. Of these, the final pathological diagnosis was SM-m in 19 lesions, and muscularis propria cancer (MP) in five lesions. The diagnostic efficiency was as follows: sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and positive likelihood ratio of 88.9%, 91.3%, 75.0%, 96.6%, 90.8%, and 10.2, respectively. In the EC diagnosis above, interobserver validation (κ) of the three endoscopists were 0.63, 0.64, and 0.69, whereas good values were obtained for intraobserver validation (κ) at 0.73, 0.79, and 0.67.

Conclusion: In the diagnosis of colorectal lesions by EC, EC3a findings of EEN and SN are important indicators of SM-m. Results also suggested that taking into consideration the findings as for EC3a may improve the diagnostic accuracy for SM-m.

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Disclosure of Interest: None declared

OP188 A RANDOMIZED THREE-ARM COMPARISON OF HIGH DEFINITION ALONE WITH HIGH DEFINITION DYE SPRAYING AND ELECTRONIC VIRTUAL CHROMOENDOSCOPY USING ISCAN FOR DETECTION OF COLONIC DYSPLASTIC LESIONS DURING IBD SURVEILLANCE COLONOSCOPY

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Introduction: Dye spraying chromoendoscopy is considered to be the standard of practise for IBD surveillance colonoscopy. However, the resolution of high definition colonoscopy has increased significantly and electronic filter techniques allow detailed assessment of mucosal and vascular patterns.

Aims & Methods: The aim of this study was to compare different techniques including high definition colonoscopy (HD), dye spraying (0.2% indigo carmine) chromoendoscopy (DSC) and electronic virtual chromoendoscopy using i-SCAN (EVC) to detect colonic dysplastic lesions in IBD patients. A randomized study (NCT02098798) was conducted to determine the detection rates of dysplasia with HD alone, DSC or EVC in patients with long standing IBD (at least 8 years from diagnosis). Consecutive patients with inactive disease (Mayo endoscopic subscore 0-1 or Harvey- Bradshaw Index < 4) were enrolled in 1:1:1 ratio into three arms of the study, using Pentax EPKi processor and high-resolution video colonoscope (EC-3490Fi; Pentax Tokyo). The endoscopic activity in UC was assessed with Mayo endoscopic subscore and in CD with the Simple Endoscopic Score (SES-CD). The colonic lesions were classified by the Paris classification and Kudo pit pattern. Neoplastic changes were classified according to the new Vienna classification. The lesions of dysplasia (polypoid/non-polypoid), SSAs, adenoma-like polyps (ALPs), hyperplastic polyps (HPs) and non-neoplastic inflammatory polyps (IPs) were identified.

Results: 155 patients (73 female, median age 48 years, range 20-77 years) were assessed by HD (n = 54, 34.8%), VEC (n = 52, 33.5%) and DSC (n = 49, 31.6%). Twenty-three SSAs were found in fourteen patients (9%); thirty-four ALPs were found in twenty-three patients (14.8%); six dysplastic lesions were found in 5 patients (3.2%); fifty HPs were found in forty patients (25.8%) and fourteen IPs were found in twelve patients (7.7%). The number and percentage of each lesion found in each group is detailed in table 1.Tubular adenoma was detected more often in the HD group than other groups ($p < 0.05$). HD had a sensitivity of 91.67%, specificity of 85%, PPV 91.67% and NPV 85% in detecting dysplastic lesions. On the other hand, DSC had a sensitivity of 81.82%, specificity of 95.65%, PPV 90%, NPV 91.6% and EVC had a sensitivity of 90.48%, specificity of 82.3%, PPV 86.36% and NPV 87.5%.

Table 1: Colonic lesions found in each surveillance group

Lesions	HD (n = 54)	DSC (n = 49)	EVC (n = 52)	p
Serrated adenoma	11(19.6%)	2 (5.9%)	10(26.3%)	0.07
Tubular adenoma	21 (37.5)	7(20.6%)	6(15.8%)	0.04
Polypoid/nonpolypoid	2 (3.6%)	1(2.9%)	2(5.3%)	0.53
Adenocarcinoma	**0 (0%)**	**1(2.9%)**	**0 (0%)**	**0.24**

Conclusion: This randomized study found that HD alone had the best detection rate for adenoma. However, we could not demonstrate superiority of DSC in sensitivity of detecting dysplastic lesions compared to HD and EVC.

Disclosure of Interest: None declared

OP189 DYSPLASIA ASSOCIATED TO INFLAMMATORY BOWEL DISEASE IS HIGHLY DETECTED WITH CHROMOENDOSCOPY BUT POORLY CHARACTERIZED: PROSPECTIVE MULTICENTER NATION-WIDE STUDY (CROMO STUDY)

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Introduction: Pan-colonic chromoendoscopy (CE) with targeted biopsies for dysplasia (N-IBD) detection in long-standing inflammatory bowel disease (L-IBD) is strongly endorsed by main scientific societies. However, effectiveness of this strategy is controversial and poorly evaluated outside controlled trials.
Aims & Methods: To assess the effectiveness of CE with targeted biopsies for N-IBD detection and characterization in a clinical setting. Patients with L-IBD were prospectively included in a multicenter nation-wide cohort study during 2 years until June 2014. Each colonic segment was evaluated with white light (WL) followed by 0.4% indigo carmine CE. Specific lesion's features selected from literature were recorded for each lesion before being sampled or removed. Endoscopists' histology prediction based on optical diagnosis was compared with histopathology as gold standard
Results: 350 patients were included: 53% male; median time evolution 15 years, 79% ulcerative colitis and 21% Crohn's disease, 70% pancolitis, 7% primary sclerosing cholangitis and 8% first degree relative with colorectal cancer. 597 lesions were detected (median per patient: 1.7; range: 0-14): 1 (0.1%) invasive cancer, 100 (16.7%) N-IBD (5 high-grade dysplasia, 95 low-grade dysplasia) and 496 (83%) benign lesions. N-IBD detection miss rate with WL was 58/100, resulting in a 56.4% incremental yield for CE. Positive and negative predictive values (PPV, NPV) for N-IBD optical diagnosis were 42% (35-49%) and 93% (90-95%) respectively. Independent lesions' characteristics predictive of N-IBD and their PPV and NPV are shown in table.

Lesions' characteristics	OR (95% CI)	P	PPV (%)	NPV (%)
Proximal location	2.0 (1.1-2.6)	0.020	21	87
Loss of Innominated lines	2.0(1.0-3.7)	0.004	22	90
Polypoid morphology	2.7 (1.5-4.8)	0.001	28	88
Kudo III-IV	5.0 (2.7-8.4)	0.000	43	86

Conclusion: Outside clinical trials, CE is an effective strategy for L-IBD surveillance and detects 2-folds more N-IBD than WLE. In vivo lesion characterization is difficult: whereas benign lesions are highly predicted, N-IBD is not well recognized. Thus, CE targeted biopsies/removal of any mucosal abnormality not highly suspicious of benignity is still recommended.
Disclosure of Interest: None declared

OP190 ACCURACY OF THE FULL SPECTRUM ENDOSCOPY (FUSE) SYSTEM FOR ASSESSMENT OF DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASES (IBD) COMPARED TO HIGH-DEFINITION ENDOSCOPY

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Introduction: In 2013, full-spectrum-endoscopy (FUSE) was introduced as a novel colonoscopy platform. In contrast to other endoscopy systems illumination with the FUSE system is achieved by LEDs and not by a xenon light source. In addition, the FUSE-system does not provide high-definition imaging yet. In patients with IBD, precise assessment of disease activity (i.e. mucosal healing) is of paramount importance to predict disease outcome and to guide therapy.
Aims & Methods: Aim of the study was to determine whether FUSE has the potential to assess disease activity in patients with IBD as compared to a matched cohort of patients undergoing high-definition white-light endoscopy (HD-WL). Therefore, consecutive patients with IBD undergoing FUSE colonoscopy were matched to patients with IBD undergoing high-definition white-light endoscopy at the same endoscopy unit. The mucosal vascular pattern and any mucosal abnormalities were recorded. Inflammation in ulcerative colitis was recorded according to Mayo ulcerative endoscopic score (MUES) and in Crohn's disease according to Crohn's Disease Endoscopic Index of Severity (CDEIS). Subsequent to endoscopic characterization targeted biopsies were obtained for histopathological analysis of disease activity.
Results: 85 cases were included. Mean age of patients was 37 years (Range 18 to 72 years). 59% of patients had diagnosis of Crohn's disease and 41% diagnosis of ulcerative colitis. Accuracy of FUSE and HD-WL endoscopy for diagnosis of disease activity in IBD were not statistically significant different (81% versus 76%). In the subgroup analysis FUSE and HD-WL endoscopy yielded in under-diagnosis and overdiagnosis of disease activity in 57% versus 46% and 43% versus 54% of not correctly predicted cases, respectively. Overall, FUSE was more accurate for diagnosis of disease activity in Crohn's disease patients while HD-WL endoscopy was more accurate for diagnosis of disease activity in ulcerative colitis.
Conclusion: Despite the use of LEDs resulting in a darker image and high-resolution imaging, the FUSE system seems to be equal effective to high-definition white-light imaging for diagnosis of disease activity in patients with IBD.
Disclosure of Interest: None declared

OP191 CONFOCAL LASER ENDOMICROSCOPY IN ULCERATIVE COLITIS: A LONGITUDINAL STUDY OF RESPONSE TO MEDICAL THERAPY

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Introduction: Confocal laser endomicroscopy (CLE) enables real-time *in vivo* microscopy during endoscopy and can predict relapse in inflammatory bowel disease patients in remission. However, little is known about how endomicroscopic features changes with time. The aim of this longitudinal study was to correlate colonic CLE features in ulcerative colitis with histopathology and macroscopic appearance before and after intensification of medical treatment.
Aims & Methods: The aim of this longitudinal study was to correlate colonic CLE features in ulcerative colitis with histopathology and macroscopic appearance before and after intensification of medical treatment. Twenty-two patients with ulcerative colitis in clinical relapse and seven controls referred for colonoscopy were enrolled. The colonic mucosa was examined with high-definition colonoscopy, histopathology, and CLE at four colonic sites. Subsequently, patients requiring medical treatment escalation were referred for re-endoscopy after 6-8 weeks enabling longitudinal data analysis.
Results: Generalized estimating equations showed that the frequency of fluorescein leakage ($p<0.001$), microerosions ($p<0.001$), tortuosity of the crypts ($p=0.001$), distortion of the crypts openings ($p=0.001$), presence of inflammatory infiltrates ($p<0.001$), and decreased crypt density ($p<0.001$) were significantly higher in endoscopically active ulcerative colitis (endoscopic Mayo Clinic subscore > 1) compared to inactive ulcerative colitis and controls. Furthermore, colonic fluorescein leakage $r_s=0.42$ ($p<0.001$), microerosions $r_s=0.54$ ($p<0.001$), crypt tortuosity $r_s=0.66$ ($p<0.001$), distortion of crypt opening $r_s=0.63$ ($p<0.001$), decreased crypt density $r_s=0.54$ ($p<0.001$), and inflammatory infiltrates $r_s=0.28$ ($p=0.004$) were all significantly correlated with the histopathological score [2]. A decrease in histopathological score after medical treatment escalation was correlated with improvement in crypt tortuosity $r_s=0.35$ ($p=0.016$), distortion of crypt openings $r_s=0.30$ ($p=0.045$), and decreased crypt density $r_s=0.33$ ($p=0.026$). No correlation was found between decrease in histopathological score and colonic fluorescein leakage, microerosions, and inflammatory infiltrates.
Conclusion: pCLE can identify subtle mucosal changes in active ulcerative colitis, which are related to the grade of severity of the disease. After medical treatment escalation, improvement of abnormal colonic crypt architecture can be detected by CLE. In contrast, we did not observe a resolution of intestinal barrier impairments, which may reflect that few patients reached complete endoscopic remission during the follow-up period. Future studies will have to assess whether CLE parameters can be incorporated into an endomicroscopic score for ulcerative colitis, which may refine the definition of mucosal healing.

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TUESDAY, OCTOBER 27, 2015 08:30–10:30

H. PYLORI: IT STILL BUGS US – ROOM E5

OP192 EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): FIRST-LINE TREATMENTS AND INTERIM ANALYSIS OF 11,272 PATIENTS

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Introduction: The most efficient management strategy of *H. pylori* infection is still to be found.
Aims & Methods: To evaluate the management of *H. pylori* infection by gastroenterologists in Europe. A systematic prospective registry of the clinical practice of European gastroenterologists regarding *H. pylori* infection and treatment (30 countries-250 recruiters). An electronic clinical research file (e-CRF) was created to systematically register all adult patients infected with *H. pylori*. Variables included: Patient's demographics, previous eradication attempts, prescribed eradication treatment, adverse events, and outcomes.
Results: Up to now, 11,272 patients have been included, and 9,181 have finished follow up (59% females, 87% caucasian). Mean age was 55 years. 4.2% had drug allergies (81% to penicillin). 20% had gastroduodenal ulcer. 77% were first-line treatments, 16% -2nd, 4.5% -3rd, 1.3% -4th. 61% were triple regimens (PPI + 2 antibiotics), 16% non-bismuth quadruple concomitant, 11% sequential, and 7% bismuth quadruple. 30% of patients had adverse events mostly mild (53%) and lasted average 6.4 days, causing treatment discontinuation in 0.3%. Overall eradication rate (considering all lines of treatment) was 80%, and only 67% of eradication failures were retreated. First-line ITT results: 10 day triple (PPI + clarithromycin + amoxicillin), sequential, concomitant and bismuth quadruple therapies achieved 78%, 87%, 88 and 92% eradication rates respectively. Expanding the regimen up to 14 days increased efficacy of triple (81%), and concomitant (90%) regimens.
Conclusion: *H. pylori* management by gastroenterologists in Europe is extremely diverse. It is important to notice that the overall eradication rate is clearly suboptimal, mainly due to the use of standard triple therapy as a first-line treatment in areas where it is not recommended. Continuation of this registry and deeper evaluation of its data may offer valuable information to improve *H. pylori* management.
Disclosure of Interest: None declared

OP193 EFFICACY OF SITAFLOXACIN-BASED HELICOBACTER PYLORI ERADICATION TREATMENT FOR PATIENTS WITH METRONIDAZOLE-RESISTANCE STRAIN

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Introduction: Bacterial resistance to antibiotics often leads to failure of *Helicobacter pylori* eradication therapy. A tailored *H. pylori* eradication regimen based on clarithromycin-susceptibility and maintaining acid secretion was developed to counter this situation. The fluoroquinolone sitafloxacin has a low minimum inhibitory concentration for *H. pylori* and has efficacy in 3rd-line eradication treatment and for patients with penicillin allergy. A sitafloxacin-based regimen with maintenance of acid inhibition might therefore have a higher success rate also in first-line treatment.
Aims & Methods: Our aim is to investigate the efficacy of sitafloxacin-based triple therapy and document its efficacy in relation to antimicrobial susceptibility.
In 180 *H. pylori*-positive Japanese patients (for first-line treatment: n = 45, second-line; n = 41, third-line: n = 94), we investigated the efficacy of a sitafloxicin-based regimen of rabeprazole 10mg four-times-daily dosing (q.i.d.), metronidazole 250mg twice-daily (b.i.d.), and sitafloxacin 100mg b.i.d. for 1 week. At eight weeks after the treatment period patients were given the [13C]-urea breath test to assess eradication status.
Results: The eradication rate was 92.2% (95% CI: 87.3% > 95.7%, 166/180) and one patient experienced appearance of nettle rashhives and dropped out from this study. Although the eradication rate was higher in patients treated as first-line therapy (100%, 95% CI: 83.4% > 100%) than in those treated as second-line (92.7%, 80.1% > 98.5%) or third-line therapy (88.3%, 80.0% > 94.0%), no significant differences were noted with respect to number of past therapy attempts (p = 0.054). Eradication rates in patients infected with sensitive- and resistant-strains to metronidazole were 96.6% (28/29) and 96.3% (77/80) (p = 0.941), respectively, while rates in sitafloxacin were 98.4% (60/61) and 50.0% (1/2) ($p < 0.001$).
Conclusion: A sitofloxacin-based triple therapy with metronidazole and rabeprazole q.i.d. achieved an eradication rate exceeding 88%, irrespective of eradication history, CYP2C19 genotypes and metronidazole resistance. Especially, higher than 95% of patients infected with metronidazole resistant *H. pylori* strain were eradicated by this sitafloxacin-based regimen, suggested that this treatment might overcome metronidazole resistance. Recently, because prevalence of metronidazole-resistant strains of *H. pylori* was increased in many geographic areas, this treatment may be rescue regimen in areas with high prevalence of metronidazole resistance.
Disclosure of Interest: None declared

OP194 HELICOBACTER PYLORI ERADICATION RATES UPON ANTIBIOTIC SUSCEPTIBILITY TESTING

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Introduction: *Helicobacter pylori* infection is a major cause of dyspepsia, peptic ulcer and recognized cause of gastric cancer.
Aims & Methods: The objectives of this study were to evaluate the antibiotics resistance, efficacy of the therapeutic guided by antibiotic susceptibility, and to identify factors associated with antibiotic resistance and treatment failure. Retrospective study of patients who underwent culture guided treatment for *Helicobacter pylori* infection (after two eradication ineffective attempts), in a tertiary center, between October 2012 and January 2015. Demographic data, history of peptic ulceration, family history of gastric cancer, the antibiotic susceptibility results and success of the antibiotic susceptibility based therapy (with Helicobacter pylori antigen in stool) were recorded. Statistical analysis was performed with SPSS version 21.0 for Windows.
Results: We performed antibiotic susceptibility test in 38 patients, 60.5% (n = 23) female and 39.5% male (n = 15), mean age 49.7 years (22-71). There was resistance to macrolides in 92.1% of patients, metronidazole in 76.3%, ciprofloxacin in 52.6%, tetracycline in 2.6%. There was no resistance to amoxicillin or rifampicin. Most patients showed resistance to two antibiotics (47.4%), 39.5% were resistant to three or more antibiotics and 10.5% were resistant to only one antibiotic. In patients over 50 years there was a significantly higher proportion of resistance to three or more antibiotics (p = 0.020). The search of *H. pylori* antigen in feces was carried out in 47.4% of patients (n = 18): negative in 61.1% and positive in 38.9%. In patients with a positive result (eradication failure) there was a significantly higher proportion with resistance to three or more antibiotics (p = 0.049).
Conclusion: The success rate of treatment guided by antibiotic susceptibility test is low. Prevalence of resistance to antibiotics is very high. Patients over 50 years are resistant to multiple antibiotics and, in turn, the failure of treatment guided by the antibiotic susceptibility is higher in patients with resistance to multiple antibiotics.
Disclosure of Interest: None declared

OP195 EFFICACY OF VONOPRAZAN-BASED THERAPY IN H.PYLORI ERADICATION

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Introduction: Proton pump inhibitor (PPI)-based triple therapy is one of the most popular eradication therapy for *H. pylori* (HP) in the world.
However, first-line eradication rate has been decreasing in Japan.
One of the major reasons of this phenomenon is that HP acquired resistance to the clarithromycin (CAM). It is known that most antibiotic agents, including CAM are not effective under strong acidic condition. Therefore, in order to improve the eradication rate, gastric acid secretion must be reduced more rapidly and strongly.
Vonoprazan is newly developed potassium competitive acid blocker (P-CAB) and more effective in reducing gastric acid secretion than PPI.
Therefore, it is expected that we are able to obtain high eradication rate by using Vonoprazan.
Aims & Methods: The aim of this study was to clarify the effect of the Vonoprazan-based eradication therapy.
The subjects were 252 patients who were positive in urine antibody test. The patients who had gastric ulcer, duodenal ulcer, or gastric cancer were excluded. HP positive patients were grouped into two: Vonoprazan group (VG) and conventional PPI group (PG). We evaluated the first-, the second-, and the third-line eradication rate.
Each regimen of VG (Feb.2015-Mar.2015) was **7 days, Vonoprazan 20mg bid + AMPC750mg bid + CAM200mg bid (first-line eradication), 7 days,**

Vonoprazan 20mg bid + AMPC750mg bid +MNZ 250mg bid (second-line eradication), 14 days, Vonoprazan 20mg bid + AMPC 1000mg bid (third-line eradication).
The each regimen of PG (Feb.2014-Jan.2015) was **7 days, PPI bid + AMPC750mg bid +CAM200mg bid (first-line eradication), 7 days, PPI bid +AMPC750mg bid +MNZ 250mg bid (second-line eradication), 14 days, PPI bid +AMPC 1000mg bid (third-line eradication).**
One of the following PPI was used: Lansoprazole 30mg, Rabeprazole 20mg, Esomeprazole 20mg. After one month, HP status was assessed by 13C urea breath test. We investigated each regimen of VG and PG.
Results: The total number of VG patients was 62 and that of PG was 190.
The number of each regimen of VG was 40 in the first-line eradication, 14 in the second –line eradication, and 11 in the third-line eradication. The number of each regimen of PG was 125 in the first-line eradication, 41 in the second-line eradication, and 24 in the third-line eradication, respectively.
The first-line eradication was achieved in 92.5% in VG vs. 76.8% in PG ($p = 0.03$).
The second eradication was achieved in 100% in VG vs. 92.7% in PG ($p = 0.3$).
The third eradication was achieved in 100% in VG vs. 33.3% in PG ($p = 0.03$).
There was no significant difference in the eradication rate among PPI.
Conclusion: Vonoprazan-based regimen was superior to conventional PPI regimen.
From our result of the third-line eradication regimen, CAM may no longer be needed for HP eradication.
Disclosure of Interest: None declared

OP196 NON-BISMUTH QUADRUPLE "CONCOMITANT" THERAPIES IN THE ERADICATION OF HELICOBACTER PYLORI: STANDARD VS. OPTIMIZED (14 DAYS, HIGH-DOSE PPI) REGIMENS IN CLINICAL PRACTICE

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Introduction: Non-bismuth quadruple "concomitant" regimen is increasingly used as first-line *H. pylori* eradication treatment.
Aims & Methods: To evaluate the efficacy and tolerability of the standard and optimized "concomitant" regimens.
Design: Prospective multicenter study. *Patients*: Consecutive *H. pylori*-infected patients. *Treatment*: In a first phase, patients received a standard concomitant therapy (CONC10): omeprazole 20 mg, amoxicillin 1 g, clarithromycin 500 mg and metronidazole 500 mg for 10 days b.i.d. In a second phase, patients received the same regimen but with esomeprazole 40 mg b.i.d. and lasting 14 days (CONC14+). *Outcome*: Eradication was confirmed with ^{13}C-urea breath test 4-8 weeks after therapy. *Compliance/tolerance*: Compliance and adverse events were determined through questioning and recovery of empty medication envelopes.
Results: 1,000 consecutive patients were included (mean age 48 years, 47% males, 21% peptic ulcer): 370 in CONC10 and 630 in CONC14+. Compliance with both regimens was 95%. Per-protocol eradication rates with CONC10 and CONC14+ were 88% (95% CI = 85-91%) and 93% (92-95%) ($p < 0.01$). Respective intention-to-treat cure rates were 87% (83-89%) and 91% (89-93%) ($p < 0.05$). Adverse effects (mostly mild) were reported in 34% of patients in CONC10, and in 46% in CONC14+ ($p < 0.05$), the most common being metallic taste, diarrhea, nausea and abdominal pain. In the multivariate analysis, only compliance (OR = 4.7) and optimization of treatment (OR = 1.7) were associated with higher efficacy.
Conclusion: An optimized (14-day and high-dose esomeprazole) non-bismuth quadruple "concomitant" regimen is more effective than the standard one for the eradication of *H. pylori*, and achieves over 90% cure rate. Although the incidence of adverse events is higher with the optimized treatment, these are mostly mild, and do not negatively impact the compliance.
Disclosure of Interest: None declared

OP197 EVOLUTION ERADICATION RATES WITH SECOND-LINE THERAPY FOR HELICOBACTER PYLORI INFECTION AND FACTORS ASSOCIATED WITH ERADICATION THERAPY

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Introduction: In Spain, the rate of eradication of *Helicobacter pylori* with the first-line treatment with an inhibitor of the proton pump, amoxicillin and clarithromycin has been decreasing due to the high prevalence of resistance to clarithromycin. Therefore the second line eradication therapy with triple therapy containing fluoroquinolones is one of the recommended treatment options.
Aims & Methods: Assess the trend of eradication rates of *H. pylori* with second-line therapy (inhibitor of the proton pump, amoxicillin and levofloxacin) in patients who failed to standard triple therapy in our health area during the last four years and identify risk factors related to eradication failure.
We reviewed test of urea in breath obtaining a total of 2652 studies in the period January 2011 to December 2014, 145 patients were included with *H. pylori* infection that failed to standard triple therapy and received second-line therapy fluoroquinolone based. We retrospectively investigated *H. pylori* eradication rates with respect to the year of therapy as well as demographic and clinical factors. *H. pylori* eradication was confirmed by a 13C-urea breath test or a rapid urease test at least 4 weeks after the completion of triple therapy.
Results: The mean age +/- SD was 50.3 +/- 16.2 years. 63.4% women. The overall H. pylori eradication rate was 83.4%. Annual eradication rates from 2011 to 2014 were 91.2%, 70.6%, 80% and 85.3% respectively, by per-protocol analysis. The eradication rate in second-line triple therapy initially decreased and started to increase in efficiency over the last year during the last four years studied ($p = 0.078$). By clinical entity *H.pylori*, the eradication was 83.3% of functional dyspepsia and 84.2% of ulcer dyspepsia. Gastric and duodenal ulcers had an eradication rate of 66.7% and 88.9% respectively. Higher eradication rate for males 88.7% has been observed. The eradication rate in smokers was 88%, while in non-smokers 81.1% (p = ns)
Conclusion: In our health area the efficacy of second-line triple therapy for *H. pylori* infection has decreased in recent years with no-significant increase in the past year, according to the last four years studies. It suggests an increase of *H. pylori* strains resistant to antibiotics. Therefore, other second-line therapies may be necessary for the eradication of *H. pylori*. This therapy has superior efficacy in ulcer dyspepsia regarding functional dyspepsia and eradication greater in males.
Disclosure of Interest: None declared

OP198 EFFECTS OF COMMUNITY SCREENING FOR HELICOBACTER PYLORI: 13-YEAR FOLLOW-UP OF A RANDOMIZED CONTROLLED TRIAL (HEP-FYN)

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Introduction: Dyspepsia is a common condition and dyspepsia-related healthcare costs are high. Dyspeptic symptoms may improve after *Helicobacter pylori* (Hp) eradication in 10% of patients
Nearly all peptic ulcers are caused by either Hp infection or non-steroidal anti-inflammatory drugs (NSAID) use, including aspirin. Eradication of Hp reduces the recurrence of peptic ulcer from 80% to a few per cent in patients with Hp related peptic ulcers.
Recurrence after Hp eradication is rare. Population Hp screening and eradication seems an attractive option; ^{13}C-Urea Breath Test (UBT) is accurate, inexpensive and non-invasive and Hp can be permanently eradicated.
Aims & Methods: The aim of this study was to evaluate the long-term effect of population screening and eradication of *Helicobacter pylori* on dyspepsia prevalence and the incidence of peptic ulcer disease (PUD) and as secondary outcomes: to assess the effect on dyspepsia related health-care consumption and quality of life.
HEP-FYN is a prospective intervention study initiated in 1998 – 1999. At baseline 20,011 individuals aged 40 – 65 years were randomized to Hp screening and treatment or to the control group. Both groups received a questionnaire on dyspepsia and quality of life, at inclusion and after 1, 5 and 13 years. Register data on contacts to hospitals and general practitioners, comorbidity, use of endoscopies and prescription medication as well as socioeconomic factors were obtained for all randomized individuals. Complete Case analysis was performed for the outcome dyspepsia, while both per protocol and intention to treat analyses were possible for the outcome PUD. Risks were examined using logistic regression, providing odds ratios (OR) and 95% confidence intervals (CI).
Results: The participation rate at baseline was 63%. During the follow-up period 12% died or moved outside the Region of Southern Denmark. Those remaining, who had participated at the 5-year follow-up were invited to the 13-year follow-up, 8,658 (78%) of these participated. Screening for Hp did not reduce the prevalence of dyspepsia or the incidence of PUD significantly. Presence of dyspepsia at baseline was a strong predictor of dyspepsia after 13 years with an adjusted OR of 5.27 (95%CI: 4.67 – 5.95). Use of high-dose acetylacetic acid (ASA) or non-steroidal anti-iflammatory drugs (NSAID) increased the risk of dyspepsia. Age above 45 and higher level of education was associated with lower dyspepsia prevalence at the 13 years follow-up.
The incidence rate of PUD in nonparticipants was higher than for those enrolled. The strongest predictor of PUD was previous PUD. Odds of PUD increased with age, use of low dose asperin, and ASA/NSAID. Higher level of education was associated with a lower OR of PUD.
Except for use of proton pump inhibitors, which was significantly higher in the screened group compared to the control group, there were no significant differences in use of health resources between groups.
Hp screening had no long-term effect on quality of life.
Conclusion: This randomized clinical trial of population Hp screening and eradication with 13-years follow-up showed no significant long-term effect when compared to current clinical practice in this low prevalence area.
Disclosure of Interest: None declared

OP199 HELICOBACTER PYLORI ERADICATION ASSOCIATED WITH DECREASING LEVEL OF AUTOANTIBODIES TO THYROID PEROXIDASE

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Introduction: Previously the close relationship between *Helicobacter pylori* (HP) infection and autoimmune thyroid disease had been described. It is not known whether it is possible to reduce the progression of autoimmune thyroiditis via *H. pylori* eradication.
Aims & Methods: The aim of the study was to investigate the influence of successful HP eradication on level of the autoantibodies against thyroid peroxidase (anti-TPO) in patients with autoimmune thyroiditis.
Ninety eight HP-positive patients with autoimmune thyroiditis aged 52 ± 3 years were prospectively included in this study. The control group consist on thirty HP-negative subjects aged 54 ± 2 years suffered from autoimmune thyroiditis. The 14 days first-line therapy - clarithromycin 500 mg, pantoprazole 40 mg, amoxicillin 1 g twice a day had been prescribed to all patients. The anti-TPO level had been measured using ELISA kits before and after (on 15th, 30th day) eradication treatment. All patients gave written informed consent.
Results: The successful HP-eradication rate was 86%. We revealed dramatic reduction in the level of anti-TPO up to 62% ($p < 0.001$) on 30th day in successfully treated patients. We also noticed significant reduction in the severity of tissue inflammation on ultrasound pictures. Meanwhile in control group as well as in patients resistant to first-line therapy the the serum changes of anti-TPO were irrelevant (-4.8%; $p > 0.05$ on 30th day after eradication).
Conclusion: Our results support the hypothesis of a strong association between infection of *H. pylori* and development of autoimmune thyroiditis. The optimistic data of HP-eradication influence on anti-TPO level suggests the need for larger clinical trials and possible optimization of autoimmune thyroiditis diagnostic and treatment protocol.
Disclosure of Interest: None declared

OP200 INTERLEUKIN-22 IS A CRITICAL MEDIATOR OF VACCINE-INDUCED REDUCTION OF HELICOBACTER INFECTION IN THE MOUSE MODEL

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Introduction: Despite the proven ability of immunization to reduce *Helicobacter* infection in mouse models, the precise mechanism of protection has remained elusive.
Aims & Methods: In this study, we evaluated the role of IL-22 in the vaccine-induced reduction of *Helicobacter* infection.
Results: We first observed that IL-22 production is increased in the stomach during the vaccine-induced reduction of *Helicobacter* infection. These high IL-22 levels were associated with an increase production of antimicrobial peptides (AMP) such as RegIIIb by stomach epithelial cells. FACS analysis revealed that the main source of IL-22 is $CD4^+$ T cells especially IL-17 producing cells. In immunized mice, intraperitoneal injection of anti-IL-22 antibodies significantly impaired the vaccine-induced reduction of *Helicobacter* infection. Importantly, IL22-Fc injections to mice chronically infected with *Helicobacter* dramatically reduced bacterial load. Finally cationic AMP (AMPc) were extracted from stomachs and incubated with *Helicobacter* to evaluate their bactericidal effects. AMPc extracted from stomachs of vaccinated mice or mice injected with IL-22Fc kill *Helicobacter in vitro*. On the contrary, AMPc extracted from stomachs of non-immunized or immunized mice injected with anti-IL-22 antibodies did not kill *Helicobacter*.
Conclusion: Collectively theses results demonstrated that IL-22 plays a critical role in vaccine-induced reduction of *Helicobacter* infection, by inducing the expression of AMPc capable to kill *Helicobacter*.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30-10:30
A GLOBAL VIEW ON LIVER CIRRHOSIS - ROOM E6

OP201 PRESEPSIN AS A NEW BIOMARKER FOR OLD EXPECTATIONS IN THE DIAGNOSIS AND PROGNOSIS OF BACTERIAL INFECTION IN CIRRHOSIS

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Introduction: Bacterial infections are frequent complications in cirrhosis with significant mortality. Early diagnosis is essential but still a diagnostic challenge from both the clinical and the laboratory part. The aim of this study is to evaluate and compare the diagnostic and prognostic value of presepsin plasma levels with CRP and PCT in bacterial infections of patients with cirrhosis.
Aims & Methods: A total of 216 patients with cirrhosis (54.4% males, age: 57.6 ± 10.3 years and median MELD score: 13 [95% CI: 10-17]) were consecutively enrolled. At admission enrollment presence of bacterial infection were assessed on the basis of conventional criteria, liver-oriented scores were calculated and plasma presepsin, CRP and PCT levels were measured. A short-term follow-up study was conducted to assess the development of organ system failure(s) and 28-day mortality associated to bacterial infections.
Results: Bacterial infection was found in 75 (34.7%) patients. Plasma presepsin levels were significantly higher in patients with infection as compared to those without (1002 pg/mL [575-2149] vs. 477 [332-680] pg/mL, $p < 0.001$), increasing correspondingly with the severity of the infection. Presepsin levels were obviously higher in infectious episodes (32%) complicated by organ dysfunction(s), namely acute-on chronic liver failure (ACLF) (32%), than those without (2358 pg/mL [1398-3666] vs. 710 pg/mL [533-1277], $p < 0.001$). The diagnostic accuracy of presepsin for identifying patients with severe infection was similar to PCT and clearly superior to CRP established by ROC analysis (AUC: 0.846, 0.845 and 0.659, respectively, p = NS for presepsin vs. PCT, and $p < 0.01$ for both the presepsin vs. CRP and PCT vs. CRP). At the optimal cut-off value of presepsin (> 1206 pg/ml) sensitivity, specificity, PPV and NPV were as follows: 87.5%, 74.5%, 61.8% and 92.7%, respectively. Rate of 28-day mortality was higher among patients with > 1277 pg/ml compared to those with ≤ 1277 pg/ml (46.9% vs. 11.6%, $p < 0.001$). In a binary logistic regression model, comprising gender, age, MELD score and acute phase proteins (APPs) one-by-one, MELD score > 21 point (OR: 5.24, p = 0.025), PCT > 0.5 pg/ml (OR: 9.10, p = 0.006) or CRP > 40 mg/l (OR: 4.03, p = 0.039) but not presepsin level were independet risk factor for 28-day mortality.
Conclusion: Presepsin is a valuable new biomarker for defining severity of infections in cirrhosis proving same efficacy as PCT. However, for the prediction of short-term mortality, liver-oriented scores and admission level of conventional APP proteins, particularly PCT are the appropriate tools.
Disclosure of Interest: None declared

OP202 SPONTANEOUS FUNGAL PERITONITIS: A RARE BUT SEVERE COMPLICATION OF LIVER CIRRHOSIS

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Introduction: Spontaneous peritonitis (SP) is the most common infectious complication in liver cirrhosis, mainly due to bacteria. Although Spontaneous Fungal Peritonitis (SFP) is a rare condition, it is associated to worse outcome. This entity remains unclear.
Objective: Characterization, risk factors and prognosis in SFP.
Aims & Methods: Retrospective case-control study of 253 consecutive admissions by peritonitis in cirrhotic patients, between 2006-2014. SP diagnosis was considered if polymorphonuclear leukocytes > 250 in ascitic fluid in intrabdominal infectious focus absence. It was selected patients with SFP (cases:8), that were compared with SBP with microbiologic analysis of ascitic fluid (controls:119). The variables evaluated were socio-demographic, clinic, cirrhosis etiology, cirrhosis severity, analysis, invasive procedures and prognosis.
Results: During period study, 231 patients developed SP and 8 SFP (3.5%; male: 75.0% vs 84.9%; p = 0.458 and mean age: 63.1 ± 11.2 vs 63.4 ± 8.6years; p = 0.955). Of SFP cases, 62.5% were co-infected with bacterial agent. In all cases were isolated *Candida spp*., mainly *Candida albicans* (37.5%) and *Candida krusei* (25.0%). Patients with SFP had more ascitic fluid lactate dehydrogenase levels (288.4 ± 266.6 vs 161.0 ± 179.5; p = 0.011), serum leukocytes (15187.5 ± 5432.3 vs 10969.8 ± 6949.5; p = 0.028), serum urea (69.8 ± 3.1 vs 36.3 ± 25.5; 9 = 0.001) and higher number of invasive procedures (colonoscopy: 25.0% vs 0.8%, p = 0.001; urinary catheterization: 87.5% vs 49.6%, p = 0.038; nasogastric intubation: 87.5% vs 26.9%, p = 0.001). There was no statistically significant difference between two groups relatively to MELD, MELD-Na and Child-Pugh scores. SFP was associated with worse prognosis, particularly more length of stay (30.0 ± 32.9 vs $18.9 \pm$ 17.0days; p = 0.031), more admission-diagnosis time (15.8 ± 24.2 vs $2.1 \pm$ 5.7dias; p = 0.001) and more global mortality (62.5% vs 31.9%; p = 0.039). The mortality rate at 30 days was statically significant higher in SFP (50.0% vs 24.4%; p = 0.034), with mean diagnosis-death time of 17.6 ± 11.5 days.
Conclusion: Despite a rare condition, SFP is a severe complication of liver cirrhosis associated with high mortality. The lactate dehydrogenase in ascitic fluid, serum leukocytes and urea, invasive procedures and more length of stay seem to be risk factors for SFP. Given only the ascitic fluid culture be able to differentiate spontaneous bacterial peritonitis and SFP, the clinical suspicion id crucial to early diagnosis and treatment.
Disclosure of Interest: None declared

OP203 BRAIN METABOLISM IN PATIENTS WITH MINIMAL HEPATIC ENCEPHALOPATHY ON 3.0-TESLA MAGNETIC RESONANCE SPECTROSCOPY

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Introduction: Minimal hepatic encephalopathy (MHE) is a clinical problem in liver cirrhosis (LC) patients. MHE involves cognitive dysfunction and poor driving skills, which lead to a decline in the patient's quality of life. Brain metabolism changes have been reported in patients with overt hepatic encephalopathy. However, these pathological changes remain to be investigated in patients with MHE.

Aims & Methods: Aims The aim of this study was to evaluate changes in the brain metabolism of MHE patients using high-resolution 3-Tesla (3T) ^{1}H (proton)−magnetic resonance spectroscopy (MRS).

Methods: We examined 21patients with liver cirrhosis [males, 15; females, 6; mean age, 60 years old (mean ± SD; 60 ± 12)].

The patients were evaluated for neuropsychiatric symptoms using the neuropsychiatric tests Digit symbol test (DST), Block design test (BDT) and Number connection test A, B (NCT A, B). MHE was diagnosed in patients who exhibited two or more abnormalities on these tests.

All patients were examined with ^{1}H (proton)−magnetic resonance spectroscopy (MRS) using 3T MRI. The findings were compared between the MHE group (7 patients) and the non-MHE group (14 patients).

Results: MRS study indicated that the brain glutamine (Gln) levels were significantly increased ($p < 0.01$) in the MHE group (Gln/Cre + PCre:2.05 ± 0.17) compared with the non-MHE group (Gln/Cre + PCre:1.05 ± 0.09) . In contrast, the brain myoinositol (mIns) levels significantly decreased ($p < 0.01$) in the MHE group (mIns/Cre + PCre:0.32 ± 0.04) compared with the non-MHE group (mIns/Cre + PCre:0.57 ± 0.04).

We also observed a significant negative correlation ($r = 0.767$, $p < 0.01$) between the brain Gln and mIns levels.

Blood tests revealed no significant differences between the MHE and non-MHE groups in the blood ammonia levels. However, a positive correlation ($r = 0.455$, $p < 0.05$) was noted between the blood ammonia and brain Gln levels, whereas a negative correlation ($r = 0.674$, $p < 0.05$) was noted between the blood ammonia and brain mIns levels .

Conclusion: The present results indicated that there is a marked increase in the brain Gln and a marked decrease in the mIns within the brain in patients with MHE compared with those without MHE. These data demonstrated that disturbed brain metabolism, similar to that observed in patients with overt hepatic encephalopathy, is also already present in patients with MHE.

In addition, the results suggested that the quantification of these phenomena using MRS could be useful for an early and objective diagnosis of MHE.

Disclosure of Interest: None declared

OP204 ASSOCIATION BETWEEN 90-DAY MORTALITY AND THE ALCOHOLIC HEPATITIS HISTOLOGICAL SCORE

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Introduction: The diagnosis of acute alcoholic hepatitis (AAH) may be based on clinical and biochemical data, but a definite diagnosis requires histological confirmation. A histological classification system has been recently proposed to predict 90-day mortality in patients with AAH.

Aims & Methods: To analyse the spectrum of histological findings in patients with AAH and assess the ability of alcoholic hepatits histological score (AHHS) to predict 90-day mortality.

Retrospective analysis of patients admitted to our department due to AAH, between November 2009 and October 2014, who underwent transjugular liver biopsy (TJLB). We analysed the following histological findings: cholestasis, steatosis, megamitochondria, Mallory bodies, necroinflammatory lesions, polymorphonuclear (PMN) infiltrate and satellitosis. The AHHS was calculated and we analysed the association between AHHS and 90-day mortality.

Results: Of 59 patients admitted due to AAH, 34 (57.6%) underwent TJLB (70.6% men, mean age 48.5 ± 8.9 years). BHTJ was performed 4.5 ± 2.9 days after admission. All patients had a METAVIR score = F4. Mortality at 90 days was 29.4%. The presence of cholestasis ($p = 0.05$), the absence of megamitochondrias ($p < 0.001$) and a higher AHHS ($p < 0.001$) were significantly associated with mortality at 90 days. There was no significant difference in steatosis, necroinflammatory lesions, PMN infiltrate and satellitosis. All patients with an AHHS ≥ 7 died (AUROC 1, sensitivity and specificity of 100%, $p < 0.001$).

Conclusion: In this group of patients with AAH, the presence of cholestasis and absence of megamitochondrias on histology were significantly associated with 90-day mortality. The AHHS was predictive of mortality at 90 days and may be used as an additional data in clinical decisions.

Disclosure of Interest: None declared

OP205 HIGH NUMBER OF OPPORTUNITIES IN PRIMARY AND SECONDARY CARE TO PREVENT ALCOHOL INDUCED CIRRHOSIS

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Introduction: Mortality from liver disease is higher in the UK than in most other European countries. As a result, recent attention has been placed on strategies that can be used to improve prevention of this disease.

Aims & Methods: The aim of this study was to describe patterns of healthcare utilisation of patients with alcoholic cirrhosis in order to identify factors that may be useful in the earlier identification of people at risk of alcoholic cirrhosis.

Methods: Patients with alcoholic cirrhosis and a matched control population of patients without the disease were identified in the UK's primary care Clinical Practice Research Datalink and secondary care Hospital Episode Statistics (HES) database (1990 and 2011). Health-care use in people with cirrhosis during the period prior to disease diagnosis was described and compared to that of the control population before a defined index date using Poisson regression. We also specifically examined co-morbidities present in patients as potential explanations to healthcare utilisation trends.

Results: 2,479 patients with cirrhosis and 24,790 controls were identified for analysis. For the 10-year period leading up to alcoholic cirrhosis diagnosis, there was a significantly higher rate of primary care visits in cases of cirrhosis than in controls (IRR 1.52, 95% CI (1.51 to 1.53)), with an average excess of 6.6 consultations per person year. The hospitalisation rate was also over two times higher for people with alcoholic cirrhosis than controls (IRR 2.49, 95% CI (2.42 to 2.54)). People with alcoholic cirrhosis were more likely than controls to present with morbidities reported to be partly attributable to alcohol. The most frequent morbidities in cases versus controls were intentional injuries (35.9% versus 11.9%) and cardiovascular diseases (23.2% versus 15.6%), followed by diabetes (12.8% versus 5.3%), digestive diseases (6.1% versus 1.2%) and epilepsy (5.0% versus 1.1%). Multivariate analyses showed that digestive diseases (OR 5.4, 95% CI 4.4-6.7), epilepsy (Odds ratio 4.4, 3.5-5.5) and injuries (OR 4.0, 3.7-4.4) had the strongest association with subsequent development of alcoholic cirrhosis.

Conclusion: Up to 10 years before alcoholic cirrhosis is diagnosed, patients have more frequent encounters with primary and secondary care than the general population, especially for conditions which are partly attributable to alcohol (e.g. injuries, epilepsy, digestive diseases). These results show that through monitoring of healthcare attendances, it may be possible to identify patients who may develop alcohol-related liver cirrhosis, and therefore intervene, at an earlier stage in the disease course.

Disclosure of Interest: None declared

OP206 ANTICOAGULANT TREATMENT AND DECOMPENSATION RATE IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Anticoagulant treatment in patients with liver cirrhosis (LC) is still controversial. Recent studies demonstrated that anticoagulant treatment could reduce decompensation and mortality rates in cirrhotic patients. Our aim was to evaluate decompensation rate in patients with LC and atrial fibrillation treated with acenocoumarol for thrombotic events prophylaxis.

Aims & Methods: The study group included patients diagnosed with compensated liver cirrhosis and atrial fibrillation treated with an oral anticoagulant (acenocoumarol), admitted in a tertiary center between January 2011 and December 2011. The control group included consecutive patients diagnosed with LC, matched by age, etiology and liver stage disease with the study group. All patients were regular follow-up since December 2014 or until first hepatic decompensation (ascites, hepatic encephalopathy, variceal bleeding) occurred.

Results: The study included 78 patients diagnosed with compensated LC and atrial fibrillation, mean age 62.36 ± 11.27 years at diagnosis, 48 (61.53%) males. The majority of the patients were diagnosed with alcoholic LC- 41 patients (52.56%). The control group included 78 cirrhotic patients who received no anticoagulant treatment. There were no differences regarding baseline characteristics and LC severity between the two study groups. Mean follow-up period was 82.5 ± 3.25 month. During the follow-up period 48 patients (30.7%) developed hepatic decompensation in both study groups of whom 5 died. The cumulative decompensation rate was 17.9% in the study group and 38.6% in the control group, respectively ($p < 0.0001$). The rate of decompensation was higher in the first year in both groups. There were two cases of epistaxis in the study group, and 4 cases of variceal bleeding in both groups, with no other major bleeding side effect to anticoagulant treatment.

Conclusion: Anticoagulant treatment in patients with LC is relatively safe, and may improve patient outcome and decrease decompensation rate, despite association of atrial fibrillation.

Disclosure of Interest: None declared

OP207 DISTURBANCES OF GASTRIC EMPTYING, INTESTINAL ABSORPTION, PERMEABILITY AND GUT HORMONES IN PATIENTS WITH CHRONIC LIVER DISEASE: POTENTIAL MECHANISMS UNDERLYING POOR ORAL INTAKE AND MALNUTRITION

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Introduction: Malnutrition is common in patients with chronic liver disease. Disturbed gastrointestinal function as well as poor appetite are thought to be the likely underlying mechanism for malnutrition in these patients. Although delayed gastric emptying and increased intestinal permeability have been reported in patients with liver cirrhosis, their relationship to gut hormones, small intestinal absorption and gastrointestinal symptoms remains unclear.

Aims & Methods: The aim was to evaluate the inter-relationship between gastric emptying, intestinal permeability, glucose absorption, gastrointestinal hormones glycaemia and post-prandial appetite in patient with chronic liver disease. **Methods:** Comprehensive physiological studies were performed in 20 patients with liver cirrhosis (16M:4F, 55.7± 1.8 years, 10 Childs A, 7 Childs B, 3 Childs C, 12 alcoholic liver disease, 8 hepatitis C), and data were compared to those from 10 healthy controls (5M:5F, 39.0 ± 6.4 years). After an overnight fast, all subjects underwent assessment of (i) gastric emptying of a mixed meal using scintigraphy, comprising of 50g beef patty (labelled with ^{99m}Tc calcium phytate) and 150mL glucose drink (labelled with 3MBq ^{67}Ga-EDTA), (ii) intestinal permeability using a dual sugar test (1g rhamnose and 7.5mL lactulose added to glucose drink), (iii) intestinal glucose absorption by 3-O-methyl-glucose absorption test (3g added to glucose drink), (iv) blood glucose and gut hormones (insulin, glucagon-like peptide-1, and peptide YY) were measured over 240minutes, and (v) post-prandial gastrointestinal symptoms using visual analogue scales (VAS).

Results: Compared to healthy controls, gastric emptying was delayed in 35% of patients with liver cirrhosis with overall prolonged meal retention (26.7 ± 4.4% vs 12.3 ± 2.9% retention at 100min, $p = 0.04$). Intestinal permeability was significantly increase in patients with cirrhosis. Patients with liver cirrhosis also had significantly higher intestinal permeability (63.8 ± 6.1 vs 3.9 ± 1.2, $p < 0.0001$), post-prandial blood glucose ($p = 0.02$) and plasma GLP-1 levels ($p = 0.018$), but attenuated rise in post-prandial plasma insulin ($p < 0.001$) and 3-OMG ($p = 0.004$). More importantly, there was a significant delay in the recovery of post-prandial appetite VAS ($p < 0.001$) at 4 hours. Small intestinal glucose absorption, as assessed by area under the curve of plasma 3-OMG, correlated inversely with both gastric half emptying time (t1/2) (r = -0.6, p = 0.025) and intestinal permeability (r = -0.76, $p = 0.001$).

Conclusion: Subjects with chronic liver diseases have a wide range of gastrointestinal dysfunction, characterising by delayed gastric emptying, impaired small intestinal barrier, reduced intestinal glucose absorption, and persistent elevation of appetite suppressing gut hormone, GLP-1. Together, these factors are the contributors of delayed recovery of post-prandial appetite, which in turn lead to a viscous cycle of nutritional deprivation, gut dysfunction, malabsorption and malnutrition. Early recognition and management of gut dysfunction, therefore, are important in patient with chronic liver diseases.

Disclosure of Interest: None declared

OP208 EFFECT OF DIFFERENT THERAPEUTIC MODALITIES ON SYSTEMIC, RENAL AND HEPATIC HEMODYNAMICS IN CIRRHOTIC PATIENTS WITH SPONTANEOUS BACTERIAL PERITONITIS

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Introduction: Spontaneous bacterial peritonitis (SBP) is a major risk factor for hepatorenal syndrome (HRS). One third of patients with SBP will develop HRS despite appropriate treatment with non-nephrotoxic antibiotics. Albumin infusion has been shown to prevent renal impairment and reduce mortality in high risk patients with SBP. However, albumin is expensive, has limited supply, and is a potential risk of infection transmission.

Aims & Methods: The study aimed to compare the effect of different therapeutic modalities on systemic, hepatic and renal hemodynamics and clinical outcome in high-risk patients with SBP. Two hundreds cirrhotic patients with SBP and bilirubin >4 mg/dL or creatinine >1 mg/dL were enrolled. Patients were randomized to receive albumin, terlipressin, low-dose albumin plus terlipressin, or midodrine. Systemic, renal and hepatic hemodynamics were estimated at baseline, 3 and 10 days of treatment. Renal impairment was diagnosed when the blood urea nitrogen or serum creatinine levels increased by more than 50% of the pretreatment value.

Results: SBP resolved in most of patients in all groups ($p > 0.05$). Cardiac output (CO) decreased and systemic vascular resistance (SVR) increased significantly in Terlipressin and albumin plus terlipressin groups compared to albumin group after 3 & 10 days ($p < 0.05$). Also, portal flow decreased significantly in both groups after 3 & 10 days ($p < 0.001$). After 10 days, plasma renin activity, renal and hepatic arteries resistive index (RI) were significantly higher in midodrine group compared to albumin group. Midodrine group didn't show any significant changes in heart rate, mean arterial pressure, CO and portal blood flow compared to albumin group after 3 or 10 days. There was no significant difference in mortality or development of renal impairment between all groups.

Conclusion: Terlipressin, low dose Albumin plus Terlipressin and Midodrine could be used as a therapeutic alternative to standard dose albumin in high-risk SBP patients.

Disclosure of Interest: None declared

OP209 SARCOPENIA AND OBESITY AMONG LIVER TRANSPLANTATION RECIPIENTS: A BODY COMPOSITION PROSPECTIVE STUDY

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Introduction: Muscle wasting, or sarcopenia, is a condition in which severe muscle depletion is observed. Recently, many studies have shown that sarcopenia is highly prevalent before transplantation (>50%) and it is considered a risk factor for increased morbidity and mortality. After transplantation, some authors have pointed out that sarcopenia arrests and, as patients gain too much weight as fat, this results in sarcopenic obesity when both conditions co-exist.

Aims & Methods

Aims: To prospectively verify changes in body composition, prevalence of sarcopenia, obesity and sarcopenic obesity in long-term liver transplantation (LTx) recipients after surgery.

Methods: Patients were evaluated in two moments for body composition, in 2008 and 2012, in average, 3.9 ± 3.2 and 7.5 ± 3.1 years after LTx. Body composition data (i.e., fat-free mass and fat mass) were obtained using bioelectrical impedance (RJL Systems® Quantum, Clinton Township, MI, USA). Fat-free mass index (FFMI) and fat mass index (FMI) (kg/m^2) were calculated and, patients classified in groups according to the following combination in: sarcopenia (low FFMI and normal FMI); obesity (normal FFMI and high FMI); sarcopenic obesity (low FFMI and high FMI) and normal body composition (normal FFMI and FMI). Low FFMI (≤ 17.4kg/m^2 in men and 15.0kg/m^2 in women) and high FMI (≥ 8.3kg/m^2 in men and 11.8kg/m^2 in women) were the cutoff values used to compare parameters (Kyle et al., 2012).

Results: A total of 113 patients were evaluated (53.1 ± 13.2 years; 58.4% male). FFMI decreased and FMI increased over the years after surgery (Table 1). Prevalence of sarcopenia, obesity and sarcopenic obesity also increased over the years, but not significantly. Sarcopenia was prevalent in 1/5 and obesity in 1/3 of patients in the long term after LTx. Although these conditions were highly prevalent in these patients, they did not coexist since only two patients (1.8%) were diagnosed with sarcopenic obesity. Less than half of the patients had normal body composition in the long-term after LTx.

Table 1: Fat-free mass and fat mass index, prevalence of sarcopenia, obesity, sarcopenic obesity and normal body composition among long-term liver transplantation recipients over four years

	Fat-free mass index	Fat massindex	Sarcopenia	Obesity	Sarcopenic obesity	Normal
2008	17.6 ± 2.5kg/m^2	7.8 ± 3.4kg/m^2	22 (19.5%)	34 (30.1%)	0 (0.0%)	57 (50.4%)
2012	17.1 ± 3.6kg/m^2	8.2 ± 3.9kg/m^2 *	24 (21.2%)	37 (32.7%)	2 (1.8%)	50 (44.2%)

Paired t and Mc Nemar test; * $p < 0.05$

Conclusion: Fat mass increased over the years after surgery and lean mass, decreased, although not significantly. Sarcopenia and obesity were highly present after LTx with increasing prevalence over the years leading to less than half of the population presenting with normal body composition. However, sarcopenic obesity was not a reality observed in these patients. As survival after liver transplantation has improved, these patients should be followed for body composition changes and early intervention.

Abstract number: OP208

Variables		Albumin N = 50	Terlipressin N = 50	Albumin plusTerlipressin N = 50	Midodrine N = 50	p
Resolution of SBP		48 (96%)	48 (96%)	47 (94%)	46(92%)	0.787
Duration of hospital stay		10.2 ±0.6	10.2 ±0.8	10.1 ±0.6	10.4 ±0.9	0.839
Renal impairment	In hospital	5 (10%)	4(8%)	4(8%)	11 (22%)	0.092
	Within 30 days	7 (14%)	7 (14%)	7 (14%)	15 (30%)	0.090
Mortality	In hospital	4 (8%)	3 (6%)	3 (6%)	9 (18%)	0.124
	Within 30 days	12 (24%)	11 (22%)	10 (20%)	17(34%)	0.377

Reference

1. Kyle UG, et al. *Clin Nutr* 2005; 24: 133–42.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30

PROGRESS IN ENDOSCOPIC BILIARY IMAGING AND INTERVENTIONS – ROOM B3

OP210 PROSPECTIVE RANDOMIZED STUDY OF ENDOSCOPIC BILIARY STONE EXTRACTION USING EITHER A BASKET OR BALLOON CATHETER: THE BASKETBALL STUDY

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Introduction: Presently, endoscopic extraction after endoscopic sphincterotomy (ES) is recognized worldwide as the first-line treatment for bile duct stones. Stones smaller than 10 mm in diameter can usually be extracted from the bile duct after ES, without crushing them. For this purpose, a retrieval basket is generally used in Japan and Europe, but a retrieval balloon is mainly used in the USA. Both of these devices appear to show similar success rates of stone extraction. However, the efficacies of these 2 devices have not been previously compared.
Aims & Methods: The present multicenter, prospective, randomized study was performed to compare the efficacies of basket and balloon catheters for endoscopic biliary stone extraction. This study included 184 patients from 6 Japanese institutions with bile duct stones smaller than 10 mm in diameter, with no limitation in the number of stones. After the stones were identified and size of the largest stone was confirmed smaller than 10 mm with ERCP, the patients were randomly assigned to either undergo endoscopic stone extraction using a basket catheter or undergo it using a balloon catheter. The primary end point was complete removal rate of biliary stones within 10 minutes, and the secondary end point was complications related to the procedure.
Results: The patients were assigned to the basket group in 91 patients and to the balloon group in 93 patients. Baseline characteristics, such as age, male/female ratio, number of stones, size of stones, and diameter of the bile duct, were not significantly different between the basket and balloon groups. Stone extraction was successful within 10 minutes in 81.3% (74/91) of patients in the basket group and in 83.9% (78/93) of patients in the balloon group (P = 0.5584). Among the patients with failed extraction within 10 minutes, complete stone extraction was successful after 10 minutes using the same device in 3 and 0 patients, and was successful with exchange of the device in 9 and 9 patients in the basket and balloon groups, respectively. Complete extraction failed at the initial session in 5 and 6 patients in each group. The main reasons for failed extraction were that the basket could not grasp small stones in the basket group and the balloon passed aside a stone impacted in the corner pocket at the lower end of the bile duct in the balloon group. The complication rates were 6.6% and 11.8% in the basket and balloon groups, respectively (P = 0.3092), and they included bleeding (2.2% vs. 6.5%), pancreatitis (3.3% vs. 4.3%), and cholangitis (1.1% vs. 1.1%).
Conclusion: Basket and balloon catheters showed similar efficacies for endoscopic biliary stone extraction. (Clinical trial registration number: UMIN000010486)
Disclosure of Interest: None declared

OP211 A MULTICENTER RANDOMIZED TRIAL OF ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION ALONE VERSUS ENDOSCOPIC SPHINCTEROTOMY FOR REMOVAL OF BILE DUCT STONES: MARVELOUS TRIAL

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Introduction: Removal of large common bile duct (CBD) stones by endoscopic papillary large balloon dilation (EPLBD) with endoscopic sphincterotomy (EST) has been proven safe and effective. Little evidence supports the benefits of a preceding EST in reducing complications. Recent studies suggest that large CBD stone removal by EPLBD alone without EST may be safe and effective.
Aims & Methods: This multicenter randomized trial was conducted at 19 institutions in Japan to compare the efficacy and safety of EPLBD alone versus EST for removal of large CBD stones (UMIN-CTR number, 000010012).
Between February 2013 and January 2015, 181 patients over 60 years of age with large CBD stones (≥10 mm) and dilated distal CBD (≥12 mm) were randomly assigned to groups that underwent EPLBD alone or EST. The primary outcome was the rate at which complete stone removal was achieved in the first session, and secondary outcomes included complete stone clearance rate, use of lithotripsy, stone removal time, early complications, and procedure cost.
Results: After randomization, 10 patients were excluded because of not fulfilling the inclusion criteria (n = 4), incorrect diagnosis (n = 4), withdrawal of consent (n = 1), and biliary cannulation failure (n = 1). 7 patients who did not receive the allocated treatment were also excluded. Finally, data from 164 patients were analyzed (82 in each group). Patient characteristics such as age, sex, ASA score, stone number, stone size, CBD diameter, and periampullary diverticulum were similar in both groups. The rate of complete stone removal in the first session was significantly higher in the EPLBD alone group than in the EST group (92.7% vs. 80.5%, $P = 0.037$). The complete stone clearance rate was similar in both groups (100% vs. 96.3%, $P = 0.245$). The use of lithotripsy was significantly less frequent in the EPLBD alone group than the EST group (28.0% vs. 46.3%, $P = 0.023$). Stone removal time was similar in both groups (36.1 min vs. 40.3 min, $P = 0.464$). The overall early complication rate was 9.8% in each group. The rate of post-ERCP pancreatitis was similar in both groups (4.9% vs. 6.1%, $P = 1.000$). No perforation occurred in either group. Hemorrhage occurred in 1 patient in the EST group. The procedure cost was significantly lower in the EPLBD alone group (USD $1354 ± 730 vs. $1619 ± 834, $P = 0.032$).
Conclusion: EPLBD alone without EST is safe and more effective than EST for the treatment of large CBD stones.
Disclosure of Interest: None declared

OP212 PEDIATRIC BIOPSY FORCEPS VS SPYBITE FORCEPS COMPARISON AT THE DIAGNOSIS OF BILIARY STRICTURES: A RANDOMIZED STUDY

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Introduction: The accuracy of histological diagnosis for biliary strictures is low and is increased using at least two ERCP-samples collections techniques (brushing, biopsies and puncture). In this context, the effectiveness of the Spybite forceps is unknown.
Aims & Methods: To compare the histological diagnosis performance of standard pediatric biopsy forceps (PS) vs Spybyte biopsy forceps (SB) in the biliary strictures by any cause diagnosis.
Methods: Open label randomized prospective controlled trial (February 2009 - January 2011). Participants: The consecutive patients with biliary strictures detected in ERCP. Intervention: A brushing cytology of strictures was done in all patients during ERCP and immediately after the biopsies were randomly obtained by SP or SB. Main outcome measures: Diagnosis performance according to forceps biopsy type. Secondary outcomes measures: Feasibility of the access into the bile duct (number of passes), endoscopist (capability to obtain tissue) and nurse (watching the biopsies in a sample jar) impression of the quality and number of samples, according to the biopsy forceps type. The biliary stricture diagnosis was confirmed by the clinical follow up during 1 year and the histology report from the surgery.
Results: 101 patients with biliary strictures were included, (Age: 72.57 ± 13.20; 41♂) 71 malignant strictures, 86% extrahepatic strictures; SP group: 44; Sb group 57. We achieved ≥4 forceps access into the bile duct in 84%; 1-3 tissue pieces in 48.4% and > 3 in 51.6%. The number of samples was greater with SP than SB (≥3: 79.5% vs 54.4%; p = 0.008) and the tissue samples were considered good by the endoscopist in 53.5% and 55.4% by the nurse. The histological analysis of ERCP-samples were: Lack or insufficient tissue 21.2%, normal biliary epithelium 23.2%, inflammatory 25.3% dysplastic 15.2% (low grade: 8.1%; high grade: 7.1%), tumor 15.2%. The correct diagnosis was done in 59.4% (n = 60); SP: 65.9% vs. SB: 54.5%; p = 0.16. The biliary access (> 3 passes) was better with SP (93.1 vs 84.1%; p = 0.048). The impression of quality samples was better with SP for the endoscopist (p = 0.186) and the nurse (SP 77.3% vs. SB 38.6%; p = 0.001).
Conclusion: The histological performance (cytology + biopsy) of biliary strictures by ERCP is 59.4% without differences in forceps type. The access and obtaining tissue in biliary strictures is better with the standard pediatric biopsy forceps.
Disclosure of Interest: None declared

OP213 EFFECT AND IMPACT OF PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY (PCLE) IN THE DIAGNOSIS AND MANAGEMENT OF INDETERMINANT BILIARY STRICTURES

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Introduction: Extrahepatic cholangiocarcinoma (ECCA) remains a highly fatal disease that is difficult to diagnose due to poor yields from standard tissue sampling methods. pCLE has been shown to improve the accuracy of diagnosis of ECCA, potentially expediting diagnosis, saving unnecessary further testing and allowing earlier initiation of treatments.

Aims & Methods: The aims of this study were to assess the diagnostic and therapeutic impact of pCLE on the management of patients with indeterminate biliary stricture, specifically comparing ERCP with tissue sampling (TS) vs. ERCP with pCLE and TS.

The FOCUS trial was a prospective multicenter evaluation of the performance of pCLE in the diagnosis of indeterminate biliary strictures. A retrospective analysis of data was performed. During the FOCUS trial, managing physicians were asked prospectively to give a presumptive diagnosis on the basis of ERCP images with pCLE information and ERCP images with pCLE and TS. Answers were recorded and compared to final diagnosis. The final diagnosis was established by positive tissue sampling or surgical pathology in cases of malignant disease, and by negative tissue sampling, negative imaging (no mass) and a benign clinical course at 6 months of follow-up. Furthermore, treatment decisions were also recorded by the managing physician, based respectively on information with and without pCLE. Treatment recommendations were considered ***"appropriate"*** if the recommended treatment corresponded to the final diagnosis or ***"inappropriate"*** if the recommended treatment did not correspond to the final diagnosis. Additional testing required for diagnosis were recorded. Time to correct diagnosis (TCD) was measured as time until positive tissue diagnosis was established OR time until a correct presumptive diagnosis was made (based on pCLE and/or TS). In cases of incorrect presumptive diagnosis in cases with malignant disease, TCD was made was deemed time to correct diagnosis. In cases of benign disease, time to correct diagnosis was considered 6 months if no presumptive diagnosis was made.

Results: 107 of the 121 patients from the FOCUS trial were evaluable.

Overall TCD was reduced from 71 days without pCLE to 15 days with pCLE. In patients with negative TS, the TCD was reduced to 89 days when pCLE information was applied.

The addition of information from pCLE to a standard approach with ERCP + TS alone increased the appropriateness of treatment management decisions from 59% to 74% (15%) and reduced the need of additional diagnostic procedure by 15%, without impairing the rate of inappropriate treatment recommendations.

In patients with indeterminate tissue sampling, the ERCP + pCLE + TS sampling approach increased the number of appropriate recommendation by 22% as compared with the standard approach and decreases the number of additional procedures by 24% without increasing the number of inappropriate procedure recommendations.

Conclusion: pCLE appears to have a beneficial effect on the diagnosis and treatment of indeterminate biliary strictures. Use of pCLE appears to decrease TCD and may reduce the number of extra diagnostic procedures required to establish a diagnosis.

Disclosure of Interest: None declared

OP214 A U.S. MULTI-CENTER FIRST HUMAN USE EXPERIENCE USING THE FULLY DISPOSABLE, DIGITAL SINGLE-OPERATOR CHOLANGIOPANCREATOSCOPE (DSOCP)

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Introduction: A new fully disposable catheter-based digital single-operator cholangiopancreatoscope (DSOCP) has recently received U.S. FDA clearance. It has a complementary metal-oxide semiconductor (CMOS) chip for high resolution, magnification, and wider field of view; a thin copper cable provides digital transmission and the lack of a separate fiberoptic probe may enhance tip articulation.

Aims & Methods

Aim: Document indications, interventions, success, and qualitative impression of the digital image. The DSOCP (SpyDS™ Boston Scientific, Marlborough, MA) has 4-way tip deflection, 10.5F tip, 1.2mm working channel, and 120 degree field of view. Data from a limited release of DSOCP to five centers with expertise in cholangioscopy was collected. Technical success was defined as achieving the intended diagnostic or therapeutic intent. Each expert qualitatively assessed the digital image and ease of use on a visual analog scale (VAS) of 0 to 10.

Results: Since February 2015, five institutions performed 124 DSOCP and 121 were evaluable. Indications: indeterminate extra- (n = 54) or intrahepatic biliary stricture (n = 17), extra- (n = 20) or intrahepatic (n = 3) stones, cystic duct stones (n = 6), extra- (n = 12) or intrahepatic ductal dilatation (n = 1), pancreatic duct stones (n = 7), and pancreatic stricture (n = 1). Eight of these patients underwent DSOCP to assess cholangiocarcinoma extent. Technical success was achieved in all cases. Directed tissue sampling using Spybite™ forceps (Boston Scientific) was obtained in 53 cases. Thus far, 32 patients have established neoplasia; 22/24 (92%) without a prior tissue diagnosis of neoplasia were confirmed by SpybiteTM forceps. One or more benign findings in patients with strictures or ductal dilatation included concentric stenosis or normal/erythematous changes (n = 17), low papillary mucosal projections (n = 9), coarse granular mucosa (n = 8), and nodular mucosa (n = 8). One or more neoplastic findings included "tumor vessels" (n = 14), infiltrative stricture (n = 14), villous or nodular mass (n = 9), and finger-like villous projections (n = 6). Two patients with DSOCP impression of neoplasia underwent surgery and were found to have benign disease. For biliary and pancreatic stones, complete ductal clearance has been achieved in 34/36 (94%). Stone fragmentation required electrohydraulic lithotripsy (n = 8) and laser lithotripsy (n = 18) and each of these cases had prior incomplete clearance. DSOCP also identified unsuspected stones or confirmed ductal clearance (n = 8). Two have ongoing therapy. The mean VAS for image quality and ease-of-use was 9.5. Complications: pancreatitis (n = 1), abdominal pain (n = 1), cholangitis (n = 1).

Conclusion: 1) This first human use report using the digital single-operator cholangiopancreatoscope demonstrates high technical success in a variety of complex pancreaticobiliary disorders. 2) The rate of obtaining confirmatory tissue sampling using directed Spybite sampling was over 90% in patients without a prior diagnosis of neoplasia. 3) The rate of ductal stone clearance is nearly 100%. 4) DSOCP provides enhanced image resolution and tip articulation and in expert hands may improve the ability to target difficult biliary and pancreatic stones, as well as, intraductal pathology for tissue sampling.

Disclosure of Interest: R. Shah Consultancy: Boston Scientific Endoscopy, I. Raijman Consultancy: Boston Scientific Endoscopy, R. Hawes: None declared, B. Gumustop: None declared, M. Hasan: None declared, B. Brauer: None declared, N. Fukami: None declared, D. Pleskow Consultancy: Boston Scientific Endoscopy

OP215 CAN ENDOSCOPIC PAPILLECTOMY BE CURATIVE FOR EARLY ADENOCARCINOMA OF THE AMPULLA OF VATER ?

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Introduction: According to the TNM classification of ampullary tumors, pT1 adenocarcinoma is limited to the ampulla of Vater without infiltration of the duodenal muscularis propria. The risk of lymph node metastasis (N+) rounds 20% in Western surgical series. The Japanese classification subdivide pT1 lesions in d0 tumours, confined to the sphincter of Oddi (risk N+ = 0%), and d1 tumours invading the duodenal submucosa (risk N+ = 30%). Japanese surgeons consider a d0 lesion without vascular embols, as an early cancer that should be cured by a local resection. At the moment, no series has evaluated if endoscopic papillectomy (EP) is curative in this situation.

Aims & Methods: To evaluate in which cases an endoscopic papillectomy could be considered as curative in ampullary adenocarcinoma.

From May 1999 to July 2014, patients with ampullary tumors (adenoma +/- adenocarcinoma), staged as uT1 at endoscopic ultrasound, undergone EP and were prospectively included in a database. Histopathological data, follow-up (FU) of patients and factors that predict lymph node metastases were analyzed retrospectively.

Results: 172 patients with ampullary tumors undergone EP during the study period. Adenocarcinoma was present on the resected specimen in 25 cases (mean age 70 years). A complementary pancreaticoduodenectomy (PD) was proposed in case of positive resection margins (R1), vascular embols, or submucosal invasion. In 11 cases (Group 1), the invasion was limited to the Oddi's sphincter (d0). In 14 cases (Group 2) there was an invasion of the duodenal submucosa (d1).

Group 1 (n = 11): Five patients (45%) had negative margins of resection (R0), no vascular embols and normal biopsies at the post resection control. No recurrence was evidenced during FU (mean 56 months (18-96)). Six patients (55%) had positive resection margins, one with vascular embols. A complementary PD was done in 3 patients (1 d1N-, 1d1N+, 1 without residual tumor). Three patients had contraindications or refused surgery and were followed. There was no cancer recurrence or disease related death in two cases (FU: 36 and 72 months). One patient had a cancer recurrence and was finally operated on 6 months later (pT3N+).

Group 2 (n = 14): Ten patients (71%) were R1 and four (29%) R0. Vascular embols were present in 5 cases (36%). Eight patients had an additional PD; 6 were N + (62%) +/- residual adenocarcinoma (n = 4; 50%) and two were free of tumor. The other six patients had contraindications or refused surgery. During FU (mean 24 months (12-48)) the cancer recurred in 3 patients (1N+, 1 local recurrence, 1 M+ liver), 2 patients died from complications of chemotherapy and one remained alive without recurrence at 24 months.

Tumor size (P = 0.027) and infiltration of the submucosae (P = 0.033) were found to be significantly related to lymph node metastasis.

Conclusion: In agreement with the Japanese classification, this study confirms that the prognosis of T1 carcinoma of the ampulla of Vater is very different whether or not submucosal invasion is present. EP can be considered as curative when the resection specimen evidence an adenocarcinoma limited to the Oddi's sphincter, no vascular embols, and R0 resection. In other cases, an additional PD should be discussed.

Disclosure of Interest: None declared

OP216 PROSPECTIVE RANDOMIZED TRIAL OF WIRE-GUIDED PAPILLECTOMY VERSUS CONVENTIONAL PAPILLECTOMY FOR AMPULLARY TUMORS

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Introduction: Concerns about endoscopic snare papillectomy (ESP) include technical difficulties and the risk of procedure-related pancreatitis. To maintain pancreatic duct access for stent placement after ESP, wire-guided ESP was introduced.

Aims & Methods: The aim of study was to compare the success rate of inserting a pancreatic stent, post-procedure pancreatitis rates, procedure time, and complete resection rates between wire-guided endoscopic snare papillectomy (WP) and conventional ESP (CP) procedures.

Methods: This was a multi-center, prospective, randomized study. Forty-five patients with ampullary tumors were assigned randomly to the WP group (a pancreatic stent was placed along a previously inserted guidewire immediately after snare resection) or the CP group (post-resection pancreatic stent insertion).

Results: A total of 51 patients were enrolled, 25 in the WP and 26 in the CP group. Complete resection was achieved in 24 patients (96%) in the WP group and 21 patients (81%) in the CP group ($p = 0.094$). A pancreatic stent was placed successfully in all patients in the WP group but in only 18 patients (69%) in the CP group ($p = 0.003$). Post-papillectomy pancreatitis occurred in 3 (11%) patients in the WP and 3 (12%) patients in the CP groups ($p = 0.960$). In the CP group, 3 of 8 (37.5%) patients without stents developed pancreatitis compared with 0 of 15 patients with stents ($p = 0.032$). One patient without a pancreatic stent experienced severe pancreatitis.

Conclusion: The WP method is a useful technique used to insert a pancreatic stent after an endoscopic papillectomy, compared with CP. However, there was no significant difference in the post-procedure pancreatitis or complete resection rates between the two methods.

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Disclosure of Interest: None declared

OP217 A PLEA FOR SELECTIVE USE OF STAGING LAPAROSCOPY FOR POTENTIALLY RESECTABLE PERIHILAR CHOLANGIOCARCINOMA: AN ANALYSIS OF 265 PATIENTS

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Introduction: Staging laparoscopy (SL) for potentially resectable perihilar cholangiocarcinoma (PHC) may detect unresectable disease and therefore prevent unnecessary laparotomy. The diagnostic yield, however, remains unclear with varying results reported in the literature and a possible decrease over years with improvement of imaging techniques.

Aims & Methods: The aim of the present study was to identify predictors of unresectable disease at SL that can be used to select patients who may benefit most from this procedure. Data of patients with suspicion on potentially resectable PHC who underwent SL between 2000 and 2014 in an academic medical centre were retrospectively analysed. The yield and accuracy (sensitivity) of SL were calculated by dividing total number of avoided laparotomies by the total number of laparoscopies or by all patients with unresectable disease, respectively. Factors that were potentially associated with unresectable disease at SL were investigated.

Results: A total of 265 patients underwent SL and unresectable tumours were detected in 39 patients (yield 15%). Eighty-three patients had unresectable disease upon laparotomy. Overall accuracy of SL was 32% with the highest sensitivity to detect peritoneal metastases (72%). Factors associated with unresectable disease at SL were Blumgart T-stage ($P = 0.007$), tumour size ($P = 0.03$), suspicious hilar lymph nodes ($P = 0.03$) and suspected metastases ($P < 0.001$) on imaging without the possibility for diagnosis by percutaneous puncture. On multivariable analysis, Blumgart T3 stage (odds ratio [OR] 2.5; $P = 0.02$), tumour size $\geq$5 cm (OR 3.6; $P = 0.04$) and suspected metastases on imaging (OR 6.5; $P < 0.001$) were revealed as independent predictors for unresectable disease at SL. The observed yield in the study cohort increased from 6% (no predictors) up to 14-43% (1 predictor), 46-100% (2 predictors) and 100% (3 predictors).

Conclusion: Staging laparoscopy in PHC should be targeted at 'high-risk' patients with Blumgart T3 stage, large tumour size or suspected metastatic lesions on imaging without the possibility for diagnosis by percutaneous biopsy.

Disclosure of Interest: None declared

OP218 MINILAPAROTOMY CHOLECYSTECTOMY VERSUS LAPAROSCOPIC CHOLECYSTECTOMY WITH HARMONIC SCALPEL – A PROSPECTIVE, RANDOMISED MULTICENTER TRIAL

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Introduction: Laparocopic cholecystectomy (LC) is the gold-standard operative technique for the treatment of symptomatic gallstone disease. However, minilaparotomy cholecystectomy (MC) has shown to have similar early recovery after surgery. Monopolar cauterization hook is most commonly used for dissection in LC because of the ease of securing haemostasis and low costs. Ultrasonic dissection (UsD) has later shown to be safe and effective in LC. Furthermore, we were the first to apply UsD in MC (1). A review of literature and our previous results suggest that UsD applied to either MC or LC leads to a shorter convalescence, less postoperative pain and complications compared to classic dissecting approaches. To our knowledge, there are no trials comparing the use of UsD in MC vs LC.

Aims & Methods: 99 patients with non-complicated symptomatic gallstone disease were randomized to MC (n = 51) or LC (n = 48) over a period of 2-years (2013-2015). UsD was used in both groups. The study was a prospective, randomised, multicentre trial and the procedures, anaesthesia protocol and postoperative care were standardized. Operative time, time at the operation theatre, perioperative bleed, complications and conversions were recorded. Postoperative pain was assessed at 1h, 2h, 3h, 4h after surgery using an 11-point numeric rating scale (NRS). Nausea, the amount of analgesics and antiemetics used, day surgery success and the length of hospitalization were recorded. Patients were interviewed at 24h after the surgery by phone.

Results: Demographic variables were similar in both groups. There was no difference in the time at the operation theatre (minutes): 116 (SD, 26) in the MC group, vs 125 (37) in the LC group, (p = 0.230), or operative time (minutes): 67 (26) in the MC group, vs 68 (26) in the LC group, (p = 0.81). No complications occurred in either group and conversion rate was alike (1 in MC vs 3 in LC, p = 0.28). Postoperative pain (NRS) was similar: at 1h in MC 3.5 (2.2) vs in LC 3.3 (2.4), (p = 0.52), at 2h (2.3 (1.8) vs. 2.4 (2.0), p = 0.91), at 3h (2.2 (1.7) vs 1.6 (2.1), p = 0.10), and at 4h (1.7 (1.8) vs 1.5 (1.8), p = 0.54) after surgery. Day surgery success rate (66% in MC vs 77% in LC, p = 0.31) and length of hospitalization (1.4 (0.6) vs 1.3 (0.5) days, p = 0.40) was similar. There was no difference in pain at 24h after surgery during rest, but LC patients reported less pain at normal activity (3.9 (2.3) vs 2.9 (2.4), p = 0.05) and quick movement 8.8 (2.3) vs 3.2 (2.6), p = 0.005. The use of analgesics during the first 24h was similar in both study groups.

Conclusion: UsD can be safely and effectively applied to MC with no significant difference compared to LC using UsD.

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Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 08:30–10:30

ABSTRACTS ON FIRE: UPPER GI CANCER-MECHANISMS AND CLINICAL ASPECTS – HOTSPOT

OP219 A PHASE II MULTICENTER PROSPECTIVE STUDY OF THE TRASTUZUMAB COMBINED WITH 5-WEEKLY S-1 AND CDDP THERAPY FOR PATIENTS WITH METASTATIC OR UNRESECTABLE HER2-POSITIVE GASTRIC CANCERS

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Introduction: S-1 and CDDP therapy was considered the standardized primary treatment for patients with metastatic or unresectable gastric cancers based on the results of SPIRITS trial. According to ToGA study, the combination therapy with trastuzumab and cisplatin plus capecitabine or 5-fluorouracil has been used as a standard regimen for metastatic or unrespectable HER2-positive gastric cancer. Regarding the effectiveness of trastuzumab combined with triweekly S-1 and CDDP therapy, it was reported that overall survival (OS) was 16.0 months, and 1-year OS rate was 67.9% in HERBIS-1 study. However, no studies have evaluated the efficacy and safety of trastuzumab combined with the 5-weekly S-1 and CDDP therapy, for HER-2 positive gastric cancer.

Aims & Methods: This study (UMIN000005792) was conducted between July 2011 and June 2014. Patients with metastatic or unresectable HER2-positive gastric cancer received S-1 (80-120mg per day) orally on days 1-21, cisplatin (60mg/m^2) intravenously on day 8, and trastuzumab (8mg/kg for first cycle on day 8, and 6 mg/ kg for subsequent cycles by every 3 weeks) intravenously. The primary end point was 1-year OS rate, and secondary end point included OS, progression-free survival (PFS), response rate (RR), and toxicity profiles.
Results: A total of 22 patients were enrolled. Two patients were ineligible for the study, and we analyzed 20 patients (16 men and 4 women; median age, 66 years old). 1-year OS rate was 66.8%, the confirmed RR was 38.4%, the median PFS was 7.5 months, and OS was a state of non-arrival.We recorded grade 3 or 4 adverse events including anorexia (30%), neutropenia (30%), general fatigue (20%), anemia (15%), nausea (15%), diarrhea (15%), and thrombocytopenia (10%).
Conclusion: Trastuzumab combined with 5-weekly S-1 and CDDP therapy was effective treatment for patients with metastatic or unresectable HER-2 positive gastric cancers. The toxicities in the patients were manageable level in the patients. 1-year OS rate in our study was nearly equal to that in HERBIS-1 study.
Disclosure of Interest: None declared

OP220 THE ASSOCIATED FACTORS FOR THE DEVELOPMENT OF METACHRONOUS GASTRIC CANCERS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCERS

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Introduction: *Helicobacter pylori (H. pylori)* is known as a major carcinogen for gastric cancer. In addition, there is evidence of an increased risk of gastric cancer related to gender, tobacco smoking, obesity, and so on. However, regarding the development of secondary gastric cancers after endoscopic resection for early gastric cancers, there are still many debates even about whether *H. pylori* is an independent risk factor. Furthermore, the other risk factors for the development of secondary gastric cancers have remained unclear.
Aims & Methods: The aim of this study was to clarify the associated factors for the development of metachronous gastric cancer in patients who underwent endoscopic submucosal dissection (ESD) for the early gastric cancers. Secondary gastric cancers detected within 1 year after ESD for early gastric cancers were considered synchronous rather than metachronous in this study. The patients with early gastric cancers treated by ESD between June 2003 and November 2012 at our institution were enrolled. The exclusion criteria were as follows: patients with a history of gastrectomy, patients with additional gastrectomy after ESD for early gastric cancer, and patients with a follow-up period of less than 12 months. In addition to the investigation of the development of secondary gastric cancers, the associated factors for the development of metachronous gastric cancers was also calculated by Cox hazard regression analysis. The estimated factors were age (<60 or ≥ 60 years), gender, BMI (<25 or ≥ 25 kg/m^2), *H. pylori* eradication, and current tobacco smoking and drinking (on the day of diagnosis of first gastric cancer). We further investigated the detailed relationship between tobacco smoking and the development of metachronous gastric cancers by pack-years (PY), classified into never, PY <20, and PY ≥ 20.
Results: A total of 539 patients (mean age = 69.4 years) were analyzed with a mean follow-up of 53.6 months. There was no missing value about the estimated factors except for PY, which had 7 missing values (1.3%). The 5-year cumulative incidence of secondary gastric cancers was 13.0% with 18 cases within 1 year and 53 cases after 1 year from the initial ESD. The rates of *H. pylori* eradication, current smoking, and current drinking were 39.3%, 42.3%, and 27.5%, respectively. Multivariate analysis exhibited that age ≥ 60 years (4.04 [1.22-13.3]) and current smoking (2.11 [1.19-3.76]) were the independent risk factors for the development of metachronous gastric cancers. There was no significant association between eradication of *H. pylori* and the development of these cancers. Regarding the detail of tobacco smoking, multivariate analysis by adjusting age, gender, BMI, eradication of *H. pylori*, and current drinking showed that PY ≥ 20 (1.52 [1.03-2.23]) was a significant risk factor for the development of metachronous gastric cancers with a dose-response relation (P for trend = 0.042).
Conclusion: In addition to age ≥ 60 years, we firstly demonstrated by multivariate analysis that tobacco smoking was an independent risk factor for the development of metachronous gastric cancers after ESD for early gastric cancers, with a dose-response relation.
Disclosure of Interest: None declared

OP221 MODULATION OF BMP4 FUNCTION BY LLAMA-DERIVED NANOBODIES: A NOVEL APPROACH TO OVERCOME CHEMORESISTANCE IN COLORECTAL CANCERS

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Introduction: Colorectal cancers (CRCs) are the most frequently occurring malignancy in western countries. Advanced stage CRCs are highly aggressive cancers characterized by chemo-resistance and poor patient outcomes. One pathway that has been shown to be disregulated in the progression of CRC is the Bone Morphogenetic Protein (BMP) pathway. BMPs are a group of about 20 growth factors for which both tumor suppressor and tumor promoting functions have been described. Albeit increased expression of BMP4 has been observed in CRCs, the exact role of BMP4 and its downstream signaling pathways with respect to cancer behavior still remains unknown.
Aims & Methods: Understanding the diverse roles of BMP4 has been hampered by the lack of highly specific BMP inhibitors. Although significant progress has been made in generating highly specific and less toxic BMP inhibitors, natural antagonists as well as chemical inhibitors are still non selective. These inhibitors present elevated off-target effects, most likely due to inactivation of other BMPs with beneficial anti-tumour effects, such as BMP6 and BMP7. Indeed, indiscriminate BMP inhibition has been shown to activate dormant metastatic breast tumour cells or increase colonic tumour burden *in vivo*. To resolve and inhibit the individual action of BMP4 in colorectal cancer, we aimed at generating potent and specific BMP4 inhibitors.
Results: We recently generated a llama-derived nanobody which selectively binds to BMP4. Its binding affinities are greater than those published for Noggin, a natural BMP antagonist, and for conventional anti-BMP4 antibodies. Nanobodies are promising clinical tools with a growing number of benefits compared to conventional antibodies such as low immunogenicity, cost-effective production, high stability, consistent activity and ease of manipulation. Here, we show how this BMP4-specific nanobody represents a promising therapeutic strategy for chemosensitization of colorectal cancer cells. First, a set of different CRC cell lines was tested for the expression and secretion of BMP4. We found that certain CRC cell lines specifically secrete BMP4, but not other BMPs, and these BMP4high profile is associated with enhanced chemoresistance. Next, an aggressive gene signature profile was identified by analyzing expression profiles of patient-derived BMP4high cancers in relation to malignant features and aggressive behavior of the tumors. Finally, selective inhibition of BMP4 using our anti-BMP4 nanobody rendered the aggressive CRC cells more sensitive to chemotherapy, supporting the therapeutic potential of anti-BMP4 nanobody in aggressive CRC.
Conclusion: In sum, we have developed a highly potent BMP4-specific antibody that represents a promising therapeutic strategy for sensitizing colorectal cancer cells to chemotherapy. Its novel structural format makes it remarkably suited to overcome the limitations that affect the clinical and research applications of current BMP inhibitors.
Disclosure of Interest: None declared

OP223 RISK FACTORS FOR PROGRESSION OF ENDOSCOPICALLY DIAGNOSED INTRAMUCOSAL GASTRIC CANCER

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Introduction: Endoscopic submucosal dissection (ESD) is now a widely accepted procedure as a curative treatment of early, especially intramucosal,

Abstract number: OP223

		Univariate analysis	Multivariate analysis	
	N	p-value	Hazard ratio	p-value
Age (per 10-yr increment)	181	0.677	1.71 (1.11-2.65)	0.015
Location (L)	42	0.783		
Location (M)	89		1.46 (0.57-3.74)	0.43
Location (U)	50		1.42 (0.49-4.07)	0.52
Morphology				
(Flat or Deplessed/Protruded or Flat elevated)	132/49	0.144	0.90 (0.31-2.64)	0.85
Mucosal background (Atrophy/Fundic glands)	164/17	0.112	3.96 (1.32-11.87)	0.014
Pathological diagnosis (Yes/No)	41/140	0.664	1.34 (0.58-3.10)	0.5
Sex (M/F)	148/33	0.334	1.78 (0.58-5.45)	0.31
Tumor size (per 10mm increment)	178	0.0412	1.32 (0.95-1.83)	0.1

gastric cancer. However, indication of ESD for patients with high age and/or severe comorbidity is still controversial.
Aims & Methods: In this study, we retrospectively investigated natural history and risk factors for progression of intramucosal gastric cancer (IGC) to help better understanding of indication of ESD in such patients. Records of 1462 lesions which were endoscopically and pathologically diagnosed as gastric cancer in our hospital between January 2011 and December 2014 were screened. Among them, previous records of esophagogastroduodenoscopy (EGD), which were performed after January 2006 and more than 6 month before the index EGD with conceivable pictures of the index gastric cancer, were available in 184 lesions. Among them, three lesions were diagnosed as gastric cancers with submucosal invasion based on their endoscopic findings at the time of previous EGD, and the remaining 181 lesions were endoscopically diagnosed as IGC and were in included in this study; a mean of intervals to the index EGD was 39 months as long as 22.6 months. One hundred and forty lesions were diagnosed at the time of this review of the records, and biopsies had been taken from the other 41 lesion with pathological diagnosis of adenoma (31 lesions) or cancer (10 lesions). Statistical differences were calculated using the Mann-Whitney U-test and the Fisher's exact test. Risk factors for progression of IGC to submucosal or advanced cancer were analyzed by Cox proportional hazards regression model.
Results: In the 181 lesions, 145 lesions were still IGC at the index EGD, and 36 lesions progressed to submucosal or advanced cancer. With regard to pathological diagnosis at time of index EGD, the proportion of well differentiated adenocarcinoma was significantly higher in the lesions which remained in IGC (118/145, 81.3%) than those which progressed to submucosal or advanced cancer (4/36, 11.1%)($p < 0.0001$, Fisher's exact test). Elder age (hazard ratio, 1.7; 95% confidence interval, 1.1-2.7, $p = 0.015$) and cancer at the fundic gland area (4.0; 1.3-11.9, $p = 0.014$) were identified as significant factors for the progression of IGC to invasive cancer by analysis with the Cox's proportional-hazards model.
Conclusion: IGC at the fundic gland area in elderly patients might be invasive and have indication for ESD.
Disclosure of Interest: None declared

OP224 THE EFFICACY OF THE SERUM PEPSINOGEN FOR PREDICTING THE METACHRONOUS GASTRIC NEOPLASM AFTER ENDOSCOPIC RESECTION FOR EARLY GASTRIC CANCER

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Introduction: The aim of this study is to evaluate the efficacy of the serum pepsinogen (PG) concentration level for predicting development of metachronous gastric dysplasia and cancer after endoscopic resection (ER) for early gastric cancer (EGC) and to evaluate other risk factors for the incidence of metachronous gastric dysplasia and cancer.
Aims & Methods: We enrolled 429 patients who were tested serum PG level at the time of ER for EGC, from January 2008 to December 2013 in Kyungpook National University medical center, Daegu, Korea, retrospectively. The baseline characteristics of the patients such as final *H. pylori* status, serum pepsinogen, pathologic findings of resected specimen after ER were analyzed for the development of the metachronous gastric neoplasm.
Results: The patients were divided on the basis of the 3 of serum concentration PG I/II ratio level. Overall, 165 patients (38.5%) were belonged into the serum PG I/II levels of ≤ 3 group and 264 patients (61.5%) were belonged into the > 3 group. During the follow-up period, 52 metachronous gastric lesions were found (10 gastric dysplasias and 42 gastric cancers). Metachronous gastric dysplasia or cancer were significantly developed in serum PG I/II ≤ 3 group ($p = 0.047$) and persistent *H. pylori* infection group ($p = 0.041$) on univariate analysis (Table 1). On multivariate analysis, persistent *H. pylori* infection (OR = 2.094, 95% CI = 1.034-4.239, $p = 0.040$), the serum PG I/II ratio ≤ 3 at the time of ER (OR = 0.027, 95%CI = 1.076-3.491, $p = 0.027$) were correlated with an increased incidence of subsequent gastric dysplasia or cancer after endoscopic resection of EGC.
Conclusion: Serum PG I/II ratio at the ER resection is a good indicator for predicting development metachronous gastric cancer after ESD for EGC and persistent *H. pylori* infection could increase the risk of metachronous gastric neoplasm after ER for EGC.
Disclosure of Interest: None declared

OP225 CLINICOPATHOLOGICAL CHANGES OF EARLY GASTRIC CANCER OVER TIME FROM SUCCESSFUL ERADICATION OF HELICOBACTER PYLORI

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Introduction: *Helicobacter pylori* (*H.pylori*) is one of important carcinogens in gastric cancer. There have been many reports that the eradication of *H.pylori* could prevent gastric cancer. However, we sometimes detect early gastric cancer (EGC) after successful eradication.
Aims & Methods: The aim of this study is to clarify the detected interval and clinico-pathological features of EGCs after successful eradication by retrospective assessment. A total of 748 EGCs were treated by endoscopic resection at University Hospital, Kyoto Prefectural University of Medicine from January 2009 to October 2014. Among them, 246 EGCs were certainly occurred in the mucosa of *H.pylori*-associated chronic gastritis (*H.pylori*-positive) and 69 EGCs were detected after successful eradication (*H.pylori*-eradicated). These 315 EGCs were enrolled in this study. Firstly, we investigated the detected interval of *H.pylori*-eradicated EGCs from successful eradication. Then, we classified *H.pylori*-eradicated EGCs into two groups: "early detection (ED) group" and "late detection (LD) group" according to their detected interval from eradication (more about this later). We compared clinico-pathological features among ED group, LD group and *H.pylori*-positive EGCs ("HP group"). Clinico-pathological features including age, gender, tumor size, location, macroscopic type, histological type were reviewed according to Japanese Classification of Gastric Carcinoma. The background gastric mucosal atrophy was assessed endoscopically according to the Kimura-Takemoto classification.
Results: The median interval from eradication to detection of EGCs was 36 months (range, 0.2-132 months). Among them, 47 EGCs (68.1%) were detected within 4 years after eradication. The number of EGCs detected within 4 years was substantially greater than those of over 4 years. Interestingly, we still detected EGCs for more than 10 years after eradication. Based on the result described above, we defined ED group as EGCs detected within 4 years after eradication and LD group as EGCs detected over 4 years. In ED group, the mean size of EGCs was significantly smaller than that found in HP group(10mm vs 12mm, P = 0.02), and the macroscopic morphology tended to be flat or depressed type(78.7% vs 65.8%, P = 0.12). In LD group, the mean age was significantly younger than HP group(65.6 y.o vs 67.9 y.o, P = 0.048). EGCs in LD group were mainly found on open type (severe) atrophic mucosa. In contrast, EGCs on close type (mild) atrophy were detected more than HP group(27.3% vs 6.9%, P = 0.006). In addition, all the histological type in LD group was differentiated predominant type.
Conclusion: In this study, the most prominent clinico-pathological feature of EGCs between ED group with HP group was the macroscopic morphological changes. After a long period having passed since eradication (like LD group),

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	Non-metachlonous lesion group (N = 377)	Metachlonous lesion group (N = 52)	Univariate P-value
Sex			0.747
Male : Female	262 (69.5%) : 115 (30.5%)	38 (73.1%) : 14 (26.9%)	
Mean age (years)	61.0 (23-82)	64.0 (45-84)	0.581
Location			0.333
Proximal	20 (9.5%)	2 (7.4%)	
Middle	52 (24.6%)	4 (7.1%)	
Distal	139 (65.9%)	21 (77.8%)	
Lesion size(mm)	15.8 (2-80)	17.3 (5-40)	0.364
Histologic type			0.832
Differentiated	360 (95.6%)	50 (96.2%)	
Undifferentiated	17 (4.4%)	2 (3.8%)	
SM invasion	22 (5.8%)	2 (3.8%)	0.451
Persistent H. pylori infection	52 (13.8%))	13 (25.0%)	0.041
Pepsinogen I/II ratio < 3	138 (36.6%)	27 (51.9%)	0.047
The change of Pepsinogen I/II ratio			0.102
Decreased	132 (35.0%)	19 (36.5%)	
Increased or not changed	245 (65.0%)	33 (63.5%)	
Follow up period (Median, Months)	46 (32-84)	38 (24-60)	0.259

different features seem to appear in detected EGCs. The endoscopist should pay great attention to these changes that occur over time after eradication therapy, and it is necessary for *H.pylori*-eradicated patient to conduct follow-up examination for a long time.
Disclosure of Interest: None declared

OP226 T1B OESOPHAGEAL ADENOCARCINOMA: RETROSPECTIVE COHORT STUDY ON PATIENT MANAGEMENT AND RISK OF METASTATIC DISEASE

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Introduction: Oesophagectomy for submucosal (T1b) oesophageal adenocarcinoma (OAC) is generally advised in order to optimize patient outcome given the risk of concurrent (occult) LN metastasis (LNM). However, not seldom, severe comorbidity precludes these patients from surgery.
Aims & Methods: Our aim was to assess the proportion patients referred for surgery, and to evaluate the incidence of metastatic disease in T1b OAC.
Methods: Between 2001 and 2011, all patients undergoing diagnostic endoscopic resection (ER) for OAC in two centres in the Netherlands were reviewed. Only patients with histopathologically proven submucosal tumour invasion were included. Based on the ER specimen, submucosal OAC's were divided into tumours which were removed radically (R0; tumour-negative vertical resection margin (VRM)) and irradically (R1; tumour-positive VRM). Subsequently, in the R0-group, OACs were classified as either low-risk (LR; submucosal invasion $<$ 500nm, G1-G2, no lymphovascular invasion) or high-risk (HR; deep submucosal invasion $>$ 500nm, and/or G3-G4, and/or lymphovascular invasion). Data on patient management (oesophagectomy versus conservative management) and outcome were assessed. Metastatic disease was defined as either LNM in surgical resection specimen, or evidence of malignant disease during follow-up (FU).
Results: 69 patients (55 male, median age 70 years) with a submucosal OAC were included, of which 23 patients underwent an endoscopic R1-resection, and 46 a R0-resection. Of the R0-resections, 14 were classified as LR, and 32 as HR. Oesophagectomy was performed in 7% of the R0-LR patients, in 38% of the R0-HR patients, and in 57% of the R1-group. None of the 14 R0-LR patients developed metastatic disease after a median FU of 60 months. In the R0-HR group, evidence of metastatic disease was found in 16% of patients (2/12 oesophagectomy patients, 3/20 non-surgical patients). In the R1 group, metastatic disease was diagnosed in 30% of patients (4/13 oesophagectomy patients, 3/10 non-surgical patients). Despite oesophagectomy, 2 surgical patients developed distant metastasis. During FU, 19 (44%) of the 43 non-surgical patients died: 5 due to disease progression (median survival 18 months), and 14 due to unrelated causes (median survival 32 months).
Conclusion: In superficial submucosal OAC (G1-G2, no LVI, radical resection), the risk of metastatic disease is very low: endoscopic treatment should thus be preferred. In deep submucosal OAC (and/or G3, and/or LVI, and/or R1-resection), the rate of metastatic disease is lower than reported in earlier surgical series. Moreover, oesophagectomy does not always cure disease. Given the reasonable disease-free survival and high background mortality, conservative management of these patients seems to be a valid alternative for surgery in selected cases.
Disclosure of Interest: D. Schölvinck: None declared, H. Künzli: None declared, S. Meijer: None declared, K. Seldenrijk: None declared, J. Bergman Financial support for research: Olympus Endoscopy, Cook Medical, Boston Scientific, Gi Solutions Covidien, Erbe, Ninepoint Medical, Consultancy: Gi Solutions Covidien, Boston Scientific, Cook Medical, B. Weusten Financial support for research: Cook Medical, Boston Scientific, Gi Solutions Covidien, C2 Therpeutics, Consultancy: C2 Therapeutics, Boston Scientific

OP227 LINE1-PCR: A NEW, CLINICALLY APPLICABLE SEQUENCING TOOL FOR THE DETECTION OF GENOMIC INSTABILITY IN GASTROINTESTINAL MALIGNANCY

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Introduction: Several gastrointestinal (GI) cancers involve the development of genomic instability during their progression. One manifestation of this is copy number aberrations (CNAs) such as amplifications and deletions- also a potential biomarker of progression from preneoplastia. Although technologies exist to recognize CNAs they may not give sub-chromosomal resolution, are too expensive to implement clinically or require technical expertise and therefore are still not automatable. Repeat genomic sequences such as LINE1 are ubiquitous. We hypothesized that these could be used to give an accurate measure of genomic instability by PCR using a single primer pair. The inherent low level of diversity in the repeats would allow us to align amplicons uniquely to the reference genome. From this we could derive sub-chromosomal copy number changes and demonstrate genomic instability.
Aims & Methods: 1) To use LINE1-PCR as a reliable, fast and simple test using a single primer pair to determine copy number changes in gastrointestinal cancer. 2) To compare the resolution of LINE1 PCR with whole genome sequencing (WGS) for the detection of clinically relevant copy number changes. A consensus sequence covering a number of LINE1 subfamilies was used to perform a two round barcoding PCR reaction optimized for next generation sequencing. To optimize the analysis of the number of raw sequences obtained 15 germline blood samples for which results were available for whole genome sequencing (WGS) were chosen. Criteria for determining the optimal number of reads with minimal variation were determined. 36 oesophageal adenocarcinoma tumour samples which had already undergone WGS then underwent LINE1 PCR and were quantitatively compared to WGS for CNA detection. An additional 51 non dysplastic Barrett's samples were also sequenced along with and 32 matched blood samples as controls. All sequencing was performed on a MiSeq (150 bp single end read) (Illumina, USA) sequencer.
Results: Comparison of CNAs between WGS and LINE1-PCR demonstrated an average detection rate of 93% (range 100-90%) for copy number changes over 0.5Mb. A score of genomic instability derived from a count of the number of $>$0.5Mb CNAs was able to distinguish tumour samples from diploid and non dysplastic samples (mean CNAs of control and tumour samples: 4.25 (range: $0-8.0$), and tumour samples 64.5 (range: $4-162$) respectively; Student's t-test p value 0.0015). Tumour samples with low CNAs (n = 4), detected by LINE1-PCR, were also confirmed to be low CNA samples as determined by WGS. The preparation for all samples from tissue collection to MiSeq submission was 3.5 hours regardless of the sample number. The current cost per sample for the entire workflow is £12. The minimum total DNA input is 2ng for FFPE and 0.5ng for frozen tissue.
Conclusion: LINE1-PCR is a fast and simple method for the determination of genomic instability. Its strength lies in its ability to localise CNAs at a comparable resolution to WGS as well as give an overall index of genomic instability with a markedly cheaper and faster workflow making it ideal for the clinic. We envisage that this new technique will be of use in the diagnosis of other malignant and premalignant diseases both within and outside of the GI tract.
Disclosure of Interest: None declared

OP228 SURGERY PLUS POSTOPERATIVE CHEMOTHERAPY AND/OR RADIOTHERAPY FOR T4 ESOPHAGEAL CANCER: TREATMENT OUTCOMES AND PROGNOSTIC FACTORS

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Introduction: Esophagectomy is the mainstay of treatment for patients with T1-T3 esophageal cancer. However, some patients are intraoperatively diagnosed as T4 esophageal cancer. Here we discuss the effectiveness of esophagectomy in these patients.
Aims & Methods: The aim of this study is to clarify the usefulness of esophagectomy in patients who were diagnosed as T4 esophageal cancer intraoperatively. Fifty-four patients (17%) were diagnosed as T4 disease intraoperatively among the 324 patients of thoracic esophageal cancer who underwent esophagectomy at our institution, between 2001 and 2012.
Results: The invasive organ was the mediastinal pleura (n = 23), the diaphragm (n = 11), the major airway (n = 12), the lung (n = 8), the pericardium (n = 7), the aorta (n = 6), and others (n = 8). Eighteen patients had invasive organs in two and more. Among these 54 patients, 16 (30%) received R0 resection, 20 (37%) received R1 resection, and the other 18 (33%) received R2 resection. As postoperative treatment, 27 patients received chemoradiotherapy, 13 received chemotherapy, and 5 received radiotherapy, while the other 9 received surgery alone. The overall median survival was 17months, and the overall 5-year survival was 26%. By univariate analysis, an improved survival was associated with tumor location (upper thoracic), residual tumor (R0/R1), postoperative treatment (present), lymphovascular invasion (absent), and the number of lymph nodes metastasis ($\leqq$ 2). Age, gender, site of other organ with invasion, number of other organs with invasion, histology, and tumor differentiation each did not affect survival. By multivariate analysis, the residual tumor (R0/R1 vs. R2: hazard ratio 0.230; 95% confidence interval 0.107–0.494; P = 0.0002), postoperative treatment (present vs. absent: hazard ratio 0.095; 95% confidence interval 0.034–0.267; $P < 0.0001$) and the number of lymph nodes metastasis ($\leqq$2 vs. 3 $\leqq$: hazard ratio 0.251; 95% confidence interval 0.112–0.538; P = 0.0003) were each an independent prognostic factor. The 5-year survival rate of those patients achieving R0/R1 was 32%, compared with 17% for R2 (P = 0.0243). The 5-year survival rate of those patients who received postoperative treatment was 32%, compared with 0% of those who received surgery alone (P = 0.0007). Of the 9 patients who received surgery alone, none survived more than two years.
Conclusion: Esophagectomy might be effective in patients achieving R0/R1 surgery, even if it is diagnosed as T4 esophageal cancer during the surgery. Furthermore, postoperative treatment may offer improvement in the prognosis for such patients with T4 esophageal cancer.
Disclosure of Interest: None declared

OP229 LONG NONCODING RNA COLON CANCER-ASSOCIATED TRANSCRIPT 2 PROMOTES TUMOR METASTASIS AND REGULATES EPITHELIAL-MESENCHYMAL TRANSITION IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Esophageal squamous cell carcinoma (ESCC) is a common cause of cancer death worldwide[1]. Long noncoding RNAs (lncRNAs) have been reported to be of crucial importance in the progresses of many diseases, and lncRNA colon cancer-associated transcript 2 (CCAT2) which was firstly found overexpressed in colorectal cancer was reported to be up-regulated in ESCC too[2, 3]. Epithelial-mesenchymal transition (EMT) is a process by which epithelial cells switch from the epithelial phenotype to the mesenchymal phenotype, accompanied with the ectopic expressions of EMT-related genes[4]. EMT is a pivotal event for most cancer cells to acquire metastasis ability, as well as for ESCC cells[5]. However, previous studies have not shown any connections between lncRNAs and EMT in ESCC.

Aims & Methods: In the present study, we mainly focused on the functional changes caused by knockdown of CCAT2 and the EMT-related genes expressions in ESCC cells. Expression of CCAT2 was analyzed in 50 ESCC tissues and 5 ESCC cell lines by quantitative reverse-transcription polymerase chain reaction (qRT-PCR). Over-expression and RNA interference (RNAi) approaches were used to study the biological functions of CCAT2 in ESCC cells. Cell migration and invasion were evaluated by transwell assays. Tail vein injection of cells was used to investigate metastasis in nude mice. Protein levels of EMT related genes were determined by western blot analysis and immunohistochemistry. Differences between groups were tested for significance using Student'st-test (two-tailed).

Results: CCAT2 expression was significantly up-regulated in ESCC tissues ($p < 0.001$) and cell lines ($p < 0.01$) compared with corresponding normal counterparts. What's more, highly expressed CCAT2 was associated with larger tumor size and advanced pathologic stage. Further studies found that the knockdown of CCAT2 markedly decreased the migration and invasion of ESCC cells *in vitro* and *in vivo*. Moreover, down-regulation of endogenous CCAT2 enhanced the expression of E-cadherin and decreased the expressions of N-cadherin and vimentin in ESCC cells.

Conclusion: Our study presents the first evidences that CCAT2 contributes a lot to the metastasis of ESCC by regulating the expressions of EMT related genes, which may lead to the development of a novel diagnostic marker and therapeutic strategy for ESCC.

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Disclosure of Interest: None declared

OP230 SEVERE ATROPHIC GASTRITIS IS A SIGNIFICANT RISK FACTOR OF METACHRONOUS MULTIPLE GASTRIC CANCER: A MULTICENTRE RETROSPECTIVE COHORT STUDY BY THE OSAKA GUT FORUM

M. Kato[1], T. Nishida[2], K. Yamamoto[3], S. Kitamura[4], T. Yamada[5], S. Egawa[6], M. Komori[7], N. Kawai[8], A. Nishihara[9], F. Nakanishi[10], M. Nakahara[11], H. Ogiyama[12], A. Mukai[13], Y. Hayashi[14], M. Tsujii[7,14], T. Takehara[14], on behalf of Osaka Gut Forum
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Introduction: Endoscopic submucosal dissection (ESD) has been a standard therapy for early gastric cancer (EGC) at negligible risk of lymph node metastasis in Japan, due to its secure local control with maintaining Quality Of Life by preservation of stomach. On the other hand, patients are at high-risk for developing metachronous multiple gastric cancers (MMGC) arising from remnant gastric mucosa. We have reported that the cumulative incidence rate of MMGC was constant and eradication therapy for *Helicobacter pylori* (HP) did not reduce the incidence of MMGC at least for three years after ESD (M. Kato et al. Gut 2013).

Aims & Methods: The aim of this study was to elucidate the detail of development of MMGC by extending the observation period and analysis of association between various factors and MMGC incidence. This is a retrospective cohort study from 12 hospitals. From April 1999 to December 2010, total 1109 consecutive patients with EGC who underwent ESD for the first time and achieved curative resection with observation period 12 months or more were included in this study. Cumulative incidence of MMGC after ESD was analyzed using Kaplan–Meier methods. The association between background factors at initial ESD (age, sex, degree of atrophic gastritis, presence or absence of synchronous multiple gastric cancer, classification of Japanese guideline for gastric cancer of initially resected lesion, and presence or absence of eradication of HP and development of MMGC) was analyzed using Cox's proportional hazards model. The degree of atrophic gastritis of background mucosa was evaluated by review of endoscopic images at initial ESD based on Kimura-Takemoto classification.

Results: Median observational period was 52.3 (IQR 37.3 – 72.6) months. The cumulative incidence increased linearly and did not reach plateau at least for five years after ESD. Three, five, and seven-year cumulative incidence rate of MMGC were 5.2%, 9.8%, and 13.9%, respectively. In univariate analysis, atrophic gastritis revealed to have a statistic significance ($p = 0.0148$) and male gender revealed to have statistic tendency ($p = 0.059$) concerning MMGC development. In multivariate analysis, only degree of atrophic gastritis revealed to be an independent risk factor (Odds ratio 1.7 [95%CI 1.1–2.8], $p = 0.0138$). In our cohort, HP eradication did not reveal to have significant association with MMGC development.

Conclusion: MMGC incidence increases constantly for at least 5 years after curative ESD. The degree of atrophic gastritis is an independent risk factor for MMGC development. Careful endoscopic surveillance is needed especially for patients with severe atrophic gastritis.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 11:00–12:30

MANAGEMENT OF SEVERE AND REFRACTORY ULCERATIVE COLITIS – ROOM B2

OP231 THE AVAILABILITY OF CALCINEURIN INHIBITORS AND INFLIXIMAB IN ACUTE SEVERE COLITIS HAVE REDUCED COLECTOMY RATES IN 283 CHILDREN ADMITTED DURING 1990-2012

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Introduction: One third of children admitted with acute severe colitis (ASC) fail intravenous corticosteroids (IVCS) and require salvage therapy. While colectomy was originally the only available salvage treatment, cyclosporine and then tacrolimus (Cys/Tac) have been used since 1996, followed by infliximab (IFX) in 2004, as second line medical treatment prior to colectomy. However, no data to date have shown whether these interventions actually managed to reduce colectomy rates in children, during the admission or thereafter.

Aims & Methods: We aimed to explore trends in colectomy rate in pediatric ASC before and after the introduction of Cys/Tac and IFX, using the largest pediatric cohort of ASC to date. 283 children treated with IVCS for ASC during 1990-2012 were included (from the prospective ($n = 128$) and retrospective ($n = 99$) OSCI studies and another 55 retrospectively reviewed patients from Jerusalem and Liverpool). Patients were followed for 1 year (46% males, age 12.1 ± 3.9 years, disease duration 2 (IQR 0-14) months, baseline PUCAI 69 ± 13 points). Data accrual was similar in the 3 cohorts, collected using the same standardized case report forms at admission, 3 days and 5 days thereafter, at discharge and at 1 year. Colectomy rates were compared between 3 periods: 1990-1996 (era1: pre medications; $n = 68$), 1997-2004 (era2: Cys/Tac and colectomy; $n = 45$), 2005-2012 (era3: IFX, Cys/Tac and colectomy; $n = 170$). No child in our cohort has been treated with IFX prior to 2005.

Results: Total 1-year colectomy rates were 40/68 (59%) during era1, 17/45 (38%) during era2, and 31/170 (18%) during era3 ($P < 0.001$). Since IVCS failure rates were different between the eras, we then focused on those failing IVCS to standardize the analysis. Of the 283 children, 89 (31%) failed IVCS and required second line therapy during admission (44 primary colectomy, 9 Cys/Tac and 22 IFX; total colectomy 56). The 3 era groups were similar in 12 pre-treatment basic variables at admission (e.g. PUCAI, CRP, albumin, disease duration etc) except for age and ESR. The rate of colectomy in those requiring salvage therapy during the admission was significantly reduced from 100% (51/51) in era 1, to 62% (8/13) in era2 and 33% (14/42) in era3 ($p < 0.001$). At 1 year after discharge, 123 children (43%), were treated with second line therapy (44 primary colectomy, 12 Cys/Tac and 53 IFX; total colectomy 88). The rate of colectomy was again significantly reduced from 100% (40/40) of children requiring salvage therapy in era1 to 77% (17/22) in era2 and 51% (31/61) in era3 ($p < 0.001$).

Conclusion: We show for the first time that the introduction of Cys/Tac and then infliximab sharply reduced the need for colectomy during admission and 1-year thereafter in pediatric ASC.

Disclosure of Interest: S. Choshen: None declared, A. Griffiths Financial support for research: Abbvie, Janssen, Lecture fee(s): Abbvie, Janssen, Consultancy: Abbvie, Janssen, H. Finnamore: None declared, M. Auth: None declared, E. Shteyer: None declared, D. Mack Financial support for research: Abbvie, Consultancy: Abbvie, Janssen, J. Hyams Consultancy: Janssen Abbvie Celgene Avaxia Takeda, D. Turner Financial support for research: Janssen, Abbvie, Ferring, Lecture fee(s): Janssen, Abbvie, MSD, Consultancy: Janssen, Abbvie,

OP232 TACROLIMUS FOR INDUCTION AND MAINTENANCE THERAPY IN PATIENTS WITH REFRACTORY ULCERATIVE COLITIS

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Introduction: In recent years, the calcineurin inhibitor, tacrolimus has been introduced to induce remission in patients with active ulcerative colitis (UC), which is refractory to corticosteroids. However, hitherto the efficacy of tacrolimus as maintenance therapy has not been investigated.

Aims & Methods: The major objective of this investigation was to see the clinical potential of tacrolimus as remission maintenance therapy following remission induction. We started with 40 patients in clinical remission with UC clinical activity index (CAI) $\leq$4 according to Lichtiger, all patients had received tacrolimus induction therapy. These 40 patients were divided into 3 groups for maintenance therapy with azathioprine (n = 13), tacrolimus (n = 13) or tacrolimus + azathioprine (n = 14), and were followed for at least one year. CAI, Ulcerative Colitis Endoscopic Index of Severity (UCEIS) and the duration of tacrolimus therapy were applied to assess treatment outcomes. Relapse was defined as patient requiring remission induction therapy by increasing the blood trough tacrolimus level $\geq$ 10 ng/ml, intravenous corticosteroid or a biologic. All patients were diligently observed for adverse side effects.

Results: The average duration of tacrolimus therapy was 402 $\pm$ 167 days in the tacrolimus group, 87 $\pm$ 12 days in the azathioprine group, and 240 $\pm$ 166 days in the tacrolimus + azathioprine group. The recurrence rates after induction of remission in the tacrolimus, azathioprine, and tacrolimus + azathioprine groups were respectively 28%, 32%, and 33% at 300 days, while the respective rates were 24%, 49%, and 55% at 600 days, showing no statistically significant differences. Further, nephropathy occurred in 11 patients, and renal failure in 5 patients, both were thought to be side effects of tacrolimus induction therapy. In patients who experienced renal failure, the dose of tacrolimus was reduced or discontinued. Additionally, headache was experienced by one patient.

Conclusion: In the present study (albeit in small subgroups of patients), tacrolimus alone appeared to be effective for remission induction as well as maintenance therapy in UC patients. Patients who are intolerant to azathioprine should benefit from tacrolimus maintenance therapy. However, the therapeutic efficacy of tacrolimus may be compromised by its renal toxicity, which needs to be regularly monitored in patients who are on long-term tacrolimus.

Disclosure of Interest: None declared

OP233 ACETARSOL SUPPOSITORIES ARE AN EFFECTIVE AND WELL TOLERATED TREATMENT FOR REFRACTORY PROCTITIS: A COHORT STUDY

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Introduction: Although conventional treatments are generally effective in the treatment of proctitis, a significant minority of patients do not respond – developing so-called "refractory proctitis". This is an incredibly debilitating and disabling condition. The use of acetarsol suppositories, which are derived from organic arsenic, was first described 1965 (Connell, 1965). The mechanism of action is unknown. Data concerning clinical efficacy and tolerability of acetarsol suppositories are limited to two small studies (Connell, 1965, Forbes, 1989).

Aims & Methods: A retrospective analysis was performed on patients with inflammatory bowel disease treated with acetarsol suppositories between 2008 and 2014 at Addenbrooke's Hospital, Cambridge, UK. Patients were identified through a hospital pharmacy database. All patients who were prescribed and received acetarsol suppositories during this period were included. Clinical response was defined as resolution of symptoms (frequency, bleeding and pain) back to baseline at the time of next clinic review. Serum arsenic levels were not routinely measured.

Results: 39 patients received acetarsol suppositories between March 2008 and July 2014 (29 UC, 9 Crohn's disease, 1 indeterminate colitis). Demographic and prior treatment details are shown in Table 1. The standard dose of acetarsol was 250mg twice daily per rectum for 4 weeks; 95% of patients received this regimen.

Clinical response was observed in 26 patients (66.7%). Of the 11 patients who had endoscopic assessment before and after treatment, 9 (82%) showed endoscopic improvement and 5 (45%) were in complete remission (p = 0.0004, median assessment at 8 months post treatment). The only clinical parameter that correlated with clinical response was the number of previously failed immunomodulators (p = 0.01, mean 1.35 in responders and 2.46 in non-responders).

One patient developed a macular skin rash one week after commencing acetarsol suppositories, which resolved within 4 weeks of drug cessation. Skin biopsy confirmed superficial perivascular dermatitis, consistent with a drug rash.

Table 1: Baseline characteristics of patients

	Total
Number of patients	39
Mean age, years ($\pm$ standard deviation)	39.3 ($\pm$ 14.8)
Sex	
Male	16 (41%)
Female	23 (59%)
Ulcerative colitis	29 (74%)
Proctitis	8 (21%)
Crohn's disease	9 (23%)
Proctitis	0
Mean duration of disease, years	6.9 ($\pm$ 5.0)
Mean follow-up, years	6.4 ($\pm$ 3.4)

Conclusion: Acetarsol was effective for 2 out of every 3 patients with refractory proctitis. This cohort had previously failed a broad range of topical and systemic treatments, including anti-TNFα therapy. The clinical efficacy was reflected in significant endoscopic improvement. Adverse effects of acetarsol were rare.

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Disclosure of Interest: None declared

OP234 INTRINSIC DEFECTS IN THE EPITHELIAL STEM CELL COMPARTMENT COULD CONTRIBUTE TO THE PERPETUATION OF ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is a chronic remitting and relapsing inflammatory bowel disease that affects the superficial mucosal barrier. Remission is characterized by clinical and endoscopic resolution of the disease; however, the transcriptional signature of remitting UC mucosa reveals long-lasting changes in the epithelial barrier[1].

Aims & Methods: The aim of our work was investigating whether primary defects are present in the epithelial stem cell (ESC) compartment of UC patients. To this end, we used a recently established human epithelial cell culture system[2]. Biopsy samples from the sigmoid colon of 11 non-IBD controls and 8 UC patients were collected. Isolated crypt units were in vitro cultured in matrigel, and ESCs were expanded as 3D spheroids called organoids. These were induced to differentiate into the main intestinal epithelial lineages, and total RNA from stem and differentiated organoids was extracted for transcriptional analysis.

Results: Our results show that stem organoid cultures derived from control and UC biopsy samples follow similar differentiation programs with comparable regulation of stem (i.e., Lgr5, AXIN2), proliferation (i.e., Myc, Ki67), and epithelial markers (i.e., MUC2, ANPEP). Microarray analysis, however, revealed a small panel of genes differentially expressed by organoid samples generated from UC patients compared to non-IBD individuals. UC-derived organoids showed a marked up-regulation of genes that are characteristic of the proximal gastrointestinal tract (e.g., lysozyme, an anti-microbial protein). Conversely, they displayed reduced transcription of genes commonly expressed by colonic epithelial cells (e.g., ZG16, a component of the mucus). Interestingly, several genes of this signature were found permanently altered in the intestinal mucosa of colitic patients in remission.

Conclusion: Overall, our findings demonstrate that sigmoid ESCs of colitic patients show an expression signature that may reflect the presence of intrinsic changes in UC epithelium. Notably, the acquisition of a ''proximal'' phenotype, including alterations in the nature of epithelial antimicrobial response and mucus composition, could contribute to the perpetuation of the disease over time.

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Disclosure of Interest: None declared

OP235 HISTOLOGICAL AND ENDOSCOPIC ASSESSMENT IN ULCERATIVE COLITIS: RESULTS FROM THE PURSUIT TRIAL

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Introduction: UC disease activity & severity is based on combined endoscopic & clinical assessments. Histologic assessment may provide more accurate measurement of disease activity than endoscopic assessment;correlation between endoscopy & histology is not understood.

Aims & Methods: To assess which features of the Geboes histological score are associated with endoscopic healing. PURSUIT-SC was a Phase 2/3 study conducted to evaluate induction therapy with SC GLM. Pts with Mayo scores of 6-12 inclusive, including endoscopic subscore >2 were randomized to placebo (PBO)/PBO, GLM 100mg/50mg (before Ph3 dose selection only), GLM 200mg/100mg, or GLM 400mg/200mg at wks0 & 2. Colonic biopsies were collected from a subgroup of pts, who consented to participate in the biopsy substudy. At wk0&wk6, pts had 2 adjacent biopsy specimens both obtained within 15-20 cm of the anal verge.A single, blinded pathologist reviewed each biopsy & used the Geboes classification system to assess the following histological features:structural change only, chronic inflammatory infiltrate, lamina propria eosinophils, lamina propria neutrophils, neutrophils in the epithelium, crypt destruction, & erosions & ulcers. Endoscopy assessments were made using the local Mayo endoscopic sub-score(as determined by local site investigators);subscores of 0 or 1 were defined as endoscopic healing. Results were summarized at wks0&6.

Results: Among 89pts consenting to the substudy, 343 biopsies, including 166 paired biopsies from wk0&6 were collected. Among the 343 biopsies, the endoscopy score distribution for scores of 0, 1, 2, or 3 were 4%, 20%, 45% & 30%, respectively. Overall, pts with endoscopic scores of 0 & 1 had very similar histological features. Histological features associated with endoscopic healing included: absence of histological evidence of ulceration & erosion, no evidence of crypt destruction, & only minimal neutrophil infiltration of the epithelia (<5%). For subsequent analysis, these pts were considered to have ''histological healing'' (histological healing by this definition does not mean complete histological normalization). ''Histological healing'' rates at wk6 by Mayo endoscopy scores of 0, 1, 2&3 were 100% (14/14), 68.1% (47/69), 19.9% (31/56), & 16.3%(17/104), respectively. Pts with histological healing had lower degrees of structural changes, chronic inflammation compared to those who did not have histological healing. There was 88% concordance rate of histological healing between multiple biopsies done at the same treatment visit. This rate was higher than observed with individual components of the Geboes score. ''Histological healing'' was associated with lower rates of rectal bleeding & decreased stool frequency vs pts without histological healing.

Conclusion: Absence of histological evidence of ulceration & erosion, no evidence of crypt destruction & only minimal neutrophil infiltration of the epithelia (<5%) may constitute a definition of histological healing in UC trials. This definition is highly reproducible in adjacent biopsy specimens. Pts who meet this definition are more likely to have endoscopic healing accompanied by reduced rectal bleeding & stool frequency.

Disclosure of Interest: R. Strauss Conflict with: Employee Janssen R & D, LLC, B. Feagan Financial support for research: Janssen R & D, LLC, J.-F. Colombel Financial support for research: Janssen R & D, LLC, C. Marano Conflict with: Employee Janssen R & D, LLC, S. Xu Conflict with: Employee Janssen R & D, LLC, L. Peyrin-Biroulet Financial support for research: Janssen R & D, LLC, G. De Hertogh Financial support for research: Janssen R & D, LLC, W. Sandborn Financial support for research: Janssen R & D, LLC

OP236 MODIFIED 2-STAGE ILEAL POUCH ANAL ANASTOMOSIS RESULTS IN LOWER RATE OF ANASTOMOTIC LEAK COMPARED TO TRADITIONAL 2-STAGE SURGERY FOR ULCERATIVE COLITIS

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Introduction: Surgical treatment options for ulcerative colitis (UC) depend on the indication for surgery, patient factors, and previous medical therapy. There is a paucity of evidence comparing traditional 2-stage (total proctocolectomy with ileal pouch anal anastomosis (IPAA) and diverting ileostomy, followed by ileostomy closure) versus a modified 2-stage (subtotal colectomy with end ileostomy, followed by completion proctectomy + IPAA, without diverting ileostomy) restorative proctocolectomy. This study examines the clinical outcomes following traditional vs. modified 2-stage IPAA for patients with UC in a single institution. Anastomotic leak and pelvic abscess following pouch creation were the primary outcomes of interest.

Aims & Methods: A retrospective cohort study was performed for UC patients who underwent IPAA between 2002 and 2013 at our institution. Individuals who received either a traditional or modified 2-stage IPAA were identified from our IBD Surgical Database. Demographic data, clinical data, and outcomes (peri- and post-operative complications) were collected from in-patient and out-patient chart review. Pouch leaks and abscesses were documented by clinical exam and diagnostic imaging. Statistical analyses were performed using the Pearson Chi-square test for categorical variables. Multivariate logistic regression and the Wilcoxon rank sum test were used for continuous variables.

Results: 758 UC IPAA patients were reviewed. 460 patients underwent a 2-stage IPAA procedure. 223 (48.5%) patients underwent traditional 2-stage IPAA and 237 (51.5%) patients received the modified 2-stage procedure. There was a trend towards more pre-operative systemic corticosteroid use (49.1 vs. 37.2%, p 0.01) and less azathioprine/6MP use (9.3 vs. 18.6%, p 0.01) prior to the first stage of the modified 2-stage group compared to that of the traditional 2-stage group. However, there was no difference in anti-TNF exposure between the two groups (13.1 vs. 9.9%, modified vs. traditional 2-stage groups, respectively). The modified 2-stage group had higher UC disease severity at presentation (94.5% patients with moderate/severe UC vs. 79.5%, $p < 0.01$) and the indication for the first stage of surgery was more likely to be for fulminant disease/toxic megacolon/perforation (22.8 vs. 0.9%, $p < 0.01$). There was no difference in post-operative wound infection (12.7 vs. 13.1%) or pelvic abscess (14.8 vs. 15.3%) between the modified or traditional 2-stage groups. However, the modified 2-stage group had a lower rate of anastomotic leak following pouch creation (4.6 vs. 15.7%, $p < 0.01$) and decreased post-operative length of stay (LOS) following pouch surgery (median 8 vs. 10 days, $p < 0.01$) compared to the traditional 2-stage group.

Conclusion: Ulcerative colitis patients who received the modified 2-stage IPAA (subtotal colectomy prior to IPAA pouch formation) had a significantly lower rate of anastomotic leak and shorter LOS following pouch creation, compared to the traditional 2-stage procedure.

Disclosure of Interest: E. Zittan: None declared, N. Wong-Chong: None declared, G. Ma: None declared, R. Milgrom: None declared, R. McLeod: None declared, H. MacRae: None declared, G. Greenberg: None declared, G. Nguyen Consultancy: Advisory Board for Janssen and Abbvie, K. Croitoru Financial support for research: Educational grant from Janssen, Abbvie and Takeda, Consultancy: Advisory Board for Abbvie and Takeda, A. Steinhart Financial support for research: Abbvie, Amgen, Pfizer, Millenium, Lecture fee(s): Abbvie, Janssen, Takeda, Shire, Consultancy: Advisory Board for Abbvie, Actives, Janssen, Takeda, Pharmascience, Shire, M. Silverberg Financial support for research: Janssen, Abbvie, Takeda, Prometheus, Consultancy: Janssen, Abbvie, Takeda, Prometheus, Z. Cohen Conflict with: Educational Grant from Janssen

TUESDAY, OCTOBER 27, 2015 11:00–12:30
PROGRESS IN ENDOSCOPIC OESOPHAGEAL INTERVENTIONS – ROOM 7.1

OP237 EFFECTIVITY AND SAFETY OF CAP-ASSISTED FLEXIBLE ENDOSCOPIC ZENKER'S DIVERTICULOTOMY (C-ZD) – RESULTS OF A PROSPECTIVE SERIES FROM ONE WORKING GROUP

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Introduction: Flexible endoscopic Zenker's diverticulotomy under propofol sedation has been established during the last years as an alternative to open surgery and transoral diverticulotomy with a rigid endoscope. Several endoscopic techniques have been reported. Data on cap-assisted endoscopic Zenker's diverticulotomy (c-ZD) are still limited. The aim of the present study was to evaluate efficacy and safety of c-ZD in a prospective series from one working group.

Aims & Methods: Patients (pt) with symptomatic Zenker's diverticulum (ZD) who underwent c-ZD were collected in a prospective database. For c-ZD, a transparent tip was mounted on the tip of the endoscope, and myotomy was performed using a needle-knife. Dysphagia and regurgitation symptoms (0 = no discomfort, 10 = extreme discomfort) were recorded using a visual analoge scale (VAS) prior to treatment and at 3- and 12 month follow-up (FU). Adverse events (AE) of c-ZD as well as symptomatic recurrence were registered.

Results: During the periods 07/09–03/14 (Wiesbaden, n = 82) and 04/14-02/15 (Offenbach, n = 34), a total of 116 pt with symptomatic ZD were referred to our working group. c-ZD was performed in 112/116 pt (77 men; mean age 71 ± 1 yr). Mean depth of diverticulum was 25 ± 9mm. Initially, dysphagia score was 6.5 ± 2, and regurgitation score was 5.8 ± 3. c-ZD was technically successful in all pt. (100%). Major AE occured in 3 pt (1 perforation, 1 fever >24h, both conservative management; 1 bleeding, haemostasis via rigid esophagoscopy). Subcutaneus emphysema was detected in 12 pt (10.7%; managed conservatively). Both dysphagia and regurgitation scores showed highly significant improvement (p< o.oo5) during 3- and 12-mo FU. Recurrence of symptoms was observed in 8% (n = 6; repeat c-ZD n = 5; surgery n = 1).

Conclusion: According to the results of this large prospective study, c-ZD appears to be an effective and safe treatment approach in experienced hands. Symptoms improved significantly during 3- and 12-mo follow-up, with a recurrence rate of symptoms of only 8%.

Disclosure of Interest: None declared

OP238 PROGNOSTIC VARIABLES FOR THE CLINICAL SUCCESS OF FLEXIBLE ENDOSCOPIC SEPTOTOMY OF ZENKER'S DIVERTICULUM

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Introduction: Flexible endoscopy septotomy for Zenker's diverticulum (ZD) is an alternative to endostapling. However, long-term data are sparse and studies are heterogeneous.
Aims & Methods: Aim was to assess the clinical efficacy of flexible endoscopy diverticuloscope-assisted septotomy and identify potential prognostic variables. Data from a prospective database including all patients with ZD undergoing septotomy followed up for ≥24 months were analysed. Septotomy used the diverticuloscope-assisted technique. Dysphagia, regurgitation and respiratory symptoms were scored according to frequency from 0 to 3 on a solid food diet. Clinical success was defined as the absence of symptoms or the presence of a maximum of two symptoms with score 1. Prognostic variables of clinical success were searched among age, sex, pre-treatment total symptom score, pre- and post-treatment ZD size, septotomy length. Kaplan-Meier method and Cox proportional-hazards model were used to calculate the crude and adjusted Hazard Ratio (HR).
Results: Septotomy was achieved in 89 patients. Adverse events occurred in 3 cases: perforation in 2 (2%); post-procedural bleeding in 1 (1%). Clinical success at the ITT analysis was 69%, 64% and 46% at 6, 24 and 48 months, respectively.
Prognostic variables for clinical failure were analysed at 6, 24 and 48 months of follow-up according to the time intervals in which clinical failures and recurrences were observed. No differences were found at 6 and 24 months. Independent variables for clinical failure were: septotomy length ≤25 mm at 6 and 48 months (HR 6.34 and HR 2.20); ZD size ≥50 mm at 6 months (HR 11.08); residual ZD size ≥10 mm at 48 months (HR 2.03).
Conclusion: The clinical success of FE septotomy is related to the ZD size, a decisive factor for both the completeness of myotomy and the size of the residual diverticulum. ZD size is the leading variable of the therapeutic algorithm: the maximal clinical efficacy of FE septotomy is expected for ZD measuring 30-50 mm in which a complete myotomy without a residual pouch can be achieved in a single procedure.
Disclosure of Interest: None declared

OP239 BALLOON DILATION WITH EPIDERMAL CELL SHEET TRANSPLANTATION TO ESOPHAGEAL STRICTURES FOR AVOIDING RE-STRICTURES - A NEW ENDOSCOPIC PROCEDURE FOR REGENERATIVE MEDICINE -

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Introduction: Endoscopic submucosal dissection (ESD) is a standard treatment for superficial esophageal cancinoma. However, post-ESD stricture is a major complication for treatments of widespread superficial esophageal carcinoma. We previously reported transplanting epithelial cell sheets (ECSs) immediately after extensive ESD was the safe and potential therapy to prevent esophageal strictures (1). In addition, the transplanting device of ECSs have been developed for improving the efficiency in the endoscopic procedure of transplanting ECSs (2). On the other hand, there were no effective treatments once esophageal strictures developed. We hypothesized that it is important to prevent the adhesion of tears after endoscopic balloon dilation (EBD) for avoiding the re-strictures. The newly endoscopic device, which make it possible to put ECS in the tears after EBD.
Aims & Methods: This study aims to develop a new endoscopic device and technique for transplanting epidermal cell sheets (ECSs) after the dilatation to esophageal strictures. A prototype of the endoscopic device was validated. Six pigs underwent circumferential esophageal ESD under general anesthesia. At 2 weeks after ESD, all pigs developed severe esophageal strictures. EBD with transplanting autologous ECSs was performed to two pigs (Trans group). EBD was only performed to other two pigs (BD group). Two remaining pigs were only endoscopically observed (Ctrl group). At 3 weeks after ESD, all pigs were clinically and endoscopically evaluated and scarified for further more study.
Results: The developed device has two phases, which are the transport mode and the releasing mode. The transport mode was set as suction by the syringe with the change of three-way stopcock. The releasing mode was set as air ejection with the three-way stopcock. In the bench test, the device was confirmed to work in the narrow tube. In the large animal study, transplantation of ECSs using the device in the tears after EBD were validated and successfully performed without adverse events. Next, we evaluated the feasibility of the therapy using ECSs with EBD to esophageal strictures after ESD. The pigs in the Ctrl group developed severe strictures and dysphagia (The rate of strictures: 92.2% and 87.7%) at 3 weeks after ESD. ECSs were successfully transplanted in all cases of the Trans group. The pigs in the Trans group avoided re-strictures and kept good clinical condition (The rate of strictures: 55.0% and 60.0%) On the other hand, the pigs in the BD group developed re-strictures (The rate of strictures: 71.7% and 78.2%).
Conclusion: The transplanting device and procedure of ECSs after EBD were developed. Covering the tears after EBD by ECSs could avoid re-strictures.

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Disclosure of Interest: S. Kobayashi: None declared, N. Kanai: None declared, T. Hosoi: None declared, N. Tanaka: None declared, M. Maeda: None declared, Y. Maruya: None declared, K. Kanetaka: None declared, S. Eguchi: None declared, M. Yamato Shareholder: Cell Seed Inc.

OP240 EFFICACY, SAFETY AND CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING A SCISSORS-TYPE KNIFE FOR EARLY ESOPHAGEAL NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) is a one of the most useful methods for the treatment of early esophageal neoplasms. Several conventional devices are used for ESD: an IT knife, hook knife, and needle knife. However, because these devices are used without being fixed to the target, there is a potential risk of complications due to an unplanned incision. To reduce the risk of complications related to ESD using a conventional knife, we used a scissors-type knife (SB knife: Akita Sumitomo Bakelite) that allows us to maintain a proper dissecting layer and prevents unexpected injury to a muscular layer. In this study, we report on the efficacy, safety and clinical outcomes of ESD performed with an SB knife for early esophageal neoplasms at our hospital.
Aims & Methods: The aim of our study was to evaluate the efficacy, safety and clinical outcomes of ESD using a SB knife for early esophageal neoplasms. ESD using a SB knife was performed on 72 lesions (47 squamous cell carcinomas, 20 high-grade intraepithelial neoplasias, 4 adenocarcinomas and 1 carcinoid tumor) in 56 patients from April 2010 to February 2015. We evaluated the en bloc resection rate, complete resection rate, size of the specimen and tumor, local recurrence rate, and complications. Complete resection was defined as an en bloc resection, where both the lateral and vertical margins were negative. In cases that underwent circumferential or semi-circumferential ESD, prednisolone was administered orally or injected into the base of ulcer after the ESD to prevent post-operative stricture.
Results: The en bloc resection rate was 100% (72/72) and the complete resection rate was 95.8% (69/72). The mean size of the resected specimens was 34.4 mm (range 11–75 mm), and that of the resected tumors was 17.3 mm (range 1–64 mm). All lesions were treated easily and safely without any unexpected incisions, and there was neither delayed hemorrhage nor perforation. Oral administration or injection of prednisolone to prevent post-operative stricture was necessary for 7 patients (9.7%) who underwent circumferential or semi-circumferential ESD, and there was no post-operative stricture in any cases. The local recurrence rate was 1.4% (1/72). In the single recurrence case, despite pathological findings that indicated submucosal invasion and vessel invasion, the patient did not undergo additional therapies because of hepatocellular carcinoma. None of the patients died of esophageal neoplasms, whereas five patients died of other diseases (mean follow-up duration, 765 days).
Conclusion: ESD using a SB knife can be adopted as an easy, safe, and technically efficient method for resecting early esophageal neoplasms.
Disclosure of Interest: None declared

OP241 LONG-TERM OUTCOMES OF ENDOSCOPIC RESECTION AND ADDITIONAL THERAPY TO SUPERFICIAL ESOPHAGEAL CANCER WITH MM OR SM INVASION

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Introduction: Recent advances in endoscopic resection (ER), such as ESD, enable us en-bloc resection of the lesions and accurate pathological diagnosis, which provide us increasing chances for resecting esophageal cancer (EC) with muscularis mucosae (MM) or submucosal (SM) invasion. However, MM or SM invasive EC have 10-50% of metastatic risks, depending on its depth, lymphovascular involvement (LI) and droplet infiltration (DI). For these cases, after ER, we perform additional therapy such as chemo radiotherapy (CRT), radio therapy (RT) or operation considering the risk of metastasis and patients' general condition.
Aims & Methods: The aim of this study is to reveal long-term outcomes of ER and additional therapy for MM and SM invasive esophageal cancer (SCC). We studied about 141 cases with MM or SM invasive esophageal cancer resected by ER (EMR or ESD), from 2003 to 2012 in Cancer Institute Hospital, Tokyo, Japan.
Results: In 141 cases (male/female 128/13, median age 66), we resected 76 cases by EMR and 65 cases by ESD, and pathological depth of invasion was MM/

SM1/SM2 85/20/36. Median observation period was 41 months (2-140). En-bloc resection rate and local recurrence rate for EMR /ESD was 47.3% /100%, 11% / 0% respectively. Of 85 cases of T1a-MM, 69 cases were observed with no additional therapy because of LI (-) and DI (-). One patient had recurrence as lymph node (LN) metastasis and received operation and CRT, surviving with no re-recurrence. The rest of 16 cases were recommended additional therapy because of LI (+) or DI (+) and 7 cases were performed additional therapy (operation/CRT 3/4). No one died of EC in T1a-MM. Of 20 cases of T1b-SM1, 11 cases were observed with no additional therapy because of LI (-) and DI (-). Of them, 2 cases had recurrence (LN metastasis and lung metastasis) and died of EC. Nine cases were recommended additional therapy, because of LI (+) or DI (+). And 5 cases were performed additional therapy (operation/CRT 1/4), although one case had recurrence (liver metastasis) and died of EC. Of 35 cases of T1b-SM2, all cases were recommended additional therapy which 23 cases were performed (operation/CRT/RT 13/6/4). Three had recurrence (2 cases of intramucosal metastasis and 1 case of LN metastasis). They were performed operation or CRT and 1 case were died of EC. Overall survival (OS) for MM/SM1/SM2 were 84.6%/71.1%/84.6% in 3 year and 81.5%/64.6%/84.6% in 5 year. In OS, additional therapy group was significantly superior to no additional therapy group ($p < 0.05$) among the cases we recommended additional therapy. Comparing OS, survival benefit was not different between operation and CRT as additional therapy. In total 7 cases had metastatic recurrence during the observation period and 4 cases died of EC.

Conclusion: The long-term outcomes of ER with additional therapy was satisfactory. With appropriate consideration for additional therapy, ER will be a good therapeutic choice for MM or SM invasive EC.

Disclosure of Interest: None declared

OP242 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Endoscopic submucosal dissection (ESD) is now widely accepted as a strategy to treat superficial gastrointestinal cancers including superficial esophageal squamous cell carcinomas (SESCCs).

Aims & Methods: The aim of this study was to analyze the long-term outcomes of esophageal ESD and to assess the feasibility of the technique as a therapeutic procedure. A retrospective cohort study was conducted in which a total of 132 consecutive patients with 177 SESCCs that underwent ESD at NTT Medical Center Tokyo between January 2007 and March 2012 were analyzed. Patients with persistent recurrence after previous endoscopic or chemoradiation therapy (CRT) before 2007 were excluded. Long-term outcomes were investigated in patients with more than 3-year follow-up. Treatment outcome, clinical course after ESD, rates of overall survival and newly developed malignancies were evaluated as long-term outcomes.

Results: The mean age of the patients and the median observation time were 64 years (range, 46-90 years) and 61months (range, 36-86 months), respectively. Regarding the histological depth, EP/LPM, MM/SM1, and SM2 or deeper were 83.0% (147 lesions), 13.0% (23 lesions), and 4.0% (7 lesions), respectively. The *en bloc* resection rate was 100% and no significant bleeding occurred, and perforation with mediastinal emphysema was observed in 5 patients (2.8%). None of the patients developed local recurrence, and metachronous SESCCs (we defined it as those detected more than one year after the ESD) were detected in 15.3%of patients (27 lesions, comprising 25 EP/LPM lesions and 2 MM/SM1 lesions, respectively). All of these metachronous lesions underwent additional ESDs. Among the 23 MM/SM1 lesions, 17 lesions including 2 cases with lymphatic vessel infiltration were closely followed up without additional treatment at the patient's decision, 4 lesions including 3 cases with lymphatic vessel infiltration underwent CRT, and 2 lesions underwent additional surgery. Among the 7 lesions with SM2 or deeper invasion, 2 lesions were closely followed up without additional treatment, 2 lesions underwent CRT, and 2 lesions underwent additional surgery. None of the patients developed regional lymph node or distant metastasis during the observation period. The 5-year overall and disease-specific survival rates were 96.4% and 100%, respectively. Cancers other than SESCCs developed in 54 out of 132 cases (40.9%) during the observation period, among which 25 cases (40.7%) were head and neck cancers.

Conclusion: ESD seems to be a feasible, effective curative treatment for SESCCs. All patients should be closely followed after ESD. It is important to follow up for not only metachronous SESCCs but also other malignancies including head and neck cancers.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 11:00–12:30
IMPROVING COMFORT AND OUTCOMES IN COLONOSCOPY – ROOM E1

OP243 NEW LOW-VOLUME BOWEL CLEANSING SOLUTION (NER1006) VS TRISULPHATE, POLYETHYLENE GLYCOL 3350 + ASCORBATE OR SODIUM PICOSULPHATE/MAGNESIUM SALT: THREE ONGOING MULTICENTRE RANDOMISED PARALLEL GROUP PHASE III STUDIES IN 1914 PATIENTS UNDERGOING COLONOSCOPY

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Introduction: Effective colonoscopy or colonic surgery requires a clean bowel. An optimal bowel preparation would have a low volume without compromising efficacy/safety. NER1006 is a new oral low-volume polyethylene glycol (PEG) solution with ascorbate, which achieved high-quality bowel cleansing in a phase II study of screening colonoscopy subjects. The phase III programme aims to establish the efficacy, safety and tolerability of NER1006 in a large population of adult patients undergoing colonoscopy.

Aims & Methods: Three multicentre, randomised, colonoscopist-blinded parallel group studies in male/female patients aged 18-85 years are underway. Main inclusion criteria: patients undergoing screening, surveillance or diagnostic colonoscopy. Main exclusion criteria: past history (≤12 months) or current episode of severe constipation; known or suspected ileus; gastrointestinal obstruction; gastric retention; bowel perforation; toxic colitis or megacolon; ongoing severe acute inflammatory bowel disease; previous significant gastrointestinal surgeries; regular use of laxatives or colon motility altering drugs (>2-3 times/week) in the 28 days prior to screening visit and/or laxative use within 72 hours prior to bowel preparation administration. NOCT (NCT02254486) will randomise (1:1) 620 patients in the USA to NER1006, 2-day split dosing regimen (to start the evening of the day before colonoscopy) or trisulphate solution (regimen per label). MORA (NCT02273167; 2014-002185-78) will randomise (1:1:1) 810 patients in Europe to NER1006, 2-day evening/morning split-dosing regimen and 1-day morning on day of colonoscopy regimen or PEG3350 + ascorbate (regimen per label). DAYB (NCT02273141; 2014-002186-30) will randomise (1:1) 484 patients in Europe to NER1006, 1-day, day before-only split dosing regimen (to start the evening of the day before colonoscopy) or sodium picosulphate/magnesium salt (regimen per label). Study duration: up to four clinic visits/patient for up to 40 days. Each study has two alternative primary endpoints: 1. Overall bowel cleansing success rate of NER1006 is non-inferior to that of comparator using the Harefield Cleansing Scale (HCS); 2. 'Excellent plus Good' cleansing rate in the colon ascendens of NER1006 is non-inferior to that of the comparator using the segmental cleansing scoring system of the HCS. Central readers will score colonoscopy videos. Key secondary endpoints include: adenoma and polyp detection rates in the colon ascendens and overall.

Results: As of March 2015, number of patients randomised were 559/620 at 12 US sites for NOCT, 251/810 at 30 sites in Belgium, France, Germany, Italy, Poland, Spain and UK for MORA, and 127/484 at 20 sites in Germany, Italy, Netherlands, Poland, Spain, and UK for DAYB. The studies are due to complete by September 2015.

Conclusion: Quality of bowel preparation is an important factor for a successful colonoscopy however the volume of lavage solution required to achieve efficacy and tolerability is often a barrier. The findings from these pivotal phase III studies of a new low volume bowel preparation may provide a better understanding of what is required in an optimal bowel preparation.

Disclosure of Interest: B. Tayo Conflict with: Employee of Norgine, M. DeMicco: None declared, R. Bisschops: None declared, S. Schreiber: None declared, L. Clayton Conflict with: Employee of Norgine

OP244 WATER EXCHANGE IS THE LEAST PAINFUL COLONOSCOPY INSERTION TECHNIQUE COMPARED WITH WATER IMMERSION AND CO2 INSUFFLATION: A META-ANALYSIS

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Introduction: Some studies suggested that, in some settings, carbon dioxide insufflation (CO_2) decreased abdominal pain and discomfort during colonoscopy. The effect of CO_2 on insertion pain is controversial: two meta-analyses showing a decrease in pain during colonoscopy by CO_2 compared with air insufflation assigned pain score recorded immediately after the procedure, or recalled pain recorded afterwards, as pain during colonoscopy. The meta-analyses did not address the need for sedation. Separate randomized controlled trials (RCTs) have shown water-aided colonoscopy techniques, water immersion (WI, removal of water predominantly during withdrawal) and water exchange (WE, removal of water predominantly during insertion) to significantly decrease insertion pain and the need for sedation compared with CO_2.

Aims & Methods: We performed a meta-analysis to determine which technique would produce the lowest real-time maximum insertion pain and lowest recalled pain at discharge, with interest also in some procedural outcomes. Medline, PubMed and Google searches (January 2011-May 2015) were done to identify appropriate RCTs that compared WE or WI with CO_2. Keywords were: water-aided colonoscopy, water exchange, water immersion, carbon dioxide colonoscopy, pain. Reviews, case reports and abstracts were excluded. Primary endpoints were real time maximum insertion pain and recalled pain at discharge. Secondary end-points were success of unsedated or minimally sedated

colonoscopy, cecal intubation rate, cecal intubation time. Fixed or random effect models were used as appropriate based on homogeneity or heterogeneity of data according to I2 statistic.
Results: 4 RCTs were identified. A total of 1501 procedures were analysed: 638 WE, 320 WI and 543 CO_2. Sex, age, BMI and previous abdominal surgery were comparable. Data are presented as Odd ratio (OR), mean difference and 95% confidence interval (CI). Meta-analysis shows that, compared with CO_2, WE achieved the lowest real-time maximum insertion pain score: -0.79 (-1.22,-0.36), $p = 0.003$. Compared with CO_2, both WE [-0.89 (-1.58,-0.19), $p = 0.01$] and WI [-0.46 (-0.9-0.02), $p = 0.06$] significantly decreased recalled insertion pain score at discharge. Compared with CO_2, proportion of procedures completed without sedation or with minimal sedation was in favour of WE [1.81 (1.19-2.75), $p = 0.005$]; WI [1.07 (0.67-1.70), $p = 0.78$]. Compared with CO_2, WE achieved significantly higher cecal intubation rate: 2.18 (1.3-3.6), $p < 0.005$. CO_2 and WI were comparable: 1.10 (0.3-3.4), $p = 0.9$. WE and WI were associated with a longer cecal intubation time than CO_2: 3.6 (2.6-4.1) and 2.8 (1.9-3.6), $p < 0.005$, respectively.
Conclusion: Compared with water exchange, which is the least painful insertion technique, insufflation with CO_2 does not decrease colonoscopy real-time insertion pain. Both WI and WE reduce recalled insertion pain at discharge. Water exchange significantly enhances completion of unsedated or minimally sedated colonoscopy, lessening patients' burdens; and achieves significantly higher cecal intubation rate, but at the expense of a prolonged insertion time.
Disclosure of Interest: None declared

OP245 BLUE WATER INFUSION DURING COLONOSCOPY DOES NOT INCREASE SIGNIFICANTLY THE ADENOMA DETECTION RATE COMPARED TO STANDARD COLONOSCOPY : RESULTS OF A PROSPECTIVE RANDOMIZED COMPARATIVE STUDY INVOLVING 984 PATIENTS IN 8 CENTERS: THE « GRAND BLEU » STUDY

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Introduction: Standard colonoscopy with air insufflation (SC) is currently the standard to detect colorectal lesions. However, the tandem colonoscopy studies reported a rate of missed adenomas between 16 and 24%. Different techniques have been developped to reduce this missed rate and the BWIC showed interesting results. This trial aimed to compare the efficacy of blue water infusion colonoscopy (BWIC) versus SC in terms of adenoma detection rate (ADR).
Aims & Methods: We designed a prospective comparative study in 8 regional gastroenterology units. Depending on the randomization, the patient received either a SC or a BWIC using warm water with 0.5/1000 indigo carmine blue. All the lesions detected (adenoma, SSP) were resected or biopsied for pathology confirmation.
Results: From Feb 2013 to Aug 2014, we recruited 983 patients with a validate indication of colonoscopy. 491 patients received a SC and 492 a BWIC by 17 endoscopists. The number of polyps, adenoma, SSP and invasive cancer detected was respectively 880, 371, 31 and 7 in the BWIC group versus 677, 293, 23 and 2 in the SC one ($p = 0.002$, $p > 0.1$). Regarding the ADR, no significant difference appeared between SC and BWIC with respectively 37.8 and 40.9% ($p = 0.32$). The mean number of adenoma and SSP detected per colonoscopy was 0.64 and 0.82 ($p = 0.11$) respectively in SC and BWIC. Time of cecal intubation was significantly longer with BWIC with 11.8 vs 7.9 min ($p < 0.0001$).
Conclusion: BWIC is effective to detect adenoma but not significantly superior to SC. In this regional study, a high ADR was observed, underlining the colonoscopy efficacy of the current screening strategy.
Disclosure of Interest: None declared

OP246 ASCENDING COLON EXPLORATION BY RETROVIEW: TECHNICAL FEASIBILITY AND DIAGNOSIS PERFORMANCE

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Introduction: The right colon lesions not visualized during the standard colonoscopy have been associated to interval cancer. The proximal fold side exploration of the ascending colon by retroview reduces the likeliness of losing those lesions. The shorter colonoscope diameter would make easier the cecal retroflexion with lower complication rate.
Aims & Methods: To determine the technical feasibility of the cecal retroflexion, the diagnosis performance and complication rate of the ascending colon exploration by retroview with a shorter colonoscope diameter.
Methods: Prospective study in a paired sample. There were included all the consecutive total colonoscopies performed by expert endoscopists during four months. The recruited patients were examined using two endoscopic **Methods:** conventional and retroview colonoscopy. We collected the visualized and resected lesions on both exploration types.
Technique: Conventional exploration of the ascending colon: Colonoscope insertion and colonoscope withdrawal in forward view from the cecum until the hepatic flexure. Retroview exploration: 1) Colonoscope re-insertion from the hepatic flexure and cecal retroflexion maneuver; and 2) Colonoscope withdrawal in retroview until the hepatic flexure. Exclusion criteria: incomplete endoscopies by any cause (obstruction, endoscopic therapy, right colon resection). All procedures were done with a Colonoscope PENTAX-i10L EC34 (Insert Ø: 11.6, Channel: 3.8, Deflection up/down: 180/180, left/right: 160/160).
Results: We included 323 colonoscopies done in the same number of patients. Age: 61.1 ± 18.2 years; 46% women. There were excluded 20 by incomplete examination. The cecal retroflexion was feasible in 76.6% ($n = 232$). In these procedures, in the right colon, were detected 42 polyps: 40 Paris Is (32 sessile and 8 semi-pedunculated) and 2 Ip, which accounted for 29.4% of 142 colonoscopies with polyps throughout the colon. Histology: 32 adenomas and 10 sessile serrated polyps without dysplasia. 28 polyps were detected and removed during the conventional exploration in forward view while 14 polyps (33.3% of all resected polyps in the ascending colon) were detected additionally only by colonoscope withdrawal in retroview. In the ascending colon, the adenoma detection rate (ADR) was significantly higher in the retroview exploration: 18.10 vs. 12.07%; $p = 0.001$. There were not complications.
Conclusion: The cecal retroflexion was feasible in greater than 75% of colonoscopies and were not registered associated complications. Over 30% of the ascending colon polyps were detected only by colonoscope withdrawal in retroview. This technique significantly increased the ADR in the right colon.
Disclosure of Interest: None declared

OP247 THE UTILITY OF EARLY COLONOSCOPY IN THE MANAGEMENT OF ACUTE LOWER GASTROINTESTINAL HEMORRHAGE

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Introduction: Differences in the safety of bowel preparation and procedures between early and elective colonoscopy have not been extensively studied. In addition, the clinical advantage of early colonoscopy in the setting of acute lower gastrointestinal bleeding (LGIB) remains uncertain. Although, there were two randomized controlled trials comparing early and elective colonoscopy for LGIB, but there were terminated before the prespecified sample size had been reached.
Aims & Methods: We aimed to investigate the safety and effectiveness of early colonoscopy in acute LGIB. We retrospectively studied 538 patients who were emergently hospitalized for acute LGIB. We used propensity score matching to adjust for differences of baseline characteristics between patients who underwent early (≤ 24 h of admission) or elective colonoscopy (> 24 h). Outcomes included rates of adverse events during bowel preparation and colonoscopy procedures, stigmata of recent hemorrhage, endoscopic therapy, blood transfusion requirement, 30-day re-bleeding and mortality, and length of hospital stay.
Results: Before propensity score matching, some differences were found between the groups. After matching using propensity scores based on 9 characteristics (elderly, sex, performance status, previous diverticular bleeding, fever, abdominal pain, diarrhea, anticoagulants, and weekend admission), 176 pairs were selected. No significant differences were found between the groups in bowel preparation-related adverse event rates (6.3% vs. 5.1%, $P = 0.645$), colonoscopy-related adverse event rates (14.2% vs. 13.1%, $P = 0.756$), blood transfusion requirement (27.8% vs. 28.4%, $P = 0.906$), or mortality (1.1% vs. 0.6%, $P = 0.562$). The early colonoscopy group had higher rates than the elective group for stigmata of recent hemorrahage (26.7% vs. 10.2%, $P < 0.001$), endoscopic therapy (25.6% vs. 9.1%, $P < 0.001$) including clipping (14.2% vs. 5.1%, $P = 0.004$) and band ligation (7.4% vs. 1.1%, $p = 0.004$), and re-bleeding (15.3% vs. 8.0%, $P = 0.031$). Length of hospital stay was shorter in the early colonoscopy group (10.3 vs. 13.3 days, $P = 0.001$).
Conclusion: Bowel preparation- and colonoscopy-related adverse event rates for early colonoscopy did not differ from those for elective colonoscopy. Although, early colonoscopy did not improve outcomes of re-bleeding, blood transfusion

requirement, or mortality, it was associated with increased rates of stigmata of recent hemorrhage and enabled more endoscopic therapy, and decreased length of hospital stay.
Disclosure of Interest: None declared

OP248 THE EFFICACY OF TREATMENT OF LOCAL RESIDUAL NEOPLASIA UNDER STANDARDIZED CONDITIONS

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Introduction: After endoscopic mucosal resection (EMR) of nonpedunculated neoplastic colorectal lesions, local residual neoplasia (LRN) has been observed in 5-54% of cases. Several treatment modalities are available to eradicate LRN. The purpose of our study is to evaluate the efficacy of LRN treatment under standardized conditions.
Aims & Methods: This prospective interventional study was conducted in two gastroenterology centers between October/2013 and September/2014. All patients positive for LRN at first follow-up colonoscopy performed 3months after EMR of laterally spreading tumors (LST) were included. The LRN was defined as histological presence of neoplasia in the post- EMR site. Based on endoscopic appearance, LRN was classified into 5 types: Endoscopically undetectable LRN (A), LRN $\leq$ 5mm (B), LRN $>$ 5mm with negative non-lifting sign (C), LRN $>$ 5mm with positive non-lifting sign (D), complex LRN (E). Corresponding treatment modalities were argon plasma coagulation (APC) for types A and B, re-EMR for type C, endoscopic submucosal dissection (ESD) for type D and surgery for type E. The treatment of LRN was considered complete if the post-EMR site was endoscopically and histologically negative for the presence of neoplasia at second follow-up colonoscopy performed after 6 months.
Results: Among 25 patients with 25 LRNs, 10 (40%) were females and 15 (60%) were males. Mean age was 69. 3 (range 52-80) years. Histology of original LST was LGIEN in 6(24%), HGIEN in 14(56%) and intramucosal carcinoma in 5(20%). The location of post-EMR site was rectum in 16(64%), distal colon in 6(24%) and proximal colon in 3(12%). The type of LRN according to the proposed classification was as follows: type A in 0(0%), type B in 12(48%), type C in 8(32%), type D in 5(20%) and type E 0 (0%). The histology of LRN was LGIEN in 12 (48%) and HGIEN in 13(52%). There was no mortality, perforation or delayed bleeding related to LRN treatment. Second follow-up colonoscopy was completed in 23(92%) patients. Remaining 2 (8%) patients were excluded due to loss to follow-up and anticoagulation treatment. The LRN treatment was complete in 21(91.3%) and incomplete in 2(8.7%) cases. Both persistent LRN were small residual adenomas (type B) suitable for additional APC therapy.
Conclusion: The local residual neoplasia after endoscopic mucosal resection of laterally spreading tumors can be eradicated endoscopically during one session in 91.3% of cases. Selection of appropriate treatment modality according to LRN type may be useful.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 11:00–12:30
INFLAMMATORY BOWEL DISEASE: NOT ALL IN THE GENES? – ROOM E4

OP249 AUTOPHAGY REGULATES DENDRITIC CELL MIGRATION THROUGH RAC1 – IMPLICATIONS FOR THIOPURINE THERAPY

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Introduction: The T300A variant of the *ATG16L1* gene reduces autophagy and is one of the few highly prevalent risk factors associated specifically with Crohn's disease. We have previously shown a regulatory role for autophagy during dendritic cell (DC) - T cell interactions, where the T300A allele results in enhanced contact time, T cell hyperactivation and Th17 skewing (Wildenberg et al, *Gastroenterology* 2012). Since a key element of the DC-T cell interaction is regulation of the cytoskeleton, we here further investigated the role of autophagy in DC cytoskeletal organization and function and correlated our findings to thiopurine therapy in IBD patients.
Aims & Methods: Autophagy deficient dendritic cells (DC) were generated using small interfering RNA, pharmacological inhibition or *CD11cCre-Atg5$^{fl/fl}$* bone marrow or generated from T300A allele carrier monocytes. DC phenotype and migratory capacity were analyzed using migration assays. Correlation between *ATG16L1* genotype and response to thiopurines in IBD patients was determined in two retrospective cohort studies.
Results: Reduced autophagy in DC resulted in loss of filopodia and increased membrane ruffling. This cytoskeletal phenotype was due to increases in Rac1 activity. As a result autophagy deficient DC showed increased adhesion to various substrates. In human DC, both random and directional migration were impaired *in vitro*, while in mice bone-marrow derived DC lacking autophagy show migratory defects *in vivo*. Strikingly, migration of autophagy deficient DC could be restored by the Rac1 inhibitor 6-thioguanin (6-TG), while 6-TG did not influence migration in autophagy sufficient DC. Similar data was obtained using monocytes carrying the *ATG16L1* T300A risk allele. Finally, we correlated ATG16L1 genotype and response to thiopurines in two IBD cohorts and found that the *ATG16L1* risk variant associates with response to thiopurine treatment specifically in patients with Crohn's disease but not ulcerative colitis.
Conclusion: Our results suggest that a defect in the autophagosomal regulation of active Rac1 underlies the association between *ATG16L1* and Crohn's disease through decreased myeloid cell migration. Since thiopurine can inhibit Rac1 activity, *ATG16L1* genotyping may be used to identify patients that will benefit from thiopurine treatment.
Disclosure of Interest: M. Wildenberg Lecture fee(s): Takeda, Falck, P. Koelink: None declared, K. Diederen: None declared, A. te Velde: None declared, V. Nuij: None declared, M. Peppelenbosch: None declared, M. Nobis: None declared, O. Sansom: None declared, C. J. van der Woude Financial support for research: Falk Pharma, Abbott Laboratories, Consultancy: AbbVie, Merck Sharp & Dohme, and Ferring Pharmaceuticals, G. D'Haens Financial support for research: Abbott/AbbVie, AM Pharma, Centocor/Janssen Biologics, Engene, Photopill, Setpoint, Novo Nordisk, MSD, UCB, Takeda, TEVA, Millenium, Boehringer Ingelheim, Elan, Ferring Pharmaceuticals, Dr Falk Pharma, Shire, Cosmo, AstraZeneca, GSK, and PDL, Lecture fee(s): Abbott/AbbVie, AM Pharma, Centocor/Janssen Biologics, Engene, Photopill, Setpoint, Novo Nordisk, MSD, UCB, Takeda, TEVA, Millenium, Boehringer Ingelheim, Elan, Ferring Pharmaceuticals, Dr Falk Pharma, Shire, Cosmo, AstraZeneca, GSK, and PDL, Consultancy: Abbott/AbbVie, AM Pharma, Centocor/Janssen Biologics, Engene, Photopill, Setpoint, Novo Nordisk, MSD, UCB, Takeda, TEVA, Millenium, Boehringer Ingelheim, Elan, Ferring Pharmaceuticals, Dr Falk Pharma, Shire, Cosmo, AstraZeneca, GSK, and PDL, G. van den Brink Financial support for research: Abbvie, Crucell, PPM Services, Lecture fee(s): AbbVie, Merck Sharp & Dohme, and Ferring Pharmaceuticals, Consultancy: Abbvie

OP250 ANTI-TNF-A INDUCTION REGIMEN MODULATES GUT MICROBIOTA MOLECULAR COMPOSITION WHILE INDUCING CLINICAL RESPONSE IN CROHN'S DISEASE PATIENTS: TOWARD A PERSONALIZED MEDICINE

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Introduction: IBD is characterized by an imbalance between immune response and microbiota composition. Anti-TNF-a is one of strongest therapeutically options with high immune modulation potential. No information exists on how and whether anti-TNF-a modulates gut microbiota composition.
Aims & Methods: Aim of our study was to evaluate gut microbiota composition in Crohn's disease patients before and after 6 weeks of anti-TNF-a therapy (mean age 41). Fecal samples were collected in 6 consecutive CD patients, (3 Infliximab, 3 adalimumab) and stored at -80°C. No antibiotic were performed 4 weeks before starting anti-TNF-a therapy or during the active treatment. Clinical response was defined as a decrease of 2 points at Harvey Bradshaw Index (HBI) compared to baseline, while clinical remission was consider for HBI $<$ 4.
Results: Bacteria amplicons were detected in all samples.Six weeks after anti-TNF-a therapy, Bacteroidetes decreased in 2 patients (one of the 2 in clinical remission) and remained stable in 4 patients. Roseburia spp increased in one patient (not in clinical remission), Ruminococcus spp decreased in 2 patients (in one not responder to treatment). F. Prausnitzii increased in 3 patients (one in clinical remission). Enterobacteriaceae increased in 3 patients (one not responder to therapy). Chao index increased in 5 patients of six after 6 week. Patients non-responder to anti-TNF by 12 weeks did not show increase in Bacteroidetes at 6 weeks.
Conclusion: Anti TNF-a treatment is associated to active modulation of intestinal microbiota while inducing clinical response. Reduction of Enterobacteriacaee and Ruminococcus were associated to clinical response to antiTNF-a, together with increase in Bacteroidetes and F. Prausnitzii. Further studies are required considering a major number of patients.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 11:00–12:30
NEW DEVELOPMENTS IN DETECTION AND MANAGEMENT OF COLORECTAL NEOPLASIA – ROOM E3

OP251 PREVALENCE OF SERRATED POLYPS; A EUROPEAN OVERVIEW

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Introduction: Serrated polyps (SP) are suggested to be precursors of colorectal cancer via the serrated neoplasia pathway and should be removed during colonoscopy. However, the true prevalence and distribution of SP is largely unknown, impeding guidance for standards in detection, resection and surveillance.
Aims & Methods: We aimed to evaluate and compare the prevalence of SP subtypes in several European countries. Cohorts of patients that underwent colonoscopies between 2009-2014 were eligible to be included in the analysis, as in

Abstract number: OP251

Country	UK	Spain	Italy	Italy	Netherlands	Netherlands	Poland
Cohort type	gFOBT screening	FIT screening	FIT screening	Case-mix	Case-mix	Primary colonoscopy screening	Primary colonoscopy screening
Cohort size (n)	205.949	6.091	17.623	1.809	2.645	1.426	12.361
Age in years (range)	60-75	50-70	60-70	50-93	50-94	50-75	50-65
Male gender (%)	58	55	55	50	53	51	47
Samples assessed by gastrointestinal pathologist	All	All	NA	All	All	All	All
Cecal intubation (%)	97	97	91	91	96	99	98
Adequate bowel preparation (%)	97	98	94	85	89	92	92
≥1 adenoma (%)	43.3	47.1	47.8	31.5	42.0	29.4	32.3
≥1 SP (%)	15.1	19.5	17.6	14.1	24.7	27.2	26.6
≥1 proximal SP (%)	4.7	6.7	9.5	6.5	11.6	12.2	9.7
≥1 large SP (%)	1.2	2.5	2.1	1.9	2.2	2.6	1.1
≥1 SSA/P (%)	NA	3.2	3.3	5.0	8.2	4.8	2.2
≥1 SP ≥10 mm and/or ≥1 proximal SP > 5mm (%)	2.1	5.0	7.8	3.4	4.4	4.3	NA
Serrated polyposis (%)(after follow-up)	NA	0.8	NA	NA	0.5	0.4	0.1

NA = not assessed

this era the neoplastic risk of SPs was known. To warrant firm estimates, only prospective cohorts of >1000 colonoscopies were included. Patients <50 years were excluded, to warrant more homogenous data. Aggregated data were collected per center. Cohort type, cecal intubation rate (CIR), adenoma detection rate and quality of bowel preparation were recorded to evaluate the quality of colonoscopies. The prevalence of SP subtypes was assessed in all cohorts, subcategorized for histology, location and size. Clinically relevant SP that could be assessed without the need of an accurate histopathologic differentiation was defined as: SP ≥10 mm and/or SP >5 mm located proximal to the splenic flexure.

Results: Seven prospectively collected cohorts from five European countries were included for analysis (table). All cohorts were representative for routine practice. The unadjusted CIR was >90% in all cohorts and bowel preparation was adequate in ≥85% of patients. In 6 cohorts, all lesions were assessed by gastrointestinal pathologists, while in one cohort the expertise of the pathologist was not registered. The prevalence of any SP ranged from 14.1-27.2% (median 19.5), of proximal SP from 4.7-12.2% (median 9.5), of large SP from 1.1-2.6% (median 1.9), of sessile serrated adenoma/polyps from 2.2-8.2 (median 4.1) and of clinically relevant SP from 2.1-7.8% (median 4.3).

Conclusion: The prevalence of SP is variable among European countries, probably due to inconsistency in detection, reporting and/or histopathological differentiation of SP subtypes. Awareness and training is needed to facilitate optimal and more consistent practice. The median prevalence of SP subtypes, as found in this study, could be used as a guidance for detection standards among Western countries.

Disclosure of Interest: None declared

OP252 UNDERSTANDING ADR PERFORMANCE IN "BOWEL SCOPE" - THE NHS FLEXIBLE SIGMOIDOSCOPY SCREENING PROGRAMME

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Introduction: A new arm of the NHS Bowel Cancer Screening Programme began in 2013. One-off flexible sigmoidoscopy (FS) is to be offered to all 55 year olds. Six pilot sites were chosen to start this screening programme, with roll out to the rest of the country planned by 2016. A benchmark adenoma detection rate (ADR) for endoscopists within the programme is being discussed.

Aims & Methods: The NHS Bowel Cancer Screening System database was interrogated for all FS performed at the pilot sites May 2013-May 2014. Data were extracted at procedural level. Participants aged 55 were included in analyses. Overall ADR was calculated. Data of endoscopists with ≥30 procedures were reviewed, and funnel plot analyses produced for ADR, and gender adjusted observed to expected adenoma detection ratio (GAADR). GAADR was calculated using the population risk of adenoma detection in females and males to predict how many adenomas each endoscopist should find based on case mix, and calculating the ratio of predicted to observed adenomas detected. Mean negative withdrawal time (time taken to withdraw the scope when no adenoma/cancer was detected) for each endoscopist was calculated and considered in three groups – those with GAADR <0.85, 0.85 to <1.1, and ≥1.1.

Results: 8582 subjects underwent FS, of which 8494 (99.0%) were aged 55. 4420 (52.0%) were male, 4074 (48.0%) female. Adenomas were detected in 507 males (11.5%) vs 273 females (6.7%, $p < 0.001$).

44 endoscopists performed ≥30 FS. These endoscopists performed 8256 FS (range 32-476). Overall programme ADR was 780/8494 (9.2%). GAADR mean 0.99 (range 0.00-2.05). Funnel plots were produced with control lines at 95% and 99.8%. The first demonstrates ADR, the second shows GAADR by endoscopist, and demonstrate the majority of endoscopists performing with these controls. Where a single outlier existed in ADR performance, review of GAADR showed that endoscopist continued to underperform even after adjusting for case mix by gender.

Increased mean negative withdrawal time (WT) was associated with higher GAADR (2.63min when GAADR <0.85, 3.02min when 0.85 to <1.1, and 3.25min when ≥1.1).

Conclusion: These data show in 55 year olds in the Bowel Scope programme, ADR is 9.2%. ADR between endoscopists varies. There is a significant gender difference in ADR, and as such, a gender adjusted ratio could be used when analysing individual endoscopists' performance should their ADR be below a defined benchmark. The funnel plots show that most endoscopists perform within an acceptable range, and highlights those that may need further investigation. More analysis of WT is needed, as well as consideration of the impact of depth of insertion on GAADR.

Disclosure of Interest: None declared

OP253 RISK FACTORS CANNOT EXPLAIN THE SEX-SPECIFIC DIFFERENCE IN DETECTION RATES OF COLORECTAL ADENOMAS AND ADVANCED ADENOMAS

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Introduction: It is insufficiently investigated whether the sex-specific difference in incidence and age of onset of colorectal cancer (CRC) is explained by the impact of risk factors.

Aims & Methods: We analyzed the impact of known risk factors on adenomas and advanced adenomas in men and women in a CRC screening cohort.

Results: This prospective cross-sectional study included 25,409 patients. Mean age was 61 years (SD 8.3) and 50.8% were women. A multivariate model showed that risk factors mediated only 8.6% of the 58% relative gender difference in adenoma and 14.2% of the 56% in advanced adenoma detection rate revealing male sex as strongest risk factor for colorectal lesions. The only sex-specific independent risk factor for adenomas (men OR 1.46, CI 1.29, 1.64, women OR 1.76, CI 1.53, 2.06) and advanced adenomas (men OR 1.06, CI 0.80,1.42, women OR 2.08, CI 1.52,2.83) was smoking. Independent risk factors for adenomas were BMI (OR 1.35 per IQR, CI 1.25-1.47) and triglyceride level (OR 1.03 per IQR, CI 1.00-1.06); for advanced adenomas physical activity (none vs regular: OR 1.54, CI 1.18-2.00, occasional vs regular: OR 1.17, CI 1.00-1.38), cholesterol level (OR 1.13 per IQR, CI 1.02-1.25), blood glucose level (OR 1.05 per IQR, CI 1.01-1.09) and alcohol score (OR 1.09 per IQR, CI 1.01-1.18).

Conclusion: Smoking is the only sex-specific risk factor for premalignant colorectal lesions. Although some risk factors significantly influence the prevalence of colorectal lesions, this does not explain the higher prevalences in men.

Disclosure of Interest: None declared

OP254 RISK OF COLORECTAL CANCER AFTER REMOVAL OF HIGH-RISK ADENOMAS

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Introduction: Recommendations for surveillance after removal of high-risk adenomas are mainly based on risk of advanced adenoma recurrence, not on risk of colorectal cancer (CRC).
Aims & Methods: We aimed to assess the association between high-risk adenoma features and CRC risk. We included individuals with high-risk adenomas removed from 2000 to 2008 in the CRC screening program in Poland. Individuals were followed for CRC through the National Cancer Registry until December 31, 2013. High-risk adenoma group was defined as that with adenomas with villous histology or high-grade dysplasia or ≥10 mm in size or with ≥3 adenomas. We compared CRC incidence by size of adenoma (≥10 mm vs. <10 mm), histological type (villous component vs. tubular), grade of dysplasia (high-grade vs. low-grade) and number of adenomas (1-2 vs. ≥3). We estimated hazard ratios (HR) and 95% confidence intervals (CI) using proportional-hazard regression models adjusted for age, sex and family history of CRC (adenoma characteristic model). Then, we grouped individuals according to their most advanced lesion and estimated the adjusted HR for CRC risk (clinical model).
Results: In total of 10,317 individuals were included, with 74,765 person-years. We identified 49 patients with CRC during follow-up. Size ≥10 mm and high-grade dysplasia were associated with CRC risk; adjusted HR 2.18 (95%CI 1.17-4.06, P = 0.014) and 2.52 (95%CI 1.40-4.55, P = 0.002), respectively (Table). No association was found for the number of adenomas and histology type. The clinical model confirmed that high-grade dysplasia and size ≥10 mm were associated with risk of CRC; adjusted HR 5.32 (95%CI 1.96-14.44, P = 0.001) and 2.71 (95%CI 1.03-7.12, P = 0.044), respectively.

Table: Risk Factors for CRC*

	Adenoma characteristics model[$]		Clinical model[†]	
Variable	**HR[95%CI]**	**P**	**HR[95%CI]**	**P**
Age				
40-49	1.00		1.00	
50-54	1.87 [0.23-15.54]	0.562	1.84 [0.22-15.30]	0.572
55-59	3.85 [0.51-28.88]	0.189	3.88 [0.52-29.04]	0.187
60-66	5.03 [0.68-37.17]	0.114	5.04 [0.68-37.26]	0.113
Size				
<10mm	1.00			
≥10mm	2.18 [1.17-4.06]	0.014		
Grade of dysplasia				
Low	1.00			
High	2.52 [1.40-4.55]	0.002		
Most advanced lesion				
HGD			5.32 [1.96-14.44]	0.001
No HGD, ≥10mm			2.71 [1.03-7.12]	0.044
No HGD, <10mm,tubular, ≥3			1.78 [0.47-6.64]	0.391
No HGD, <10mm, villous/tubulo-villous, ≥1			1.00	

Abbreviation: HGD, high grade dysplasia. *HR reported for variables found significant in stepwise selection. [$]Sex, family history of CRC, number of adenomas and histological type were tested for inclusion in the model. [†]Sex and family history of CRC were tested for inclusion in the model.

Conclusion: The highest risk of CRC after removal of high-risk adenomas was associated with high-grade dysplasia or size ≥10mm.
Disclosure of Interest: None declared

OP255 SAFETY AND EFFICIENCY OF COLD POLYPECTOMY FOR DIMINUTIVE OR SMALL COLORECTAL POLYPS

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Introduction: Cold Polypectomy (CP) is becoming more widely used for the removal of diminutive or small colorectal polyps. Moreover a few studies reported the possibility of CP for polyps even in patients who are currently receiving antiplatelet or anticoagulant therapy. However, the safety and efficiency of CP have not been fully evaluated.
Aims & Methods: The aim of this study was to clarify the safety and efficiency of CP. 237 consecutive patients with colorectal polyps < 10mm were removed by Cold Forceps Polypectomy (CFP) or Cold Snare Polypectomy (CSP) between June 2014 and March 2015. In principle, polyp < 5mm was removed by CFP and one < 10mm by CSP. All polyps were evaluated by using a high-definition endoscope with magnification before CP to exclude invasive cancer. Polypectomy sites after CP were observed attentively with same method to assess the presence of residual polyp tissue. We retrospectively assessed the characteristics of polyps, retrieval rate, histological result, and complications.
Results: A total of 506 polyps in 237 patients (160 males and 77 females, 4.2% on antiplatelet or anticoagulant agents) were removed by CP (155 for CFP and 351 for CSP). Their mean age was 66.6 ± 10.7 years. The mean number of polyps per patient was 2.1 ± 1.8. The morphology of polyps was as follows: sessile, 216 lesions (42.7%); semipedunculated, 198 lesions (39.1%); slightly elevated, 92 lesions (18.2%). Among the 506 polyps, 312 (61.7%) were located in the right colon and 194 (38.3%) in the left colon. The mean polyp size was 3.7 ± 0.9 mm in the CFP group and 6.1 ± 1.9 mm in the CSP group, respectively. The retrieval rate was 96.2%. Histopathological evaluation showed that advanced adenoma (AA) was detected in 36 lesions (7.1%), of which 2 were removed by CFP and 34 by CSP. All of AAs were achieved complete histological resection. Neither delayed bleeding nor perforation occurred, and moreover no patient was admitted to hospital owing to other complication such as abdominal pain or discomfort after CP in our series.
Conclusion: CP is safety and effective technique for removal of diminutive or small polyp. Especially, patients receiving anticoagulants or antiplatelet agents may benefit from CP. The appropriate selection of device in accordance with polyp size is important to achieve the complete resection.
Disclosure of Interest: None declared

OP256 ACROMEGALY AND COLONIC POLYPS REVISITED: TIME TO CHANGE THE GUIDELINES?

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Introduction: Previous studies (including an important study from our own unit published nearly 20 years ago) have highlighted an increased risk of pre-malignant colonic polyps in patients with acromegaly (1). Current clinical guidelines suggest colonoscopic surveillance for these patients. Advances in detection and treatment of acromegaly may have influenced polyp prevalence in this group, and may mean revision of current guidelines is needed.
Aims & Methods: We aimed to re-evaluate polyp prevalence in a more recent cohort of patients with acromegaly undergoing colonoscopy at the Royal London Hospital.
We interrogated our database to identify patients with acromegaly undergoing surveillance colonscopy between 2010 and 2015. In these patients we reported detection of premalignant and malignant lesions.
Results: We identified 89 patients (41 males, age range 36-82, median age 64) who had undergone colonoscopy. In this cohort we identified 16 patients (18%) with at least one adenomatous polyp. Of these polyps, 69% were tubular adenomas and 31% were tubulovillous adenomas. Polyps in only two patients displayed high-grade dysplasia, the remainder displayed low grade dysplasia. No cancers were found.

	1996 cohort	2015 cohort
Tubulovillous adenoma detection rate	26%	6%
Maligancy	5%	0%
Any premalignant or malignant lesion	30%	18%

Conclusion: In comparison to the 1996 cohort we show a significantly (p = 0.04) lower detection rate of precancerous lesions in our patient group. In fact adenoma detection rates are similar to those seen in healthy colonoscopic screening populations. The reasons for this are likely complex but may in part be accounted for advances in the diagnosis, management and monitoring of acromegaly. Consideration may be given to revisiting surveillance guidelines in these patients.

Reference

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Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 11:00–12:30
DIAGNOSIS AND TREATMENT OF GI MOTILITY DISORDERS – ROOM E5

OP257 PREVENTION AND TREATMENT OF ADVANCED DENTAL EROSION DUE TO GASTRO-OESOPHAGEAL REFLUX

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Introduction: Approximately 60% of patients presenting to dentists with dental erosion have significant gastrooesophageal reflux (GERD)[1]. The paucity of typical GERD symptoms complicates the initial diagnosis, as well as the appraisal of a response to preventative measures. No treatment studies have been reported, except a small pilot study[2] and the natural history of GERD in these patients is unknown.

Aims & Methods: Detailed dental and endoscopic assessments and exclusion of other causes of dental erosion were performed in 72 successive male and female patients of mean age 34 years presenting to dentists with significant dental erosion, who had increased GERD by 24-hour multichannel intraluminal pH-impedance measurement (pH-MII). None had previously had proton pump inhibitor treatment and their median Reflux Disease Questionnaire score (interquartile range) was 3 (1-5). All were subsequently treated with esomeprazole 20mg twice-daily. After a median follow-up of 1 year, pH-MII was repeated off-PPI and dental erosion was reassessed for progression.

Results: At follow-up, reflux had normalized in 27 (38%) of patients with dental erosion. Normalization of reflux occurred in similar numbers of patients with (41%) and without (37%) progression of erosion. No progression of erosion was observed in 53 (74%) of patients treated with esomeprazole 20 mg twice-daily. None of the baseline demographic, clinical, endoscopic or pH-MII characteristics were significantly associated with progression of dental erosions at follow-up.

Conclusion: In a subset of patients with oligosymptomatic GERD and dental erosion, reflux appears to normalize after a median follow-up of one year. Progression of erosion did not occur in the majority of patients with esomeprazole 20 mg twice-daily. No baseline characteristics were predictive of progression of erosion. As no treatment guidelines for this increasingly encountered group of patients with GERD-associated oral pathology exist, we currently recommend preventative twice-daily proton pump inhibitor treatment with biannual expert dental and pH-MII evaluation.

References

1. Wilder-Smith CH, et al. *UEGJ* 2014. Published online before print September 11, 2014, doi: 10.1177/2050640614550852.
2. 2.Wilder-Smith CH, et al. *Am J Gastroenterol.* 2009;104:2788-2795.

Disclosure of Interest: None declared

OP258 DIGESTIVE SYMPTOMS AFTER SLEEVE GASTRECTOMY: USEFULNESS OF ESOPHAGEAL HIGH-RESOLUTION MANOMETRY WITH IMPEDANCE

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Introduction: Sleeve gastrectomy (SG) has become the most frequent bariatric surgery perfomed in western countries. Digestive symptoms are less frequent than after gastric banding, but the volume reduction of the gastric cavity may lead to GER or food intolerance. Gastric stasis and post-prandial regurgitations have been shown to occur after SG (1).

Aims & Methods: The goal of this retrospective study was to evaluate the impact of esophageal high resolution manometry together with impedance (HRMI) on the management of upper GI symptoms occuring after SG.

Twenty-four patients (18 women), mean age 39 years-old (range 38-58) underwent HRMI (Manoscan, Given Imaging, Duluth, GA) within a mean delay of 3 months (range : 2-50) after SG. All but 4 patients had upper GI symptoms at the time of HRMI. The procedure was performed with 10 swallows of 5 ml water in supine position, repeated swallows of 2 ml of water, and with the rapid ingestion of 200 ml of water in the sitting position. The analysis of HRM was performed according to the Chicago classification. Intra-gastric pressure (IGP) was also measured after ecah swallow. Thirteen patients also underwent an abdominal CT scan with filling of the stomach with gastrobubbles, and 3D reconstruction, to measure the volume of the sleeve. Results are expressed as mean (SD), and comparisons between groups performed by ANOVA.

Results: An increase IGP during 5 ml-swallows was observed in 18 patients (75%) : when present, this IIGP occurred in 30 to 100% of swallows (mean 35%). This IIGP was not correlated to the presence of digestive symptoms, weight loss, to the residual volume of the gastric pouch as measured by 3D-CT scan, nor to the time between the surgery and the HRMI.

Reflux episodes were detected by impedance in 47% of cases, and occurred between 10 and 100% of 5 ml-swallows (mean 20%). Patients with reflux episodes detected by impedance had more often GER symptoms (63% vs 10%, $p < 0.02$), less vigorous esophageal peristaltis (mean DCI = 1307 (663) mmHg.cm.s vs 3510 (629), $p < 0.03$), and a smaller gastric pouch volume (138 (28) ml vs 232 (31), $p = 0.054$). There was no correlation between IIGP and reflux episodes.

Conclusion: Increased intra-gastric pressure during 5 ml-swallows is very frequent after SG : it indicates a decrease of the compliance of the gastric pouch, but seems independant of digestive symptoms, since it may be present in asymptomatic subjects after SG. Reflux episodes are also very frequent and are significantly associated with typical GERD symptoms, hypotonic esophageal peristalsis and a smaller volume of the gastric pouch. HRMI may thus be uselful for the diagnosis of GERD after SG.

Reference

1. Del Genio, et al. *Obes Surg* 2014; 24: 71–7.

Disclosure of Interest: F. Mion Financial support for research: Given imaging, Consultancy: given imaging, S. Marjoux: None declared, E. Pelascini: None declared, J.-R. Risson: None declared, M. Robert: None declared, S. Roman Financial support for research: Given imaging, Consultancy: Given imaging

OP259 PER-ORAL ENDOSCOPIC MYOTOMY FOR ACHALASIA. HOW ARE THE PATIENTS DOING AFTER MORE THAN TWO YEARS?

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Introduction: Per-Oral Endoscopic Myotomy (POEM), for the treatment of achalasia, combines the benefits of a minimally invasive approach with the long term efficacy of a surgical procedure. The short-term efficacy of POEM has been the object of various publications. However, only scanty data on the long-term follow-up are available nowadays. We report on a consecutive series of patients with achalasia who underwent POEM more than 2 years ago.

Aims & Methods: A total of 252 patients underwent POEM in a single tertiary referral endoscopy center between 2011 and April 2015. Sixty-four patients (mean age 47.5 years, 24 males) were treated more than 2 years ago and were included in the study.

After POEM patients underwent a close follow-up, including high-resolution manometry, EGD, pH-metry and timed barium swallow (TBS). Data on the clinical history, procedure and follow-up were prospectively collected and analyzed. Clinical success was defined by and Eckardt score < 4. ANOVA and Fisher's Exact test were used to identify factors related with clinical failure.

Results: Forty-two patients (68.8%) have a 2-year follow-up, 16 (26.2%) a 3-year follow-up and three (4.9%) a 4-year follow-up. Three patients (4.7%) were lost-at-follow-up.

At the last follow-up visit (mean 26.7 months), POEM was successful in 53/61 patients (86.9%). Clinical success decreased with time, being 98.4%, 95.2%, 91.7%, 90.0% and 83.3% at the 3-month, 6-month, 1-, 2-, and 3-year follow-up, respectively. Symptoms recurred in 8 patients, in 3 cases within the first year, in 3 cases after 2 years, in 1 patient after 3 years. Pneumatic dilation (PD) was proposed as initial rescue therapy in case of recurrence. Two patients refused PD and preferred surgery. Four patients underwent PD (30mm balloon); in 2 patients (50%) symptoms persisted after PD and additional sessions were scheduled. Two patients are still awaiting PD. During follow-up, esophagitis was diagnosed in 16.9% of patients (10/59 with EGD). Altered esophageal acid exposure was seen in 51% of patients (26/51 with pH-metry); 19.7% of patients complained with heartburn. In all the cases, esophagitis and heartburn completely disappeared with medications.

At univariate analysis, no differences were observed in patients with or without a successful treatment in terms of gender, age, type of achalasia, total length of myotomy, post-operative LES pressure (4sIRP). In case of clinical success, the myotomy on the gastric side was significantly longer than in cases with symptoms recurrences (3.5cm vs 2.75cm, $p < 0.05$). At postoperative TBS, patients with recurrences had a larger esophagus (5.0cm vs 2.8, $p < 0.001$), and an higher column of barium at the end of the barium swallow (12.8cm vs 4.3cm), after 1 minute (11.7cm vs 3.4cm), 2 minutes (11.8cm vs 3.1cm), and 5 minutes (10.7cm vs 2.4cm) ($p < 0.001$).

Conclusion: Our study confirms the efficacy of POEM for the management of achalasia also at a mid-term-follow-up. However, success rate seems to decrease with time. Achalasia is a chronic illness, and the efficacy should be especially evaluated at long term. A long myotomy (>3cm) on the gastric side is likely associated with better outcomes

Disclosure of Interest: None declared

OP260 PER ORAL ENDOSCOPIC MYOTOMY: A PROSPECTIVE EVALUATION OF 86 CONSECUTIVE CASES

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Introduction: Per oral endoscopic myotomy (POEM) is an endoscopic alternative to laparoscopic myotomy. Herein, we report single-center mid-term results of POEM in the Czech Republic.

Aims & Methods: Since 2012, a total of 87 POEM procedures have been performed in 86 patients (38 women, 48 men, mean age 46). All patients had a

diagnosis of achalasia (n = 85) or jackhammer esophagus (n = 1) based on endoscopic, manometric and radiologic examinations. A follow up at 3, 6, 12 and 24 months was completed in 66, 60, 41 and 12 patients. The primary outcome was treatment success defined as an Eckardt score < 3. Three months after POEM, high resolution manometry and 24-hours pH metry monitoring were performed.
Results: A. PROCEDURE: POEM was successfully completed in all patients. The median length of the procedure was 70 minutes (range 32-145). The median myotomy length was 13 cm (8-19). In 42 patients (49%), capnoperitoneum had to be decompressed and 45 patients (52%) experienced a subcutaneous emphysema which resolved spontaneously. Fever was present on the first postoperative day (POD 1) in 9 patients (10%). Eighty five patients (99%) were discharged on the POD 2 or 3 and only one patient required prolonged hospitalization due to thoracic drainage of haemothorax. We observed the following minor complications: inadvertent mucosotomy 9x (treated with clips), respiratory instability during POEM 2x, bleeding at the entry site 2x, difficult entry site closure 2x (necessary to use high resolution clips) and large subcutaneous emphysema 2x.
B. TREATMENT RESULTS: 3, 6, 12 and 24 months after POEM, treatment success (Eckardt score < 3) was achieved in 65, 57, 41 and 10 patients (98%, 95%, 100% and 83%), median score pre- vs. post-treatment 7 vs. 0 at 3, 6 and 12 months, and vs. 1 at 24 months; $p < 0.001$. The median percentage of overall symptomatic improvement was 90%. Quality of life significantly improved (median score 104 before POEM vs. 130, 137, 139 and 138 at 3, 6, 12 and 24 months after POEM, $p < 0.001$). Manometric parameters (IRP and LES pressure) normalized in a majority of patients.
Heartburn has been present in 24% of patients and 19% of patients have been treated with proton pump inhibitors. Three months after POEM, a mild reflux esophagitis (LA A) was diagnosed in 19 patients (29%) and a pathological gastro-esophageal reflux (DeMeester score > 14) was detected in 24 (36%) patients.
Conclusion: POEM is a safe and effective treatment modality in patients with achalasia with excellent mid-term results which seems durable. Although post-POEM gastroesophageal reflux is present in 36% of patients, it causes no or mild symptoms and/or mild esophagitis in some patients.
Disclosure of Interest: None declared

OP261 EVALUATION OF ENDOSCOPIC ULTRASONOGRAPHY IN THE DIAGNOSIS OF SPHINCTER OF ODDI DYSFUNCTION

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) with manometry is the definitive investigation for the diagnosis of sphincter of Oddi dysfunction (SOD) but caries a significant risk of pancreatitis in ~15% of cases. Endoscopic ultrasonography (EUS) has been adopted in many centres as a preliminary investigation in patients considered to have SOD. This study aimed to examine the referrals for EUS to a tertiary hepatobiliary specialist centre with a potential diagnosis of SOD.
Aims & Methods: In all cases referred for evaluation of suspected SOD between January 2012 to April 2015, data was captured for age, sex, reason behind the SOD suspicion, derangement of liver function tests (LFT), findings at EUS and subsequent SOD classification.
Results: Of 1195 EUS procedures performed in this period, 5.9% (71/1195) were referred with a suspicion of SOD due to characteristic biliary pain of whom 34% (24/71) also had suggestive imaging (abnormal US/CT/MRCP). 83% (59/71) subsequently had findings consistent with SOD. Of these, the mean age was 43 years (SD ± 14) and 81% were women (48/59). In this group, 47% (28/59) had a normal EUS, 36% (21/59) biliary duct dilatation, 1 of whom also had pancreatic duct dilatation (1.7%; 1/59), 12% (7/59) had features of chronic pancreatitis, 10% (6/59) had fatty infiltration of the pancreatic parenchyma, 2% (1/59) had a duodenal diverticulum and 2% (1/59) had air in the biliary tree. Combining compatible EUS features with LFT derangement classified 10% (6/59) as Type 1 SOD, 56% (33/59) as Type 2 SOD and 34% (20/59) as Type 3 SOD. EUS revealed alternative diagnoses in 17% (12/71) of SOD queries. Of these, 42% (5/12) had microlithiasis, 25% (3/12) a biliary stricture, 17% (2/12) had pancreatic cysts, 8% (1/12) a pancreatic stricture and 8% (1/12) a duodenal diverticulum causing their symptoms and/or suggestive imaging.

Table 1: Subgroup analysis of suspected SOD referrals

	n	%
Outcome post EUS for all referrals	**71**	
SOD	59	*83*
Non-SOD	12	*17*
SOD classification post EUS	**59**	
Type 1	6	*10*
Type 2	33	*56*
Type 3	20	*34*
Alternative diagnosis post EUS	**12**	
Microlithiasis	5	*42*
Biliary Stricture	3	*25*
Pancreatic Cysts	2	*17*
Pancreatic Stricture	1	*8*
Duodenal diverticulum	1	*8*

Conclusion: Our findings highlight the importance of EUS in the evaluation of patients with a history or imaging suggestive of SOD. While the majority had EUS features consistent with this diagnosis, a significant proportion had alternative diagnosis. Precise evaluation of suspected SOD cases therefore avoids the need and risk of ERCP with manometry in a subgroup of patients who would subsequently have received it without EUS.
Disclosure of Interest: None declared

OP262 PERCUTANEOUS TIBIAL NERVE STIMULATION: A SUCCESFULL TREATMENT FOR PATIENTS WITH ANAL INCONTINENCE (URGENCY), LEADING TO A SUSTAINED RESPONSE AND MODULATING ANAL SPHINCTER PRESSURE AND RECTAL PERCEPTION

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Introduction: Little is known about the efficacy of PTNS treatment in urge anal incontinence. Our objective was to assess the long-term symptomatic response, anorectal motor and sensory function in incontinent patients treated by PTNS
Aims & Methods: This is a retrospective analysis of prospective sequential gathered data of 100 patients with anal urge incontinence treated with PTNS in a 3 year period (2010-2013). Patients had 21 treatment sessions within 8 months. St. Marks Incontinence-score and Visual Analogue Scale (VAS)-score of well-being in relation to their incontinence were collected at baseline, after 3, 8, 10 and 20 months. All patients had a high resolution manometry (sphincter pressure and rectal sensory testing) at baseline and after 12 weeks.
Results: A successful clinical response, defined as ≥ 50% reduction of the St. Marks, resp. VAS-score was reached at end of treatment (8 months) in 74% resp. 82.2% and at one year after end of treatment (20 months) in 71.1%, resp. 80.6% of the patients ($p < 0.001$). The sphincter squeeze pressure significantly improved from 126.5mmHg at baseline to 137.6 mmHg ($p < 0.001$) at 12 weeks. The constant perception for urge changed from 101.4ml to 120ml ($p = 0.002$), the maximal tolerable volume from 155.5ml to 183.7ml ($p < 0001$) after 12 weeks PTNS treatment. A significant, although weak correlation between clinical response and improvement of rectal sensory function was observed ($p = 0.04$, Spearman coefficient = -0.25)
Conclusion: PTNS is a minimal invasive treatment, with negligible side effects and a response rate of 80%. The therapeutic effect sustains at least one year after end of treatment. The treatment leads to a significant improvement of the sphincter squeeze pressure as well as the rectal perception.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 11:00–12:30
NUTRITION AND GI DISEASES – ROOM E6

OP263 THE CLINICAL AND PHENOTYPIC ASSESSMENT OF ULTRA-SHORT COELIAC DISEASE

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Introduction: Data suggests that an additional duodenal bulb (D1) biopsy may increase the diagnostic yield for coeliac disease (CD) by up to 10%. However no consensus exists on necessity of D1 biopsy. One reason may be that it is not clear if these patients with Ultra-Short Coeliac Disease (USCD) have the same phenotype or are at risk of the same consequences as conventional CD. We aimed to assess the clinical phenotypes of patients with USCD compared to those with conventional disease.
Aims & Methods: All patients attending a specialist CD endoscopy list were invited to take part. All patients had duodenal biopsy taken as routine. Patients had standard quadrantic biopsies taken from the second part of the duodenum (D2) and at least one biopsy taken from D1. Biopsies were analysed separately according to the Marsh classification system. Marsh 3 disease was required to diagnose CD. Patients had concurrent tissue tranglutaminase (tTG) and endomysial antibodies (EMA) and total IgA. All patients with VA were followed up in the CD specialist clinic where routine hematology, biochemistry, HLA typing and DXA scans were requested. Presenting symptoms and immunology were compared for all presentations. Hematology and biochemistry results were compared to a control group of patients that had CD excluded with normal serology and histology.
Results: 1378 new presentations (62% female; mean age 50.3) underwent duodenal biopsy. 268 (19.4%) new diagnoses of CD were made (66% female; mean age 41.6). CD patients were significantly younger than controls ($p < 0.0001$). 25/268 (9.3%) of new CD patients had USCD. Univariate analysis showed fewer USCD patients had diarrhoea than conventional CD (3.8 vs 24.0%, $P < 0.0001$). Decision tree analysis to identify USCD showed the absence of diarrhoea was the single discriminating factor (Adj $P = 0.018$). Rates of osteoporosis ($p = 0.78$) and anaemia ($p = 0.14$) were equal. Ferritin deficiency ($P = 0.007$) and folate deficiency ($P = 0.003$) rates were higher in conventional CD than USCD and controls. On multivariate analysis, patients with USCD were younger than

those with conventional CD 36.6 vs. 42.1 (AOR 0.97 (0.94 – 0.998) $P=0.03$), had lower tTG titres (AOR 0.89 (0.81 - 0.98) $P=0.02$) and were less likely to have folate deficiency (AOR 1.17 (1.01 - 1.36) $P=0.03$) compared to conventional disease.
Conclusion: USCD appears to represent early disease with younger age and lower tTG titres and may represent a milder form of CD with lower rates of diarrhoea and folate deficiency. Long-term follow-up of patients with USCD is required to fully assess the clinical impact of diagnosis.
Disclosure of Interest: None declared

OP264 POTENTIAL CELIAC DISEASE IN ADULTS: CLINICAL FEATURES AND NATURAL HISTORY

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Introduction: Potential celiac disease (PCD) is characterized by the positivity for serological and genetic markers with absent or minimal small intestinal damage. Little is known on PCD natural history in adults.
Aims & Methods: Our aim was to define the clinical features of adult PCD and to evaluate its evolution to overt CD in cases left on a gluten-containing diet. Seventy-seven (F/M 3.2:1; mean age 25 years) of 735 CD cases, consecutively diagnosed at our center, met the diagnostic criteria of PCD. Clinical and laboratory findings of PCD patients were evaluated at diagnosis and during a follow-up ranging from one to 10 years (mean 3 years).
Results: Sixty-one of the 77 PCD were symptomatic, whereas 16 did not complain of any symptom. Of the 61 symptomatic, 10 showed diarrhea and weight loss, while 51 had other gastrointestinal (alternating bowel habit/constipation) and extra-intestinal manifestations (anemia, osteopenia, aphthous stomatitis, hypertransaminasemia, recurrent miscarriages). IgA tissue transglutaminase (TGA) and endomysial antibodies (EmA) were positive in all but one patient with IgA deficiency (TGA IgG+). HLA typing displayed DQ2 in 73 cases, whereas 3 and 2 patients had DQ8 and DQB1*02. Duodenal biopsy showed normal mucosa in 20 and high IELs count in 57 cases. All the 61 symptomatic PCD started a gluten-free diet (GFD) with a significant clinical improvement. The 16 asymptomatic PCD remained on a gluten-containing diet and were periodically followed up by serology and duodenal biopsy. Only one patient became symptomatic and developed flat mucosa, whereas the other 15 did not develop either symptoms or villous atrophy and 4 of them became antibody-negative.
Conclusion: PCD frequency is increasing in adults, accounting for about 10% of the total diagnoses. The majority of PCD cases in adulthood is symptomatic and significantly benefits from GFD. In contrast, our study indicates that GFD is not recommended in adult asymptomatic PCD, since these patients do not tend to experience symptoms over time with a possible antibody disappearance and without progression to severe intestinal damage.

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Disclosure of Interest: None declared

OP265 HLA-DQ8 CELIAC SUSCEPTIBILITY GENE IS IMPORTANT IN THE DEVELOPMENT OF BEHAVIOURAL AND MOTILITY CHANGES ASSOCIATED WITH GLUTEN SENSITIVITY

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Introduction: Non-celiac gluten sensitivity is a frequent disorder, which shares many clinical features with irritable bowel syndrome and celiac disease, including gastrointestinal symptoms and frequent psychiatric comorbidity. Its pathophysiology is poorly understood and may involve immune and genetic factors, as 50% of these patients express celiac risk alleles. Gluten sensitization and challenge in genetically predisposed mice generates immune activation and gut cholinergic nerve dysfunction, however the *in vivo* correlates of these findings are unknown.
Aims & Methods: Our aim was to investigate the effect of gliadin sensitisation and challenge on behaviour and motility in wild type and mice expressing the human HLA-DQ8 gene.
SPF C57Bl/6 and NOD-DQ8 mice maintained on a gluten-free diet were orally sensitized with cholera toxin (CT) and gliadin weekly for 3 weeks, while control mice received CT alone. Two weeks later, mice were challenged with gliadin (2mg/mouse) or vehicle 3 times per week for 2 weeks by oral gavage. Gastrointestinal motility and behavioural profile were assessed before and after gliadin challenge. Mice were sacrificed thereafter and tissue samples were collected. Motility was assessed by bead videofluoroscopy (Reed *et al* 2014), behaviour was studied by the step-down, light preference and tail suspension tests. Statistical analysis was performed using Mann-Whitney or t-tests, as appropriate.
Results: Gliadin sensitization, without gliadin challenge, did not affect motility or behaviour in C57Bl/6 or in NOD-DQ8 mice. After gliadin challenge, no changes in motility or behaviour were observed in sensitized C57Bl/6 mice. However, NOD-DQ8 mice displayed anxiety-like behaviour, as they stepped down from an elevated platform with longer latency compared to controls and they tended to spend less time in the illuminated compartment. Videofluoroscopy showed delayed gastrointestinal transit in challenged NOD-DQ8 mice compared to controls. Although a mild reduction in the villi/crypt ratio was observed in NOD-DQ8 compared to C57Bl/6 mice, no marked inflammatory or atrophic lesion was observed. Mice with higher levels of serum anti-gliadin (AGA) IgG antibodies displayed more anxiety-like behaviour and slower transit time than mice with lower AGA titers. IgA anti-transglutaminase antibodies were not detected in any experimental group.
Conclusion: Gliadin sensitization and challenge induced anxiety-like behaviour and gastrointestinal dysmotility in NOD-DQ8 mice, but not in C57Bl/6 mice. These changes were observed in the absence of mucosal atrophy or TTG antibodies, but were associated with gliadin specific antibody responses. This study suggests that the HLA-DQ8 celiac susceptibility gene is important in the development of altered behaviour and gut dysfunction associated with gluten sensitivity. These changes occur in the absence of atrophy and thus supports the concept of an underlying "celiac light" condition in gluten sensitivity.
Disclosure of Interest: None declared

OP266 COMPARISON OF LYOPHILIZED MONO- AND THREE-STRAIN PROBIOTIC AND ALIVE MULTISTRAIN PROBIOTIC ADMINISTRATION FROM CHILDHOOD FOR PREVENTION OF OBESITY IN ADULT

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Introduction: Today it is well known the association between obesity and alteration of microbiota composition in gut. Obesity contributes to destroying microbiocenosis of intestine, and in turn dysbiosis leads to excessive energy storage via various molecular pathways including increased production of short chain fatty acid and decreased expression of fasting-induced adipose factor and AMP-activated protein kinase. Such feedback loop explains the efficacy of probiotic in obesity treatment but there is still a gap in knowledge of which probiotics are more effective. Our study was aimed to compare the antiobesity effects of intermittent introduction by short courses of lyophilized three-strain and alive multistrain probiotic.
Aims & Methods: Seven groups of rats (control, MSG- and 5 MSG + probiotic group) were included. All newborn rats except control were injected with monosodium glutamate (MSG) (4 mg/g) at 2-10th days of life. MSG + probiotic groups were treated intermittently from one-month age with lyophilized monoprobiotics *B.animalis VKL*, *B.animalis VKB*, *L.casei IMVB-7280*, mix of these three probiotic strains and alive multiprobiotic "Symbiter" containing concentrated biomass of 14 alive probiotic bacteria (*Bifidobacterium, Lactobacillus, Lactococcus, Propionibacterium)*. Anthropometric parameters (weight, body length) of rats were measured, body mass index (BMI) and index Lee were calculated, total visceral adipose tissue (VAT) was weighed, biochemical parameters of lipid metabolism and level of adipocytokines (adiponectin and leptin) in serum were estimated. The clinical studies of anti-inflammatory properties of the most effective probiotic were performed.
Results: We established the beneficial effect of all probiotics intermittent administration from childhood on obesity parameters in adult rats. The most pronounced effect was detected in group treated with alive multistrain probiotic. In this group we found the greatest lowering of body weight, BMI, index Lee, improvement of biomarkers of lipid metabolism in blood (the decrease of very low-density lipoproteins and raise of content of high density lipoproteins). The normalization of hormonal activity of VAT was observed in rats treated with multistrain probiotics: the level of leptin reduced by 14.3% ($p < 0.05$) and adiponectin raised by 89% ($p < 0.05$) compared to MSG-group. In obese humans with elevated transaminases we assessed levels of proinflammatory cytokines (TNF-α, IL1β, IL6, IL8, INFγ) and showed their decreased after multistrain probiotic treatment.
Conclusion: The comparative study suggest the beneficial role of probiotic bacteria for visceral obesity treatment and confirmed the most significant antiobesity properties of alive multistrain probiotic.
Disclosure of Interest: None declared

OP267 IMPACT OF GASTRIC EMPTYING AND SMALL INTESTINAL TRANSIT ON BLOOD GLUCOSE, INTESTINAL HORMONES, GLUCOSE ABSORPTION IN THE MORBIDLY OBESE

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Introduction: The superiority of Roux-en-Y gastric bypass over gastric banding in inducing weight loss and improving glycaemic control may relate to the

exaggerated release of gut hormones from the distal intestine which plays important roles in the regulation of appetite and blood glucose. We have shown that rapid gastric and small intestinal transit is a major determinant of changes in blood glucose, intestinal hormones, and glucose absorption after gastric bypass (Nguyen et al. *Obesity* 2014), suggesting that slower small intestinal (GI) transit may be important in the pathogenesis of obesity.

Aims & Methods: The aim is to evaluate gastric emptying and small intestinal transit of the morbidly obese and their relationship to glycaemia, incretin hormones, and glucose absorption. Gastric emptying and caecal arrival time (CAT) of a mixed meal were assessed in 27 morbidly obese (age: 50.2 ± 2.5yrs; 18F:9M; BMI: 48.6 ± 1.8kg/m^2) and 10 lean healthy (age: 38.6 ± 8.4yrs; 5F:5M; BMI: 23.9 ± 0.7kg/m^2) subjects, using scintigraphy. The mixed meal consisted of a 50g beef patty (584 kJ) labelled with 15MBq ^{99m}Tc-sulfur colloid and a 150ml glucose drink (50g of glucose, 840 kJ), containing 3MBq ^{67}Ga-EDTA and 3g 3-O-methylglucose (3-OMG, to assess glucose absorption). Blood glucose, plasma 3-OMG, insulin, glucagon, glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) were measured over 240 min. Insulin resistance was also assessed by HOMA-IR score.

Results: Compared to lean subjects, gastric emptying (GE-t50: 60.7 ± 6.5 vs. 41.1 ± 7.3min; P = 0.04) and CAT (221.5 ± 9.8 vs. 148.0 ± 7.1min; P < 0.001) were prolonged in the morbidly obese, and associated with smaller rises in GLP-1 (P = 0.04), GIP (P < 0.001), insulin (P = 0.02) and 3-OMG (P < 0.001). In contrast, both fasting (P = 0.045) and post-prandial (P = 0.012) plasma glucagon concentrations were higher in the obese. Although both fasting (P < 0.01) and post-prandial (P < 0.001) blood glucose were higher in the obese, the magnitude of the post-prandial glycaemic rise was less than that in lean subjects (P = 0.03). HOMA-IR score was higher in the obese subjects (4.5 ± 0.7 vs. 1.5 ± 0.2; P = 0.01).

Conclusion: Gastric emptying and small intestinal transit are slower in the morbidly obese, which is associated with lower plasma GIP and GLP-1 but higher glucagon concentrations. Given rapid gastrointestinal transit is a major determinant of weight loss after gastric bypass surgery, the current finding of slower gastric emptying in the morbidly obese may be central to the pathogenesis of obesity and warrants further evaluation.

Disclosure of Interest: None declared

OP268 ELECTROMAGNETIC GUIDED BEDSIDE VERSUS ENDOSCOPIC PLACEMENT OF NASOENTERAL FEEDING TUBES IN SURGICAL PATIENTS: A MULTICENTER RANDOMIZED CONTROLLED NON-INFERIORITY TRIAL

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Introduction: Gastroparesis in surgical patients frequently leads to the need for enteral feeding through a nasoenteral feeding tube. Endoscopic tube placement is relatively cumbersome for patients and labour-intensive for hospital staff. Electromagnetic (EM) guided bedside placement by nurses may reduce patient discomfort, workload, and costs, but evidence from comparative studies is lacking.

Aims & Methods: In this investigator-initiated, multicenter, randomized controlled non-inferiority trial, adult patients admitted to gastrointestinal surgical wards in five Dutch hospitals requiring nasoenteral feeding, were randomly assigned (1:1) to undergo EM guided or endoscopic nasoenteral feeding tube placement. The primary endpoint was the need for reinsertion of an endoscope and/or tube (e.g. after failed initial placement or dislodgement/blockage of the tube). Successful tube placement was defined as a position of the tip beyond D2 (or in the efferent jejunal limb if applicable) on imaging followed by successful delivery of enteral feeding. The trial was designed to assess non-inferiority of EM guided placement with a pre-specified non-inferiority margin of 10% more patients requiring reinsertion. The trial is registered in the Dutch Trial Register, number NTR4420.

Results: Between March 2014 and March 2015, a total of 154 patients were enrolled (88% after gastrointestinal surgery, 12% managed non-operatively). Reinsertion of an endoscope and/or tube (primary endpoint) occurred in 27 of 80 patients (34%) in the EM guided group and 31 of 74 patients (42%) in the endoscopic group (absolute risk difference -8%, upper limit of one-sided 95% CI 5%, p for non-inferiority = 0.01). No significant differences were noted in success rates of primary tube placement (56 [71%] vs. 52 [70%], RR 1.01 (95% CI 0.82-1.24), p = 0.93) or tube related complications, such as dislodgement and blockage (43 [54%] vs. 36 [49%], RR 1.11 (95% CI 0.81-1.51), p = 0.52). Conscious sedation was used in none of the 79 (0%) patients undergoing EM guided placement vs. 61 of 69 (88%) patients undergoing endoscopy. Although the level of discomfort (visual analogue scale) was higher in the EM guided group (median [IQR] 3.9 [2.0-6.6] vs. 2.0 [0.2-5.6], p = 0.009), pain, social embarrassment, anxiety and total burden were not significantly different between the two groups and EM guided placement received higher recommendation scores than endoscopy (median [IQR] 8.2 [4.8-9.9] vs. 5.5 [2.3-7.8], p = 0.008).

Conclusion: EM guided bedside placement of nasoenteral feeding tubes by nurses was non-inferior to endoscopic placement and may therefore be considered the preferred technique for nasoenteral feeding tube placement in surgical patients.

Disclosure of Interest: A. Gerritsen Financial support for research: This study was supported by Stichting Agis (Amersfoort, the Netherlands), Stichting Achmea Gezondheidszorg (Leiden, the Netherlands) and CORPAK MedSystems UK (Gatwick, United Kingdom). The sponsors had no influence on the design of the study; neither did they have any influence on the data collection, interpretation or decision to publish the results. The authors have no individual agreements, affiliations with or involvement in any of these organizations., T. de Rooij: None declared, M. Dijkgraaf: None declared, O. Busch: None declared, J. Bergman: None declared, D. Ubbink: None declared, P. van Duijvendijk: None declared, G. W. Erkelens: None declared, P. Kruyt: None declared, D. J. Bac: None declared, C. Rosman: None declared, A. Tan: None declared, I. Q. Molenaar: None declared, J. Monkelbaan: None declared, E. Mathus-Vliegen: None declared, M. Besselink: None declared

TUESDAY, OCTOBER 27, 2015 11:00–12:30

NEW INSIGHTS INTO THE PATHOPHYSIOLOGY AND PATHOGENESIS OF FUNCTIONAL BOWEL DISORDERS – ROOM B3

OP269 THE ROLE OF ZONULIN IN NON-CELIAC GLUTEN SENSITIVITY AND IRRITABLE BOWEL SYNDROME

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Introduction: Zonulin, the human homolog of the zonula occludens toxin secreted by *Vibrio cholera*, is the only known endogenous modulator of epithelial tight junctions (TJs) and intestinal permeability. Intestinal bacterial infections and gluten evoke zonulin release in the intestinal milieu and in the bloodstream. A role for zonulin has been demonstrated in different diseases such as celiac disease (CD). Increased intestinal permeability has been reported in Non-Celiac Gluten Sensitivity (NCGS) and Irritable Bowel Syndrome (IBS) although the mechanisms involved are not clear. Zonulin serum levels and its diagnostic value in NCGS and IBS remain undetermined

Aims & Methods: In the present study, we aimed at characterizing zonulin serum levels in patients with NCGS (n = 27) and IBS-D (n = 15) compared with CD (n = 15; positive control) and healthy controls (n = 15; HC, negative control). ELISA assay was used to evaluate zonulin serum levels; qPCR was used to evaluate zonulin gene expression in the colonic mucosa. Clinical data, abdominal symptoms and bowel habit were recorded and analysis of HLA alleles was performed. Zonulin serum levels were evaluated in a subgroup of NCGS patients during gluten containing diet (GCD) and gluten free diet (GFD).

Results: CD patients showed significantly higher zonulin serum levels compared to HC (0.033 ± 0.004 vs 0.007 ± 0.001 ng/mg total proteins, p < 0.0001) and to IBS-D patients (0.012 ± 0.002 ng/mg total proteins, p < 0.001). NCGS showed significantly higher zonulin serum levels compared to HC (0.030 ± 0.006 vs 0.007 ± 0.001, p < 0.05) and IBS-D (p < 0.05). IBS-D patients showed higher zonulin serum levels and colonic mRNA expression compared to HC. Zonulin levels were positively correlated with the titer of anti-TTG antibodies (r:0.6; p < 0.05) and anti-DGP antibodies (r:0.6; p < 0.05). A decrease in zonulin serum levels was observed during GFD compared to GCD (p = 0.06) and a comparable decrease was observed for AGA IgG levels (p = 0.06). Only HLA-DQ2-positive patients showed a significant decrease in zonulin serum levels during GFD compared to GCD (p < 0.05). A significant difference was observed in zonulin serum levels during GFD between HLA-DQ2-positive patients and HLA-DQ2/DQ8 negative ones (p < 0.05).

Conclusion: Zonulin serum levels are increased in IBS-D and NCGS, in addition to CD. A positive and significant correlation was found between zonulin serum levels and both anti-DGP and anti-TTG antibody titers. A comparable decrease of AGA IgG and zonulin serum levels was observed during GFD. Interestingly, only HLA-DQ2-positive patients showed a significant decrease of zonulin serum levels during GFD compared to GCD. Our data suggest that a zonulin-dependent TJ dysfunction may play a role in the pathophysiology of IBS and NCGS, particularly in a subset of patients.

Disclosure of Interest: None declared

OP270 PRINCIPAL COMPONENT ANALYSIS (PCA) WITH REPLICATION CONFIRMS FOUR INDEPENDENT ETIOLOGICAL FACTORS IN IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: Multiple variables have been identified that separate IBS patients from healthy controls, including visceral hypersensitivity, motility, stool consistency abnormality, and psychological traits. It is not yet known if these variables are separate or mutually dependent.

Aims & Methods: We aimed to determine whether the variables discriminating a large sample of IBS patients from a demographically similar group of healthy individuals cluster together in distinct patterns that suggest independent pathophysiological factors in IBS. We tested 530 IBS patients (Rome II or III criteria+ physician diagnosis; 79.4% females; mean age = 35.8 years) and 337 control subjects without gastrointestinal problems (78.7% females; mean age = 34.7 years). Subjects completed psychological and gastrointestinal symptom questionnaires, as well as barostat tests to measure bowel sensory thresholds with the ascending method of limits (AML) method and the colonic motility index at rest,

after the AML, after recovery, and after a standard meal. In the control group, barostat testing was only conducted in a sub-set of 41 individuals. All variables that significantly ($p < 0.05$) differentiated IBS and control subjects (listed in the Table) were entered into PCA analysis (a statistical method useful for discovering independent dimensions among inter-correlated variables) with varimax rotation. The PCA was run twice, on randomly divided equal-size halves of the total IBS sample, to examine the stability of the generated model.
Results: Significant differences between IBS and control subjects were found on all test variables except motility post-meal, which was excluded from the PCAs. The initial PCA, on half the total IBS sample, yielded 4 factors that were easily identifiable as representing psychological functioning, motility, visceral sensitivity, and abnormal stool consistency, and collectively explained 63.9% of the total variance (see Table). The replication PCA conducted with the other half of the IBS sample yielded the same 4 factors with similar loadings, confirming the IBS factor structure, and explained 63.4% of the variance.

Numbers in table are factor loadings: Factors scoring < 0.35 have been set to 0 for clarity

	Factors:			
Psychological Functioning	**Motility**	**Visceral Sensitivity**	**Abnormal Stool Consistency**	
Hard stools by Rome II and III	0	0	0	-0.776
Soft stools by Rome II and III	0	0	0	0.798
Motility Index (baseline)	0	0.827	0	0
Motility Index (distension)	0	0.692	0	0
Motility Index (recovery)	0	0.816	0	0
AML Pain Threshold	0	0	0.939	0
AML Urge Threshold	0	0	0.934	0
Catastrophizing	0.659	0	0	0
RPSQ Somatization	0.621	0	0	0
BSI Depression (BSI-18)	0.838	0	0	0
BSI Anxiety (BSI-18)	0.838	0	0	0
Neuroticism (NEO-PI)	0.724	0	0	0

Conclusion: Our findings of four robust and replicable factors in our large IBS sample confirm that psychological variables, motility, visceral sensitivity and stool consistency abnormalities are all independent and prominent etiological contributors to IBS. [Supported by grant RO1 DK31369]
Disclosure of Interest: None declared

OP271 DIFFERENTIAL EXPRESSION OF MIRNAS IN THE JEJUNAL MUCOSA OF IBS-D IS INVOLVED IN INTESTINAL EPITHELIAL BARRIER DYSFUNCTION THROUGH MODULATION OF SPECIFIC TIGHT JUNCTION PROTEINS

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Introduction: miRNAs play a crucial role in the control of intestinal epithelial barrier function by modulating stability and translation of mRNAs encoding tight junction proteins. We have previously shown differential mRNA expression associated to ultrastructural abnormalities of the epithelial barrier, mast cell activation and symptoms in IBS-D patients. However, the role of miRNAs modulating intestinal dysfunction in IBS-D has not been fully addressed.
Aims & Methods
Aims: to identify dysregulated miRNAs in the small bowel mucosa of IBS-D patients and to identify targets specifically involved in intestinal epithelial barrier function.
Healthy controls (n = 31) (HC) and non-allergic, non-celiac, IBS-D patients (n = 45) were studied. Total RNA and protein from jejunal tissue were analyzed to identify potential candidates by: a) miRNA/mRNA profiling, by RNAseq and nCounter analysis; b) Pathway analysis and upstream regulator identification; and c) miRNA and target validation by nCounter nanostring analysis, qPCR and Western blot.
Results: Thirty-two miRNAs and 3086 mRNAs were differentially expressed (FDR < 0.05) between HC and IBS-D. Pathway and network analysis identified miR-125b as playing a central role by targeting genes involved in molecular functions and pathways relevant for modulation of epithelial barrier function like tight junction and cytoskeleton signaling pathways. Validation of selected genes showed consistent up-regulation in 7 out of 9 mRNAs involved in epithelial barrier function (Table 1). Moreover, six miRNAs (including miR-125b) identified as down-regulated in IBS-D in our miRNA profiling experiment were also highlighted as predicted to be inhibited based on the expression pattern of their targets. Down-regulation of all six miRNAs was validated by qPCR ($P < 0.05$). Bioinformatic analysis of putative miRNA binding sites by TargetScan identified miR-125b and miR-16 as potentially regulating expression of cingulin (*CGN*) and claudin 2 (*CLDN2*). Consistently, expression of these two proteins was up-regulated in IBS-D samples (*CGN* fold-change 1.5; $P < 0.01$; *CLDN2* fold-change 1.7; $P < 0.01$). Down-regulation of both miRNAs negatively correlated with bowel habits ($r > -0.55$; $P < 0.01$) and mast cell numbers ($r > -0.52$; $P < 0.01$) while up-regulation of *CGN* and *CLDN2* protein positively correlated with bowel habits ($r < 0.60$; $P < 0.001$).
Conclusion: Modulation of the intestinal epithelial barrier function in IBS-D involves both transcriptional and post-transcriptional mechanisms. These molecular mechanisms include miRNAs as master regulators in controlling the expression of TJ proteins and are associated with major clinical symptoms and mast cells.
Disclosure of Interest: None declared

OP272 AUTOMATING THE ANALYSIS OF HIGH-RESOLUTION COLONIC MANOMETRY DATA

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Introduction: The introduction of high-resolution manometry to record colonic motor patterns has helped to quantify and define both normal and abnormal colonic motor patterns in health (1) and disease (2). However, the recording also generates large quantities of data that makes manual analysis both time consuming and subject to bias, and therefore the findings are difficult to standardize amongst different research groups.
Aims & Methods: We have used colonic manometry data recorded for two previous publications (1, 2). Data were recorded with a 72 sensors (spaced at 1cm intervals) fibre-optic manometry catheter from 12 healthy controls (5 men; median age 51 years; range 27 - 69 yrs) and 14 patients (2 men; median age 52 years; range 24 - 76 years) with scintigraphically defined STC. The manometric recordings were taken for two hours pre and post a 700cKal meal. The approach used in this work was adapted from a technique developed in the field of meterorology (3), and effectively identifies wave forms in adjacent channels of data and determines the likelihood that the wave forms are associated with one-another; it therefore identifies propagating events. Utilising the baseline-corrected data from each study, the automated analysis applied a cross wavelet transform between each pair of adjacent sensors, for each region in the colon (proximal, descending and sigmoid colon). The technique averages the phase of the transformed data over the duration of each period, weighted by the amplitude of the transformed data. The result is then averaged over all pairs of adjacent channels per region. The value for each region, in each of the groups (health and patients) was then averaged across each of the subjects within each group. The end result indicates a distribution of propagating activity (antegrade / retrograde) over the propagation-velocity and frequency of the propagating activity.
Results: The group mean data for each region in healthy controls and patients with slow transit constipation is shown in fig 1. In health (post meal) motor activity in the proximal and descending colon is characterized by predominantly antegrade propagating events that occurs at > 1 per min and travel at ~0.5cm/s. In contrast in the sigmoid colon, propagating activity is

Abstract number: OP271

	RNAseq			nCounter		
Gene	**Mean Reads**	**Fold-change**	**FDR- adjusted P-value**	**Mean Counts**	**Fold-change**	**FDR- adjusted P-value**
CDH1	5220	1.8	0.00001***	10283	1.8	0.0002***
CELF1	524	1.3	0.003**	768	1.5	0.0001***
CGN	2188	1.5	0.0001***	1048	1.4	0.05*
CTNNA1	2875	1.5	0.002**	4671	1.6	0.007**
CTNNB1	1998	1.4	0.01*	5892	1.3	0.01**
F11R	3013	1.8	0.0001***	2429	1.6	0.007**
JAM2	119	-1.3	0.03*	278	1.2	0.34
JAM3	70	1.5	0.02*	113	1.3	0.06
PLEKHA7	692	1.8	0.002**	465	1.6	0.01**

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	vehicle	antibiotic treatment	2 wkspost antibiotic discontinuation	4 wkspost antibiotic discontinuation	6 wkspost antibiotic discontinuation
GI motility(geometric centre)	7.50 ± 0.33	8.63 ± 0.08*	8.24 ± 0.15*	8.49 ± 0.38*	7.81 ± 0.25
muscle tension(EFS, 40Hz)	126 ± 12	45 ± 8*	43 ± 11*	93 ± 14	102 ± 10
damage of the ENS (score)	-	+++	++++	++	+
GDNF mRNA levels (ΔC_T)	7.3 ± 0.2	1.7 ± 0.5*	2.3 ± 0.3*	2.7 ± 0.2*	2.5 ± 0.5*

*$P < 0.05$ *vs* vehicle

predominantly retrograde, occurring at 2-4/min, traveling at speeds between 0.5-8cm/s. No dominant post-prandial propagating activity is seen in the patient data.
Conclusion: This automated technique clearly defines both regional differences of propagating activity within the healthy human colon, and differences between patients with slow transit constipation and healthy controls.

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Disclosure of Interest: None declared

OP273 SEARCHING FOR GENES WHERE THE SUN DON'T SHINE: A PILOT GENOME-WIDE ASSOCIATION STUDY (GWAS) OF STOOL FREQUENCY IN A SWEDISH POPULATION-BASED SAMPLE

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Introduction: Normal gut function, including regular defecation, is of key relevance to human wellbeing. This is evident, for instance, from alterations of stool frequency and pattern frequently observed in functional disorders such as irritable bowel syndrome (IBS), where these are in fact regarded as intermediate phenotypes or endophenotypes of disease. While stool frequency appears to be a rather stable intra-individual phenotype from clinical observations, anecdotal evidence suggests it may have familial aggregation although this has never been scientifically investigated. We explored the potential correlation between genotype and stool frequency/pattern by studying GWAS data in relation to daily bowel function recordings in 251 Swedish healthy individuals.
Aims & Methods: 251 participants from the Population-based Colonoscopy cohort (PopCol) were included, with available genome-wide genotype (Illumina HumanOmniExpressExome+) and recorded questionnaire data including daily recordings of bowel movements (BM) scored on the Bristol Stool Form Scale (BSFS) over 1 week. 637,607 SNP markers from 247 individuals passing quality control (QC) filters were studied in relation to quantitative measures of stool frequency and pattern (BM/day, total BSFS/day) using linear regression adjusting for age and gender under an additive genetic model. Enrichment of Gene Ontology (GO) terms was performed with hypergeometric test based tools.
Results: Genome-wide association testing of bowel movement frequency and BSFS scores identified a total of 86 suggestive (P < 5x10-5) association signals, spread over 41 genes. Among these, strongest associations were detected respectively in the *TEAD1* gene on chr 11 (P = 6.42x10-7 for rs10766003) and the *PLIN3*promoter on chr 19 (P = 6.57x10-7 for rs3760949). Gene set enrichment analysis highlighted specific GO pathways including smooth muscle contraction, cellular response to organic cyclic compound and almost reassuringly, response to caffeine.
Conclusion: "Outside-the-box" approaches to gene-hunting in gastroenterology may provide valuable clues to human gut function and physiology, and therefore improve our understanding of GI disease. Massive-scale efforts are required to reach adequate statistical power for the analyses of "loose" phenotypes, though these appear feasible if existing epidemiological and genetic data from several population-based cohorts are combined and exploited. We provide preliminary evidence that specific genes and associated pathways may be relevant to the control of bowel movement frequency, and establish a set of candidate targets for follow-up and replication in independent datasets.
Disclosure of Interest: None declared

OP274 ANTIBIOTIC TREATMENT INDUCES LONG LASTING EFFECTS ON MURINE ENTERIC NERVOUS SYSTEM AND IMPAIRS GUT MOTILITY

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Introduction: The most common side-effects of antibiotic treatment such as diarrhoea, bloating and abdominal pain are considered the direct consequence of intestinal dysbiosis. Indeed, a balanced gut microbiota is known to support the integrity of the enteric nervous system (ENS) which in turn controls gastrointestinal (GI) neuromuscular functions.
Aims & Methods: In this study we investigated the long-term effects of antibiotic-induced microbial dysbiosis on the ENS and we studied the impact of the spontaneous re-establishment of the gut microbiota on GI functions. C57Bl/6 mice were treated daily for 2 weeks (wks) with a cocktail of antibiotics. After 0-6 wks of antibiotic wash-out we determined a) gut microbiota composition by quantitative PCR (qPCR) on faecal DNA, b) GI motility by measuring fluorescein-isothiocyanate dextran distribution in the gut; c) changes in isometric muscle tension in ileal segments; d) integrity of the ENS by immunohistochemistry (IHC) on ileal whole-mount preparations; e) neurochemical code by qPCR and IHC; f) inflammatory damage by histological examination.
Results: Two wks of antibiotic treatment reduced the bacterial 16S rRNA genes copy number by 300-fold and resulted in a higher *Firmicutes*/*Bacteroidetes* ratio compared to vehicle-treated mice. Mice treated with antibiotics experienced delayed GI transit time, impaired electric-field stimulation (EFS)-elicited contraction, altered expression and distribution of the neurofilaments peripherin and βIII-tubulin, and deregulated expression of Substance P and nNOS (see Table). Histological examination of ileum and colon sections revealed nearly normal structure in mice after 2 wks of antibiotic administration and after 2-6 wks of antibiotic discontinuation. At the 6th week from antibiotic interruption bacterial DNA load re-established at normal levels but the composition of gut microbiota greatly diverged from the one of vehicle treated mice. As assessed by qPCR, Bacteroides and Lactobacillus groups drastically decreased in antibiotic-treated mice while the Clostridium became the predominant group. The functional and structural anomalies of the ENS still persisted 4 wks after antibiotic interruption whereas the expression of glial marker S100β and the glial derived neurotrophic factor (GDNF) did not recover.
Conclusion: In this study we strengthened the idea that antibiotic-induced GI dysmotility directly correlates with gut dysbiosis and structural and functional damage in the ENS. Therefore, fostering the recovery of gut microbiota (i.e. probiotic supplementation) could be helpful for restoring the neurochemical code of the ENS and reducing the antibiotic-induced adverse effects on GI motility.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 14:00–15:30
DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN GORD – ROOM B2

OP275 USE OF ACID-SUPPRESSIVE THERAPY BEFORE ANTI-REFLUX SURGERY. A NATIONWIDE REGISTER-BASED STUDY IN DENMARK

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Introduction: Guidelines recommend that patients with gastroesophageal reflux disease are adequately treated with acid-suppressive therapy before undergoing anti-reflux surgery (ARS). Little is known of the use of acid-suppressive drugs before ARS.
Aims & Methods: This study aimed to determine the use of proton pump inhibitors and histamine-receptor-2-antagonists in the year before ARS.
We performed a nationwide retrospective study of all patients aged ≥18 undergoing first-time ARS in Denmark during 2000 – 2012 using data from three different sources: the Danish National Register of Patients, the Danish National Prescription Register, and the Danish Person Register. We extracted data for prescriptions on acid-suppressive therapy (proton pump inhibitors and/or histamine-receptor-2-antagonists) within five years before ARS and prescriptions of non-steroidal anti-inflammatory drugs (NSAID) and antiplatelet drugs for the year leading up to ARS. We also extracted data for the pre-surgical procedures upper endoscopy, esophageal manometry, pH monitoring and impedance monitoring within three years before ARS.
We defined inadequate dosing as redeeming < 180 defined daily doses (DDD) of acid-suppressive therapy in the year before ARS and factors associated with inadequate dosing was analyzed using logistic regression and presented as odds ratio (OR) with 95% confidence intervals (CI).
Results: The study population included 2,922 patients (median age: 48 years, 55.7% male). The annual proportion of patients redeeming ≥180 DDD of acid-suppressive therapy increased from 17.0% five years before ARS to

64.9% one year before. Of the 1,895 patients redeeming ≥180 DDD in the year before ARS, 1,121 (59.2%) redeemed ≥360 DDD. Of the 1,027 patients redeeming <180 DDD one year before ARS, 839 (81.7%) redeemed <180 DDD every year in the five years leading up to surgery.
The probability for inadequate dosing one year before surgery (<180 DDD) was significantly increased for younger patients aged 18 - 39 (OR 1.8; 95% CI: 1.4 - 2.2), patients operated in the period 2000 – 2003 (OR 1.7; 95% CI: 1.4 - 2.1), patients, who had not undergone pre-surgical manometry, pH- or impedance monitoring (OR 1.6; 95% CI: 1.3 - 2.0), and patients, who had not redeemed prescriptions on NSAID or antiplatelet drugs (OR 1.3; 95% CI: 1.1 - 1.6).
Conclusion: Compliance to medical therapy should be evaluated thoroughly before planning anti-reflux surgery since a high proportion of patients received inadequate dosing of acid-suppressive therapy prior to the operation.
Disclosure of Interest: None declared

OP276 A NOVEL PROSTANOID EP1 RECEPTOR ANTAGONIST ONO-8539 REDUCES ACID-INDUCED HEARTBURN SYMPTOMS IN HEALTHY VOLUNTEERS

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Introduction: Prostaglandin E_2 (PGE_2) is a key mediator in the processing of pain hypersensitivity via the EP1 receptor, and the previous study showed that an EP1 receptor antagonist (ZD6416) has been shown to attenuate the development of oesophageal hypersensitivity in humans [1]. Recently, we have also reported that oesophageal PGE_2 expression is associated with degree of heartburn induced by mucosal acid exposure [2-3]. In the present study, we investigated the effects of ONO-8539, a novel EP1 receptor antagonist, on the induction of heartburn symptoms by acid perfusion in healthy men.
Aims & Methods: The present prospective, double-blinded, placebo-controlled, 2-period cross-over study was performed over 3 visits in 20 healthy men. A novel prostanoid EP1 receptor antagonist, ONO-8539 (450 mg), was administered once 4 h prior to an acid perfusion test. During the test, hydrochloric acid (0.15 mol/L) was perfused into the lower oesophagus for 30 min. We evaluated heartburn symptoms during acid infusion using a validated categorical rating scale. Further, we calculated and assessed the area under the curve (AUC) as a total symptom score.
Results: Compared with placebo, ONO-8539 significantly extended the time (min) to first sensation of heartburn (5.7 ± 4.3 min for placebo and 9.7 ± 7.2 min for ONO-8539; $P < 0.05$), and ONO-8539 significantly reduced the AUC for heartburn (83.5 ± 10.2 for placebo and 56.5 ± 7.2 for ONO-8539, $P < 0.05$).
Conclusion: ONO-8539 attenuated acid-induced heartburn in healthy men. EP1 receptor plays a key role in generation of heartburn symptoms and ONO-8539 may be a novel therapeutic option for controlling these symptoms in patients with gastroesophageal reflux disease. Clinical Trials Registry no: UMIN000015753.

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Disclosure of Interest: None declared

OP277 PROTON PUMP INHIBITORS AND THE RISK OF PNEUMONIA USING A NEW ANALYTICAL TECHNIQUE: PRELIMINARY RESULTS FROM A RETROSPECTIVE COHORT STUDY USING PRIMARY CARE DATABASE

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Introduction: Research examining the association between use of proton pump inhibitors (PPIs), and risk of pneumonia has been inconsistent. Due to the difficulties associated with conducting trials, the majority of existing studies that aimed to investigate this association were observational in nature. These observational studies have been criticised due to a lack of control for unmeasured confounding. The prior event rate ratio (PERR) adjustment method, an analytical method to control for unmeasured confounding(1), may overcome this problem.
Aims & Methods: The aim of this study was to determine whether the association between PPI use and pneumonia is independent of confounding through the use of the PERR method. A cohort study was conducted using anonymised records from a primary care database between the years 1990 and 2013. Adult patients newly prescribed a PPI (exposed) were selected and individually matched, according to age, gender and year of prescription, to subjects not prescribed a PPI (un-exposed). The primary outcome was the occurrence of first pneumonia event before and after a prescription of PPI. PERR was estimated by dividing the unadjusted hazard ratio for pneumonia during the year after initial PPI prescription (of the exposed group versus the unexposed group), by the unadjusted hazard ratio for pneumonia before the PPI prescription (of the exposed versus the unexposed group).
Results: There were 1,176,632 subjects included in this study. The rate of pneumonia was higher (3.04 per 1,000 person years of follow-up) before the PPI prescription compared with the rate after a prescription for the exposed patients (2.85 per 1,000 person years of follow-up). Exposed patients were at 3.05 (95% confidence interval 2.78-3.25) times more risk of pneumonia than patients not prescribed a PPI in the period before the first PPI prescription, and 2.41 (95% confidence interval 2.20-2.63) times the risk afterwards(see table). Giving a PERR for pneumonia of 0.79.
Table unadjusted hazard ratio (95% confidence interval) before and after prescription of proton pump inhibitor .

Patients matched for dateTotal number of patients(1,176,632)	PPI exposed Number of patients588,316	Non-PPI exposed Number of patients588,316
Before PPI prescription		
Pneumonia event (%)	1790(0.30)	587(0.09)
Person years follow-up	587.69	588.02
Incidence per 1,000 per person year(95%CI)	3.04 (2.90-3.19)	0.99 (0.92-1.08)
Hazard ratio (95%CI)(PPI/non-PPI)	3.05 (2.78-3.25)	
After PPI prescription		
Pneumonia event (%)	1,675(0.28)	695(0.11)
Person years follow-up	587.43	587.97
Incidence per 1,000 per person year(95%CI)	2.85 (2.71-2.99)	1.18 (1.09-1.27)
Hazard ratio (95%CI)(PPI/non-PPI)	2.41 (2.20-2.63)	

Conclusion: The outcome of the study indicates that commencing PPI use does not increase the association between the eventually PPI exposed group and the risk of pneumonia. It is likely therefore that confounding factors present before PPI use rather than the PPI itself were the main contributors to an increased rate of pneumonia in patients who have been prescribed PPI.

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Disclosure of Interest: None declared

OP278 INVOLVEMENT OF LEPTIN IN THE SEVERITY OF REFLUX OESOPHAGITIS

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Introduction: Obesity has widely been recognized to promote a wide variety of diseases including Gastroesophageal reflux disease (GERD), Barrett's esophagus and ensuring arising of esophageal adenocarcinoma (EAC) which incidence depicts sharp rise in the western countries over the last 3 decades.[1] Leptin, adhipokine that exerts pleiotropic functions such as regulation of food intake and energy consumption as well as inflammatory response, is increased in obese individuals.[2] In humans, women's serum leptin level is about 3-fold as high as men, however there is profound male-predominance in GERD related diseases.[3, 4] On the other hand, postmenopausal women have a higher incidence of these diseases. We hypothesize that the discrepancy of the gender difference attributes to sex hormones.
Aims & Methods: Male and female wistar rats were subjected to a surgically induced GERD model. Groups of rats were treated continuously subcutaneous injection of leptin. Divided female rats underwent ovariectomy to diminish serum 17b-estradiol (E2). Intensity of GERD was assessed both macroscopically and histologically. Expression in tissue TNF-a was measured by immunohistostaining and serum leptin level was measured by ELISA.
Results: A significant increase in inflammation of reflux esophagitis was observed in leptin-administered male rats compared to control rat, followed rising of serum leptin level (injury area: $17.7 \pm 11.3\%$ vs $5.4 \pm 2.9\%$, $p < 0.01$), whereas a slight decrease in severity of reflux esophagitis was seen in leptin-injected female rats compared to controls (injury area: $2.9 \pm 1.5\%$ vs $2.5 \pm 1.0\%$). Additionally significant deterioration in esophagitis was observed in ovariectomized and leptin-applied female rats (injury area: $5.8 \pm 3.5\%$ vs $2.9 \pm 1.5\%$, $p < 0.01$). Leptin administration caused TNF-a expression in esophageal epithelium to increase in both male and ovariectomized female rats compared to respective controls.
Conclusion: We showed that high level of leptin profoundly intensified inflammation induced by acid reflux in male and ovariectomized female rats, while the leptin tended to decrease the inflammation in non-ovariectomized female rats. Sex hormones secreted from ovary such as E2 could downregulate TNF-a expression induced by leptin and strengthen an epithelial defense system in lower esophagus to ameliorate an inflammation caused by GERD.[5] Severe GERD is reported to correlate high prevalence of Barrett's esophagus and

subsequent development of EAC. [6]Thus, this molecular process might shed light to develop a new therapeutic strategy for EAC.

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Disclosure of Interest: None declared

OP279 NOVEL IMPEDANCE PARAMETERS IMPROVE THE DIAGNOSTIC YIELD OF IMPEDANCE-PH MONITORING IN GERD – A MULTICENTER STUDY

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Introduction: Recently, two novel impedance parameters evaluating esophageal chemical clearance and mucosal integrity, namely the post-reflux swallow-induced peristaltic wave (PSPW) index and the mean nocturnal baseline impedance (MNBI) have been proposed. According to the results of preliminary studies, they appear as potentially useful to improve the diagnostic accuracy of impedance-pH monitoring in gastroesophageal reflux disease (GERD).
Aims & Methods: We aimed to assess whether the PSPW index and the MNBI can improve the diagnostic yield of impedance-pH monitoring in typical GERD. Off-therapy impedance-pH tracings from 289 patients with proton pump inhibitor (PPI) responsive heartburn, 68 with erosive (ERD) and 221 with non-erosive (NERD) reflux disease, and from 50 healthy controls were blindly reviewed. The PSPW index, the MNBI, the esophageal acid exposure time, the number of total refluxes, and the bolus exposure were calculated as well as the symptom association probability (SAP+ if $\geq$ 95%) and the symptom index (SI+ if $\geq$ 50%). In particular, a PSPW was defined as an antegrade 50% drop in impedance relative to the pre-swallow baseline originating in the most proximal impedance site, reaching all the distal impedance sites, and followed by at least 50% return to the baseline in the distal impedance sites (bolus exit). Only PSPWs with bolus exit occurring within 30s from the end of reflux episodes were taken into account. For each impedance-pH tracing, the number of refluxes followed within 30s by a PSPW was divided by the number of total refluxes in order to obtain the PSPW index. MNBI was assessed from the most distal impedance channel during nighttime recumbent period. Three 10-minute time periods (around 1.00 am, 2.00 am, and 3.00 am) were selected. Time periods including swallows, refluxes and pH drops were avoided. The mean of the three measurements was calculated to obtain the MNBI.
Results: At receiver operating characteristic (ROC) analysis, the area under curve (AUC) of the PSPW index (0.977, 95% CI 0.961-0.993) was significantly greater than that of the other impedance-pH parameters ($P < 0.001$). The PSPW index and the MNBI showed the highest sensitivity in ERD (100% and 91%) and in 118 pH-positive (99% and 86%) and 103 pH-negative (77% and 56%) NERD cases. In pH-negative NERD, the PSPW index and the MNBI had the highest sensitivity in 65 SAP/SI positive (82% and 52%) and in 38 SAP/SI negative (68% and 63%) cases. NERD diagnosis was confirmed by pH-only criteria, including SAP/SI positivity, in 165/221 (75%) cases and by impedance-pH criteria in 216/221 (98%) cases ($P = 0.001$).
Conclusion: The PSPW index and the MNBI improve the diagnostic yield of impedance-pH monitoring in typical reflux disease. Impedance-pH criteria, including calculation of the PSPW index and the MNBI ensure significant diagnostic gain as compared to pH-only criteria.
Disclosure of Interest: M. Frazzoni: None declared, E. Savarino Lecture fee(s): Given Imaging, N. de Bortoli: None declared, M. Furnari: None declared, I. Martinucci: None declared, L. Frazzoni: None declared, S. Marchi: None declared, R. Conigliaro: None declared, V. Savarino: None declared

OP280 MAGNETIC SPHINCTER AUGMENTATION VERSUS TOUPET FUNDOPLICATION: A LONGITUDINAL STUDY FOCUSED ON QUALITY OF LIFE

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Introduction: Only about 1% of the patients with gastroesophageal reflux disease (GERD) are offered a surgical option. This is mostly due to the fear of potential side effects, the variable success rate, and the extreme alteration of gastric anatomy with the current gold standard, the laparoscopic Nissen fundoplication. Laparoscopic Toupet Fundoplication (LTF) and laparoscopic magnetic sphincter augmentation (LINX) seem to prevent reflux more physiologically and with a lower incidence of side-effects and reoperation rate. We present the first case-control study comparing LTF and LINX.
Aims & Methods: Between March 2007 and December 2014, 135 LINX and 97 LTF patients were compared by using the propensity score full matching method. Outcomes were measured by GERD-HRQL scores, PPI use, dysphagia rate, bloating and reoperation rate. HRQL-GERD and bloating were analyzed over the time using Generalized Estimating Equation (GEE) with logit link function. Dysphagia was analyzed using logistic or Firth logistic regression and PPI use with chi square test.
Results: At 7-year follow-up, patients in both groups had similar GERD-HRQL scores (OR 1.01 CI 0.82-1.30 $p = 0.80$) and PPI use (14% of LINX and 11% of LTF, $p = 0.7$). No significant differences were detected in the incidence of dysphagia (9% of LINX and 9% of LTF, $p = 0.89$) and bloating (OR 0.69 CI 0.21-2.28 $p = 0.54$) between the two groups. Reoperation rate was 7.4% in LINX and 2% in LTF ($p = 0.13$).
Conclusion: In two contemporary cohorts of patients matched by propensity score analysis, control of reflux symptoms was similar after both LINX and LTF. No statistically significant difference was found in the incidence of dysphagia, bloating, and reoperation rate. These results suggest a possible paradigm change and a new concept of antireflux surgery.

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Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 14:00–15:30

ENGAGING IBD PATIENTS IN THE MANAGEMENT OF THEIR DISEASE – ROOM 7.1

OP281 IMPACT OF AN EDUCATION PROGRAM ON IBD PATIENT'S SKILLS: A RANDOMIZED, CONTROLLED MULTICENTER STUDY (ECIPE)

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Introduction: Inflammatory bowel diseases (IBD) may induce difficulties in everyday life of patients. Treatment is aimed at reducing symptom burden, progression of damage and impact on quality of life. An improvement of patients' skills, in terms of knowledge, competences and behavior could have a positive impact on therapeutic efficacy, control of the disease and quality of life. The aim of our study was to demonstrate that an education program could have a significant impact on IBD patient's skills with regards to their disease.
Aims & Methods: GETAID centers, which promoted therapeutic education through the EDU-MICI program, were eligible. Patients were randomized into "educated" or "non-educated" groups for 6 months. A crossover then allowed uneducated patients to benefit from the educational program the next 6 months. Inclusion criteria were: - patients with a recent diagnosis (<6 months), - or need to optimize medical therapy. Education was performed by dedicated staff (mainly nurses) using an illustrated book, covering the different dimensions of life with an IBD. A psycho-pedagogic score (ECIPE score) was performed by a "blinded" physician (independent from the education team) at M0, M6 and M12. The primary endpoint was the variation of ECIPE score at M6. A variation of more than 20% was considered as significant. Different questionnaires, including SIBDQ, RFIPC, and WPAI were completed by patients.
Results: 263 patients were included in 18 centers (40% Male; median age: 30.8; 73% CD; 27% UC): 133 patients were randomized in the educated group and 130 in the non-educated group, with no marked differences regarding baseline characteristics. The primary endpoint was reached with a 27.8% variation [IQR: 9-47] of the ECIPE score at M6 in the educated group vs. 9% [0-20] in the non-educated group ($p = 0.0007$). Variation in ECIPE score of more than 20% was observed in 46% vs. 24% in the educated and non-educated groups, respectively ($p = 0.0003$). Within ECIPE score, variations were significant for items regarding competences and behavior, but not for those regarding quality of life. A total of 92 patients experienced an increase in ECIPE score of at least 20%. In multivariate analysis, randomization in the educated group (OR = 2.61) together with no past surgery (OR = 2.00) remained associated with an increase of ECIPE score of at least 20%. These patients who had an increase in ECIPE score of at least 20%, also significantly improved all ECIPE sub-scores (competences, behavior, quality of life) and SIBDQ, RFIPC and WPAI scores, except for the observance score.
Conclusion: This large prospective controlled multicenter study shows for the first time, that an educational program improve the skills of IBD patients, as

demonstrated by a significant increase of a psycho-pedagogic score in the educated group.

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Disclosure of Interest: None declared

OP282 PATIENTS PERCEPTIONS OF QUALITY OF CARE AND FOLLOW-UP IN INFLAMMATORY BOWEL DISEASE

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Introduction: Quality of care (QoC) is increasingly used in evaluation of health care performance. In IBD, a better QoC is often linked to the number of patients on corticosteroid-free remission, number of hospitalizations and surgery. Factors of equal importance to patients may however be health-related quality of life (HRQoL), patient-care provider communication, access to care, autonomy and shared decisions. Recently the IMPACT study (1) revealed that IBD patients may be experiencing sub-optimal care related to some of these issues.

Aims & Methods: The aim of this study was to assess patient perceived QoC and patient centeredness in follow-up among IBD outpatients in Norway. Furthermore to identify potential clinical and epidemiological associations to QoC scores. A purposely designed questionnaire was developed, based on clinical assessment, patient input and literature review. Questionnaire items covered aspects related to specialist care, primary care and hospitalizations. Clinical and epidemiological data was gathered by interview, medical records and laboratory tests. Validity was tested with Cronbach's alpha, while descriptive analysis was used to describe the material. Associations between QoC and background variables were investigated with t-tests, chi-square and Pearson's correlation coefficient.

Results: In all, 414 patients gave informed consent to participate in the study. Of these, 411 had complete datasets, CD; n = 231, UC; n = 180, female (202/411, 49.1%). Internal consistency (Cronbach's alpha) was 0.90. In total, 86.1% (354/411) reported to be either satisfied or very satisfied with the quality of IBD follow-up. In contrast 4.1% (17/411) of patients were dissatisfied or very dissatisfied with QoC. There were no significant differences between the two diagnostic groups (Mean UC = 4.3, CD = 4.2). Moreover, no significant correlations were found between QoC scores age, calprotectin levels, CRP or number of relapses (prior 365 days). In UC, but not in CD, female gender was associated with decreased scores in general satisfaction ($p = 0.05$). In CD, elevated SCDAI score correlated negatively ($p = 0.03$), while a longer disease duration was correlated positively with QoC scores ($p = 0.04$). The highest level of dissatisfaction in IBD follow-up was related to general practitioners' (GP's) knowledge of IBD (75/411, 21.9%), and communication with primary health care after hospitalizations (26/278, 12.6%). Moreover, 19.2% (62/411) and 32.4% (75/411) of patients reported little focus on quality of life and on relatives in IBD follow-up.

Conclusion: Contrary to the findings presented in the IMPACT study, this large, multicenter study revealed that a majority of IBD patients are satisfied with IBD care and follow-up. In CD, patients with shorter disease duration and increased symptoms seem to have lower satisfaction scores. Furthermore, many patients perceive little focus on the psychosocial impact of IBD in follow-up.

Reference

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Disclosure of Interest: None declared

OP283 MEDICATION ADHERENCE IN INFLAMMATORY BOWEL DISEASE IN THE GLOBAL ALIGN STUDY: IMPACT OF CONCERNS AND PERCEIVED NECESSITY OF IMMUNOSUPPRESSANTS, 5-AMINOSALICYLATES, AND TUMOR NECROSIS FACTOR INHIBITORS

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Introduction: Relatively little is known about the relationship between patients (pts') beliefs (eg, concerns, necessity) regarding inflammatory bowel disease (IBD) therapies and medication adherence; a better understanding could enhance interventions to optimize adherence.

Aims & Methods: The global, cross-sectional ALIGN study determined pts' beliefs about, and adherence to, systemic therapies in > 7000 pts with 6 immune-mediated inflammatory diseases including Crohn's disease (CD) and ulcerative colitis (UC). Consecutive pts completed the Beliefs About Medicines Questionnaire (BMQ) and 4-item Morisky Medication Adherence Scale (MMAS-4) at a routine visit. Here, CD and UC pts were divided into 3 treatment groups (**Table**). The reference for comparisons was immunosuppressant (IS) monotherapy for CD and 5-aminosalicylate (5ASA) monotherapy for UC. Multiple random-effect linear and logistic regression analyses explored pts' beliefs regarding their therapies and associations with adherence.

Results: 1146 CD pts and 613 UC pts were analyzed. In CD, BMQ-Specific *Concern* ratings were similar for IS, 5ASA, and TNFi. In UC, TNFi (alone or combined with IS) and IS (in combination therapy) were associated with increased concerns vs 5ASA monotherapy. For CD and UC, TNFi (alone or combination) was associated with higher BMQ-Specific *Necessity* beliefs vs IS monotherapy. Older age and higher necessity beliefs were associated with higher treatment adherence in multivariable regression. Higher proportions of CD and UC pts reported high adherence (MMAS-4 = 4) to TNFi vs other therapies (73%–82% vs 29%–59%). Regression analyses revealed that, in CD and UC, adherence was significantly higher with TNFi therapy (alone or combined with IS) vs IS monotherapy; in UC, adherence was significantly higher with IS and TNFi (alone or in combination) vs 5ASA monotherapy (**Table**).

Conclusion: This large cross-sectional study indicates that concerns regarding TNFi are similar to conventional therapies in CD and UC, but are higher compared with 5ASA treatment in UC. In both CD and UC, pts express high treatment necessity beliefs for TNFi therapy, which is associated with increased adherence rates.

Disclosure of Interest: P. Michetti Lecture fee(s): AbbVie, Ferring Pharmaceuticals, MSD, and Vifor, Consultancy: AbbVie, Ferring Pharmaceuticals, Merck Serono, MSD, Nestlé Health Sciences, Takeda, UCB Pharma, and Vifor, L. Peyrin-Biroulet Lecture fee(s): AbbVie, Ferring Pharmaceuticals, H.A.C. Pharma, Janssen, Merck, Norgine, Therakos, Tillotts Pharma AG, and Vifor, Consultancy: AbbVie, Boehringer Ingelheim Inc, Bristol-Myers Squibb, Celltrion, Eli Lily, Ferring Pharmaceuticals, Genentech, Hospira, Janssen, Merck, Mitsubishi, Norgine, Pharmacosmos, Pilège, Shire Pharmaceuticals, Takeda, Therakos, Tillotts Pharma AG, UCB

Abstract number: OP283 Table: Multivariable Logistic Regression Analysis On High Adherence (MMAS-4 = 4) to IBD Treatments in CD or UC

CD			
Treatment Group	**MMAS-4 Adherence Rating**	**N**	**Odds Ratio (95% CI)**
IS monotherapy(IS ± 5ASA ± steroids)	IS (Reference) 5ASA	26262	–0.4 (0.1–1.1)
TNFi monotherapy(TNFi ± 5ASA ± steroids)	TNFi 5ASA	577122	7.3 (3.8–13.9) 1.6 (0.7–3.6)
IS-TNFi combination therapy (IS + TNFi ± 5ASA ± steroids)	IS TNFi 5ASA	27728065	1.5 (0.8–3.0) 17.5 (7.8–39.3) 1.5 (0.5–4.7)
UC			
5ASA monotherapy(5ASA ± steroids)	5ASA (Reference)	157	–
IS monotherapy(IS ± 5ASA ± steroids)	IS 5ASA	12689	6.2 (1.8–21.0) 1.9 (0.5–6.5)
TNFi monotherapy(TNFi ± 5ASA ± steroids)	TNFi 5ASA	18587	67.7 (13.8–331.1) 5.5 (1.3–22.7)
IS-TNFi combination therapy (IS + TNFi ± 5ASA ± steroids)	ISTNFi 5ASA	929446	19.2 (4.1–88.8) 185.2 (27.5–1245.6) 21.0 (3.5–126.6)

Pharma, and Vifor, E. Louis Lecture fee(s): Abbvie, Ferring, MSD, Chiesi, Mitsubishi Pharma, Hospira, and Janssen, Conflict with: Educational grants from MSD and AbbVie, as well as advisory board fees from AbbVie, Ferring, MSD, Takeda, Mitsubishi Pharma, and Celltrion, M. Silverberg Financial support for research: AbbVie, Janssen, and Prometheus, Lecture fee(s): AbbVie, Janssen, Takeda, and Prometheus, Consultancy: AbbVie, Janssen, Takeda, and Prometheus, J. Weinman Conflict with: Employee of Atlantis Healthcare, J. Sommer Conflict with: Employee of GKM Gesellschaft fuer Therapieforschung mbH, J. Petersson Conflict with: Is an AbbVie employee and may own AbbVie stock and/or options, B. Pappalardo Conflict with: Is an AbbVie employee and may own AbbVie stock and/or options, P. Nurwakagari Conflict with: Is an AbbVie employee and may own AbbVie stock and/or options, N. Selenko-Gebauer Conflict with: Is an AbbVie employee and may own AbbVie stock and/or options

OP284 INFLUENCE OF ALEXITHYMIA ON THE CLINICAL COURSE OF INFLAMMATORY BOWEL DISEASE (IBD)

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Introduction: Alexithymia is a personality trait characterized by difficulty to perceive and express emotions. Previous studies have reported a high prevalence of alexithymia in IBD patients, but its influence on the clinical course of the disease is unknown.

Aims & Methods: The aim of this study was to assess the influence of alexithymia on the clinical course of IBD patients.

Methods: A prospective observational cohort study was designed. Crohn's disease (CD) and Ulcerative Colitis (UC) patients older than 18 years of age were included. Alexithymia was evaluated using the Toronto scale (TAS-26). This scale is a self-report instrument consisting of 26 items with a response format of a five-point scale (range 26 to 130). Alexithymia was defined as a total score of > 73 points. In order to assess the clinical course of IBD, all unscheduled or emergency visits and hospitalisations related with IBD were recorded over a 18-month follow-up time. The influence of alexithymia on clinical course was analysed by logistic regression analysis.

Results: 470 patients were included; 219 (46.6%) male, mean age 44 years, range 18 to 85 years, 60.8% with UC and 39.2% with CD. The overall prevalence of alexithymia was 67.4%. Mean emergency or unscheduled visits was 1.08 (SD 1.50, range 0-14) and mean hospitalizations of 0.38 (SD 1.04, range 0-9). Higher alexithymia scores at baseline were not associated with more emergency visits (B = 0.06; 95%CI 0.93-1.21; p = 0.364) nor more hospitalizations (B = -0.02; 95% CI 0.82-1.18;p = 0.838).

Conclusion: Alexithymia is highly prevalent in IBD patients but it has no influence on the number of emergency visits and hospitalizations.

Disclosure of Interest: None declared

OP285 EVALUATION OF FERTILITY IN MEN WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel diseases (IBD, Crohn's disease-CD and ulcerative colitis-UC) are chronic conditions, with the highest incidence rates during the peak reproductive years. Our aims were to compare the fertility status in men with IBD and controls (CTR) and to investigate the pathophysiology.

Aims & Methods: A multicentre, transversal groups study was performed between April 2010 and March 2014. Patients with varicocele, altered FSH, LH, prolactine (PRL) or testosterone levels (TST), pathology related to subfertility, ≥ 5 white blood cells in semen or positive culture were excluded. Age, smoking status, activity of IBD (by Harvey and Simple clinical colitis activity index), semen characteristics (million sperm/ml, progressive motility, morphology and vitality), hormone levels (FSH, LH, PRL and free TST), plasma and seminal zinc, 24 hour urinary zinc,antisperm antibodies (ASA), and plasma TNF-α were measured in each patient.

Results: Seventy-four patients [30 CD (40.4%), 22 UC (29.7%) and 22 CTRL (29.7%)] were included. Mean age was 30.5 ± 5.5 in CD, 34.0 ± 6.0 UC and 31.3 ± 5.1 CTRL (p = 0.780), smokers 14 patients in CD, 8 in UC and 8 CTRL (p = 0.221[FB1]).[h2] 86.6% of IBD patients were asymptomatic. Differences in FSH, LH and TST levels were not found. Regarding to PRL levels, the difference observed was close to statistical significance (CD 15.2 ± 6.7; UC 16.7 ± 6.6 ;CTRL 12.3 ± 4.0; p = 0.062). In sperm analysys differences in sperm/ml (CD 35 (19.7-53.0), UC 71.5 (37.7-124.2), CTRL 81 (10.0-110.0; p = 0.038) were obtained, without difference in progressive motility (CD 42.3 ± 22.9; UC 47.8 ± 19.7, CTRL 50.6 ± 16.6, p = 0.324), vitality (CD 64.1 ± 19.7; UC 65.6 ± 19.2; CTRL 71.8 ± 12.6; p = 0.300 or morphology (CD 9.9 ± 6.5; UC 9.1 ± 4.3; CTRL 7.9 ± 3.7; p = 0.422). Although, this stadistical significance was lost when the results were adjusted for age and smoking status (p = 0.162). When comparing CD and UC, we found that patients with CD had worse progressive motility-astenospermia- (CD 35.1 ± 22.1; UC 49.1 ± 19.2; p = 0.036) and sperm/ml -oligospermia- (CD 34.5 (19.2-48.0); UC 70 (34.5-127.5); p = 0.02) without differences in vitality (CD 59.5 ± 21.0; UC 67.4 ± 17.8; p = 0.205 and morphology (CD 7.6 ± 4.9; UC 8.8 ± 4.2). All ASA were negative. TNF α levels were similar in CD and UC patients, and lower in CTRL (CD 4.49 (3.65-12.2), UC 4.51 (3.9-5.385), CTRL 4.755 (3.932-6.280), p = 0.433). Patients with CD had lower seminal zinc levels than UC patients(CD 1455.0 ± 860.1 μmol/L ; UC 2193.3 ± 1152.8; CTRL 1522.9 ± 937.2, p = 0.012)without difference in serum zinc (CD 11.6 ± 2.7; UC 12.6 ± 2.6; CTRL 12.4 ± 2.4; p = 0.211) and urinary zinc (CD 10.3 ± 6.9; UC 9.9 ± 4.6; CTRL 6.5 ± 2.9,; p = 0.823). Seminal zinc showed possitive correlation with progressive motility(r = 0.243, p = 0.086)

Conclusion: Male CD patients have a worse fertility status than UC patients or control which is characterized by lower sperm count, reduced progressive motility and lower seminal zinc levels. The alterations observed do not seem to be related to ASA or ant-TNF levels in these patients.

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OP286 ADALIMUMAB AND INFLIXIMAB CLEARANCE IN NEONATES (ERA STUDY)

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Introduction: Anti-TNF-alpha (ATNF) therapy in pregnancy results in transfer of drug to the foetus. Neonatal levels and clearance of ATNF therapy are poorly understood.

Aims & Methods: We investigated neonatal ATNF levels after exposure in utero and correlated these with maternal levels, therapy duration, time to clearance and factors affecting clearance.

Pregnant IBD women exposed to infliximab (IFX) or adalimumab (ADA) were enrolled at 14 sites in Denmark, Australia, and New Zealand. Drug levels were measured by ELISA. If positive at birth, infants were tested three monthly. Demographics, disease activity, medication, and pregnancy outcomes were prospectively collected. Multivariate and logistic regression analysis determined factors correlated with drug levels at birth in mothers and newborns, time to and factors influencing clearance in newborns.

Results: Of 80 women (44 IFX, 36 ADA) recruited, 49% were on combination therapy with thiopurines. There were 3 (4%) preterm births, 3 (4%) babies who were small for gestational age and 3 (4%) with congenital malformations. There was an inverse correlation between duration since last dose and both cord drug levels (IFX: r = -0.77; ADA: r = -0.64, both p < 0.0001) and maternal levels (IFX: r = -0.80; ADA: r = -0.80, both p < 0.0001). At delivery the cord/maternal ratio was 1.96 (95% CI 1.5-2.4) for IFX and 1.21 (95% CI 0.93-1.48) for ADA. Last ATNF dose was at median gestational week (GW) 30 in IFX, (8-37) and 35 in ADA (14-41) treated mothers. Median maternal and cord drug concentrations were 2.0 (0-22.2 mcg/ml) and 5.9 (0.12-28.7 mcg/ml) for IFX and 1.5 (0-10 mcg/ml) and 2.0 (0-12.1 mcg/ml) for ADA. Concentrations were significantly lower when ATNF was stopped prior to GW 30 (p < 0.002). Cessation prior to GW 30 in 31% of mothers did not increase the risk of disease activity in the 3rd trimester or postpartum. Median time to neonatal clearance was 6 months (range 3-12) for IFX and 6 months (range 0-9) for ADA. The average decrease in neonatal ATNF concentration from birth to 3 months of age was 82% (95% CI 77-87%) for IFX and 91% (95% CI 88-94%) for ADA, p = 0.002. The number of weeks since last dose in pregnancy predicted likelihood of neonatal clearance by 3 months (p = 0.01). Child development was normal on routine infant checks and no serious infections were noted.

Conclusion: Maternal and cord ATNF levels inversely correlated with duration since last exposure. Stopping before week 30 reduced drug levels but did not prevent transfer to the neonate. The rate of ADA clearance was faster than IFX clearance within the first 3 months of life. Neonatal clearance of ATNF took up to 12 months, emphasizing the importance of avoiding live vaccines the first year. Despite recordable neonatal drug concentrations, no increased risk of infections or adverse developmental outcome was reported.

Disclosure of Interest: M. Julsgaard Lecture fee(s): Ferring, MSD, UCB, L. A. Christensen Lecture fee(s): Ferring, MSD, UCB, Takeda, AbbVie, Conflict with: Member of the advisory board for MSD, P. R. Gibson Financial support for research: Janssen, AbbVie, Ferring, Lecture fee(s): Janssen, AbbVie, Abbott, Fresenius Kabi, Astrazeneca, Consultancy: AbbVie, Janssen, Ferring, Takeda, Nestle, Danone, R. Gearry Financial support for research: AbbVie, Ferring, Lecture fee(s): AbbVie, Janssen, MSD, Consultancy: AbbVie, Janssen, MSD, J. Fallingborg Financial support for research: AbbVie, Ferring, Lecture fee(s): AbbVie, Janssen, MSD, Consultancy: AbbVie, Janssen, MSD, J. Kjeldsen: None declared, S. Wildt Financial support for research: Dr Falck Pharma, Conflict with: Member of Advisory Board: MSD and Tillots, L. Svenningsen: None declared, W. Connell: None declared, C. L. Hvas Lecture fee(s): AbbVie, MSD, Tillotts, Ferring, M. P. Sparrow Financial support for research: Ferring, Lecture fee(s): AbbVie, Janssen, MSD, Conflict with: Advisory Board: Janssen, A. Walsh Consultancy: Janssen, AbbVie, S. J. Connor Financial support for research: Ferring, Shire, Orphan/Aspen, Abbvie, Lecture fee(s): Ferring, Abbvie, Shire, Janssen, Consultancy: Abbvie, Janssen, Vifor, G. Radford-Smith: None declared, I. Lawrance: None declared, J. M. Andrews Financial

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TUESDAY, OCTOBER 27, 2015 14:00–15:30

PREVENTION AND MANAGEMENT OF PROCEDURE-RELATED GI COMPLICATIONS – ROOM E1

OP287 ENDOSCOPIC TREATMENT OF POST-SURGICAL FISTULAS INVOLVING THE GASTROINTESTINAL TRACT: A LARGE CASE SERIES

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Introduction: Post surgical fistula (PSF) or anastomotic leak is surely a dreadful event. It is generally managed with a surgical approach, which is mandatory when peritonitis, mediastinitis or severe sepsis are present. Several endoscopic devices have been introduced in the last decades, so that such a complication could be treated conservatively in selected cases without a re-intervention.

Aims & Methods: The aim was to assess the pivotal role of endoscopic treatment of PSF involving the gastrointestinal (GI) tract **Methods:** Data of all pts with a PSF involving the GI tract were prospectively collected. Information on the previous surgical approach, time, site and diameter of fistula, the endoscopic device used, technical success, the need of an additional approach, the hospital stay and the clinical outcome were recorded. The fistula was defined 'early' when occurring within 7 days, 'delayed' when later. The endoscopic treatments included: placement of a covered SEMS; over-the-scope clip positioning; fibrin glue injection (Tissucol); endo-sponge application. Single or multiple endoscopic devices were used, based on site of fistula and the therapeutic outcome. In those pts with a fluid collection cavity, drainage by either radiological or surgical approach was also performed (combined treatment).

Results: From April 2009 to September 2014, 76 pts (36 M; mean age: 63 yrs) with a PSF involving the GI tract were treated. The surgery was performed for a neoplastic (52 pts) and benign (24 pts) disease. An open or laparoscopic surgery was performed in 42 and 34 pts, respectively. Our series included fistulas after gastric-oesophageal anastomosis: 5 pts; bariatric surgery: 10 pts; gastric resections:22 pts; pancreatic surgeries: 5 pts; small bowel resections: 5 pts; colorectal resections: 24; urologic surgeries: 5 pts. The fistula was classified as early in 36/76 pts, and delayed in 40/76 pts. 35 and 24 pts were managed with only endoscopic treatment for either upper or lower GI fistula, respectively, whilst a combined approach was performed in the remaining 17 pts. Following the endoscopic therapy (single or combined) the fistula was successfully closed in 61/76 treated pts (80%) pts, without a statistically significant difference between single (48/59; 81%) and combined (13/17; 76%) treatment. The median of hospital stay was 16 days (5-180). The fistula closure was achieved in 45/53 (85%) pts managed by using only one type of device, and in 18/23 pts (78%) following a combination of devices., without a statistically significant difference. A similar success rate was achieved in pts with early (29/36; 81%) and those with a delayed (32/40; 80%) PSF

Conclusion: Endoscopic approach is successful and safe in the majority of pts with GI fistula specially when performed by skilled endoscopist. It should be always attempted before resorting in more invasive, costly and risky re-intervention. Therefore, a closed collaboration among the endoscopist, surgeon, radiologist and nutritional staff is required.

Reference

1. Manta R, Magno L and Conigliaro R, et al. Endoscopic repair of post-surgical gastrointestinal complications. *Dig Liver Dis* 2013; 45: 879–85.

Disclosure of Interest: None declared

OP288 SHOULD ANTITHROMBOTIC AGENTS BE STOPPED FOR GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION ?

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Introduction: As usage of antithrombotic agents increases, how to manage these drugs in perioperative period becomes a great concern. Recent Japanese guideline is converted to permit gastric endoscopic submucosal dissection (ESD) without cessation of low dose aspirin because thrombosis is usually more severe than bleeding[1]. American and British guidelines also admit to continue low dose aspirin during high-risk procedure, however, there are limited data of bleeding risk. Moreover, how to manage antithrombotic agents other than low dose aspirin is hardly reported.

Aims & Methods: The aim of this study is to compare the delayed bleeding rate in the patients who take antithrombotic agents with matched controls during the perioperative period of gastric ESD. We also compare the delayed bleeding rate of continuing antithrombotic agents with that of heparin bridging or cessation of antithrombotic agents.

Patients who underwent gastric ESD with or without cessation of antithrombotic agents between January 2009 and October 2014 were reviewed. Antithrombotic agents were defined as anticoagulant and antiplatelet, such as low dose aspirin, thienopyridine derivatives or cilostazol. Delayed bleeding was defined as the cases of emergent hemostasis after gastric ESD with a sign of bleeding.

Results: A total of 2105 patients underwent gastric ESD in the relevant period. Among them, 317 patients on antithrombotic therapy were reviewed. The patients on antithrombotic agents were divided into 3 groups according to existence of cessation or bridging therapy: 42 patients (13%) without cessation (continuation group), 29 patients (9%) with cessation and bridging therapy of heparin (heparin group), and the other 246 patients with cessation and without bridging therapy (cessation group). The period of cessation was determined according to the Japanese guideline in most cases[1]. A total of 683 patients without antithrombotic therapy were selected as controls. Controls were matched with a 1:2 ratio by location of the lesion and resected size of the specimen.

Overall bleeding rate of the patients on antithrombotic agents was 11% (35/317). This rate was significantly higher than that of matched controls (4.1% 28/683). The bleeding rate of continuation group, heparin group, and cessation group was 11.9%(5/42), 13.8%(4/29), and 10.6%(26/246), respectively. No significant differences were seen in bleeding rate, procedure time, tumor size and resected specimen size among these 3 groups.

During the perioperative period, a total of 4 thrombotic events occurred only in cessation group (1.6%).

	Continuation group(n = 42)	Heparin group(n = 29)	Cessation group(n = 246)	P value
Delayed bleeding	11.9%(5/42)	13.8%(4/29)	10.6%(26/246)	0.81
Procedure time (min)	44.7 ± 26.8	58.5 ± 51.6	48.7 ± 35.4	0.68
Tumor size (mm)	21.0 ± 16.8	23.5 ± 17.0	19.7 ± 15.2	0.18
Specimen size (mm)	49.3 ± 19.7	47.8 ± 20.7	45.9 ± 16.1	0.63
Thrombotic event	0%	0%	1.6% (4/246)	0.36

Conclusion: Patients who regularly take antithrombotic agents had higher risk of delayed bleeding than controls during the perioperative period of gastric ESD. No differences were seen in delayed bleeding rate with or without cessation. Taking into account the risk of thrombosis, gastric ESD without cessation of antithrombotic agents may be feasible.

Reference

1. 1 Fujimoto K, et al. *Dig Endosc* 2014;26:1-14.

Disclosure of Interest: None declared

OP289 PREDICTING DELAYED BLEEDING AFTER PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION OF COMPLEX COLORECTAL POLYPS

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Introduction: Delayed bleeding is the most common severe adverse event after p-Endoscopic Mucosal Resection (p-EMR) but factors that may predict delayed bleeding are not well-defined.

Aims & Methods: The primary objective of this study was to identify potential patient, polyp and technique-related risk factors for delayed bleeding using univariate and multivariable logistic regression analyses. A prospective p-EMR database of complex colorectal polyps included a description of the final post-EMR defect. We also aimed to analyse the inter-observer agreement between two blind assessors for 4 polypectomy defect-related factors (visible vessels, visible muscle fibres, submucosal haematoma (''cherry red spot'') and APC > 30% base). A checklist telephone call at 15 days post p-EMR documented the incidence of delayed bleeding.

Results: Of 323 patients/341 complex colorectal polyps (mean size 3.7cm), seventy-two patients (22%) had delayed bleeding (39/72 did not require hospitalisation, 22/72 required hospitalisation but no therapeutic intervention, 11/72 required blood transfusion and 1/11 had a segmental bowel resection). Univariate analysis demonstrated that delayed bleeding was associated with **patient** (female gender), **polyp** (rectosigmoid site, increasing size, Paris classification Is + IIa, Kudo pit pattern type IV, incomplete lift, previous polypectomy

attempt), **technique** (longer procedure time, mixed - saline and hyaluronate - injection solution type, greater solution volume, spiral p-EMR) and **post-polypectomy defect** (''cherry red spot'' and visible muscle fibres) related factors (Table).

Factors	Category	Delayed BleedingN (%)	Odds Ratio (95% CI)	P-value
PATIENTGender	Female	34/122 (28%)	1.73 (1.02, 2.93)	**0.04**
POLYPSite	R. sigmoid/rectum	37/112 (33%)	1	**0.007**
Size (cm)	-	-	1.27 (1.12, 1.43)	**<0.001**
Paris classification	IIa /IIb	13/104 (13%)	0.51 (0.26, 1.01)	**<0.001**
Kudoclassification	IV	39/130 (30%)	2.17 (1.28, 3.68)	**0.004**
Polyp Lift	Incomplete	50/173 (29%)	2.49 (1.43, 4.36)	**0.001**
Previouspolypectomy	Yes	29/91 (32%)	2.13 (1.23, 3.70)	**0.007**
TECHNIQUE				
Procedure time (*)	-		1.18 (1.07, 1.31)	**0.002**
Solutiontype	Saline/hyaluronate	19/51 (37%)	2.57 (1.35, 4.89)	**0.004**
Solution volume(*)	-		1.15 (1.06, 1.25)	**0.001**
DEFECTSRed cherry spot	Yes	18/41 (44%)	3.31 (1.63, 6.73)	**0.001**
Visible muscle fibers	Yes	23/51 (45%)	3.87 (1.99, 7.51)	**<0.001**

(*) Odds ratios reported for a 10-unit increase in predictor variable

Multivariate analysis confirmed that delayed bleeding was associated with female gender (OR 2.2,p = .02), previous polypectomy attempt (OR 2.58,p = .006), longer procedure time (OR 1.2,p = .007), visible muscle fibres (OR 4.51,p < .001), Paris classification Is + IIa (OR 2.51,p = .002), mixed injection solution type (OR 2.53,p = .02) and spiral p-EMR (OR 1.89,p = .02). The presence of visible vessels within the polypectomy defect, the use of APC and aspirin were not found to be significant predictive variables. The inter-observer agreement for all four defect measures was moderate, with kappa values from 0.5-0.6.
Conclusion: Risk factors for delayed bleeding post p-EMR were identified. A global risk assessment may be developed using patient (female gender), polyp (previous polypectomy), technique (prolonged procedure time) and defect (visible muscle fibers) related factors.
Disclosure of Interest: None declared

OP290 MULTICENTER STUDY ABOUT HEMORRHAGE AFTER THERAPEUTIC ENDOSCOPY IN HEMODIALYSIS PATIENTS

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Introduction
Background: Therapeutic gastrointestinal endoscopy in hemodialysis patients is becoming a usual procedure, as the prevalence of maintenance hemodialysis is increasing every year, with the number of dialysis patients in Japan exceeding 300 thousand at the end of 2011 and continuing to increase. The increased risk of post-procedural hemorrhage among dialysis patients is empirically known, but has not been well documented.
Aims & Methods
Aim: We aimed to characterize hemorrhage after therapeutic endoscopy in hemodialysis patients.
Methods: Between 2009 and 2011, a nationwide multicenter survey using questionnaire was performed about hemodialysis patients undergoing therapeutic endoscopy (i.e., gastric endoscopic mucosal resection [EMR], gastric endoscopic submucosal dissection [ESD], colonic EMR/polypectomy, and colonic ESD) . For controls, non-dialysis patients who underwent therapeutic endoscopy were also included.
Results: We collected data from 113 dialysis patients and 10297 control patients at 13 medical institutions. Of the 113 dialysis patients, 46 had undergone therapeutic gastroscopy and 67 therapeutic colonoscopy. Of the 10297 control patients, 3386 had undergone therapeutic gastroscopy and 6957 therapeutic colonoscopy.
The overall incidence of post-procedural hemorrhage was 14.2% (16/113) in the dialysis group and 2.6% (272/10297) in the control group ($p < 0.001$).
By site, the incidence of hemorrhage after therapeutic gastroscopy was 23.9% (11/46) in the dialysis groupand 4.8% (160/3340) in the control group; and that after therapeutic colonoscopy was 7.4% (5/67) in the dialysis group and 1.6% (112/6957) in the control group ($p < 0.001$).
As for background factors, overall, use of antithrombotic drugs ($p = 0.03$) and pre-procedural dialysis using nafamostat mesilate ($p = 0.002$) were detected as significant factors. Multivariate analysis using logistic regression analysis revealed that duration of dialysis (in years) was also a significant factor ($p = 0.001$).
A similar analysis performed separately for gastroscopy and colonoscopy, demonstrated that post-procedural dialysis using nafamostat mesilate ($p = 0.01$) was a significant factor for hemorrhage after gastroscopy, and duration of dialysis (in years) ($p = 0.03$) was a significant factor for hemorrhage after colonoscopy.
The hemorrhage after therapeutic endoscopy tended to be of delayed onset in dialysis patients compared with control patients.
Conclusion: The risk of hemorrhagic complications after therapeutic endoscopy was significantly higher in hemodialysis patients. Dialysis itself can be a risk factor, rather than age and use of antithrombotic drugs. Increased caution is warranted in monitoring dialysis patients after therapeutic endoscopy.
Disclosure of Interest: None declared

OP291 POST POLYPECTOMY BLEEDING (PPB) IN THE ENGLISH NHS BOWEL CANCER SCREENING PROGRAMME (NHSBCSP)

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Introduction: Colonoscopies in the English NHSBCSP are offered to 60-74 year olds with an abnormal Faecal Occult Blood Test. Colonoscopies are performed at 61 Bowel Cancer Screening Centres (BCSCs) which are divided geographically between five regions of England. Polypectomy breaks the adenoma-carcinoma sequence but carries a risk of Post Polypectomy Bleeding (PPB). The NHSBCSP has a longstanding robust mechanism for capturing adverse events. Adverse Events are graded by severity using the NHSBCSP framework, based on the American Society of Gastrointestinal Endoscopy grading system.[1,2]
Aims & Methods: We aimed to (1) determine the rate of PPB, broken down by severity grading, in one region of the NHSBCSP (2) describe PPB management and outcomes and (3) explore the factors that contribute to PPB's severity grading. This prospectively collected observational case series identified patients with PPB at 5 BCSCs within the North East Region of the English NHSBCSP from 06/12/2010 to 15/07/2014. We defined PPB as bleeding presenting following completion of the procedure and that resulted in medical consultation, admission to or prolongation of an existing hospital stay or another intervention. Patient co-morbidity, use of anticoagulation, polyp location, morphology, size, polypectomy method, time to presentation, subsequent patient management and outcome were all recorded. PPB was graded into major, intermediate or minor as per the NHSBCSP grading system.
Results: From a total population of 4,191,507, 15,285 colonoscopies were subsequently performed on 11,564 patients leading to 23,766 polypectomies. 68 patients with PPB were identified; a PPB rate of 0.44% per colonoscopy and 0.29% per polypectomy. 2.9% of cases were major due to need for surgery or admission to ITU for > 1 night; median time to presentation was 3.5 days (range 1-6 days), median hospital stay was 3 days (range 2-4) days. 42.6% were intermediate, the majority due to requiring an interventional procedure or a haemoglobin drop ≥ 2g/dL; median time to presentation was 4.5 days (range 0-19 days), median hospital stay was 2 days (range 0-6 days). Of all patients with PPB, 8.8% presented with symptoms or signs of haemodynamic compromise. 19.1% required resuscitation with intravenous fluids and/or red blood cells. Repeat endoscopy was performed in 27.9% with repeat endoscopic therapy in 10.3%. Surgery was performed in 1.47% of cases. 1.47% of patients required a second admission and were managed radiologically.
Conclusion: (1) We believe this detailed, robustly collected and prospectively categorised dataset gives a true reflection of PPB rate among experienced colonoscopists. (2) A PPB rate of 0.44% is therefore excellent when compared with other similar series. (3) Clinically significant PPB, defined as major or intermediate severity, occurred in less than half of the cases reported.

References

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Disclosure of Interest: None declared

OP292 ESTABLISHMENT OF OVER-THE-SCOPE-CLIPS (OTSC) IN DAILY ENDOSCOPIC ROUTINE: A LONG-TERM SINGLE CENTRE EXPERIENCE

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Introduction: Alongside with the evolution of interventional endoscopy, the need for a more sophisticated closure tool tailored to the treatment of new challenging indications has been increasing rapidly. In 2007, the first small case series (11 cases) of Over-The-Scope-Clip (OTSC, Ovesco, Tübingen) placement in the gastrointestinal tract was reported.
Aims & Methods: We here present our collected data on 223 OTSC placements in a total of 198 interventions at out institution. Follow up was focused on clinically lasting success in regard to the different indications.
Results: Acute gastrointestinal perforation (39.9%; 79/198), fistulas or anastomotic insufficiency (34.3%; 68/198), gastrointestinal bleeding (23.2%; 46/198) and diameter reduction of the gastrojejunal anastomosis after bariatric surgery (2.5%; 5/198) were the four main indications for OTSC placement.
Acute gastrointestinal perforations were located in the esophagus (10.1%; 8/79), in the stomach, (17.7%; 14/79), in the duodenum (21.5%; 17/79), in the colon (44.3%; 35/79) and in the rectum (6.3%; 5/79).

Anatomic locations of the *fistulas or anastomotic insufficiencies* were defined by their gastrointestinal origin. 20.6% (14/68) of the lesions originated from the esophagus, 29.4% (20/68) from the stomach, 1.5% (1/68) form the duodenum, 16.2% (11/68) from the small intestine, 11.8% (8/68) from the colon and 20.6% (14/68) from the rectum.
Gastrointestinal bleeding was located in the esophagus in 6.5% (3/46), in 19.6% (9/46) in the stomach, in 54.3% (25/46) in the duodenum, in 2.2% (1/46) in the small intestine, and in 17.4% (8/46) in the colon.
Overall immediate success of OTSC deployment was achieved in 84.8% (168/198) of the cases. The main causes for failure of OTSC placement (15.2%; 30/198) were non-suitable anatomic structure (30%; 9/30), rigidity of the lesion-surrounding tissue (30%; 9/30) and lesion size exceeding OTSC size (40%; 12/30). In 3 cases (1.5%; 3/198) the passage of the mounted OTSC through the upper esophageal sphincter was not possible, but OTSC-passage became successful after loading a smaller sized OTSC. In 8.1% of the cases (18/223), proper OTSC placement was not achieved and clip removal was performed during the same procedure.
At *thirty-day follow-up*, 61.1% (121/198) of the cases were granted as successful OTSC treatment, whereas 34.8% (69/198) of the cases had to be considered as failed treatment. Four percent (8/198) of the cases were either lost to follow up at 30 days or no follow was indicated. OTSC application in the stomach, duodenum or colon was shown to be favourable in order to reach success at day 30, whereas the treatment of fistulas and anastomotic insufficiency was less promising.
After one year, 42.4% (84/198) of the cases were followed up. Eighty-one per cent (68/84) of these cases were considered as permanent successful OTSC treatment. 9.5% (8/84) were declared as failure of OTSC treatment at one year follow up, whereas another 9.5% (8/84) were lost of follow up at this point.
Conclusion: In conclusion, the OTSC device has been shown to be a must-have tool when performing frequent interventional endoscopic procedures and may be a valuable tool to spare the surgeon. Yet, before a safe and purposeful OTSC application can be guaranteed, the endoscopist has to earn experience in handling the device. An issue to overcome in the near future is the removal of the clip if indicated.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 14:00–15:30
BRAIN-GUT INTERACTIONS IN HEALTH AND DISEASE – ROOM E4

OP293 FOOD-INDUCED DOPAMINE RELEASE IN EXTRA-STRIATAL REGIONS OF THE BRAIN REWARD SYSTEM PREDICTS FOOD INTAKE IN HEALTHY HUMANS

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Introduction: Several studies have tried to assess the role of dopamine (DA) in human food reward by measuring either baseline DA $D_{2/3}$ receptor availability or DA release in response to some food cue. However, results have been inconsistent and often rely on the use of pharmacological stimulation of DAergic neurons and/or scanning before and after rather than during presentation of food stimuli. Moreover, research on the role of extra-striatal DA signaling in human food reward is completely lacking to date, even though it is generally accepted that DA release in these regions is also implicated in food reward.
Aims & Methods
Aim: To assess DA release in both striatal and extra-striatal brain regions in response to food stimuli in healthy volunteers.
Methods: 7 healthy females (age = 25 ± 8.25 years; BMI = 21.62 ± 2.02 kg/m^2) underwent a single dynamic Positron Emission Tomography (PET) scanning session after intravenous administration of 183.25 ± 7.01 MBq of the highly selective DA $D_{2/3}$ PET radioligand [^{18}F]fallypride. A food reward task was initiated at 180 min post-injection and comprised a set of visual stimuli consisting of high-calorie food images, combined with the delivery of a small amount (8ml/8sec) of chocolate milkshake every 4 min. PET data were analyzed using the linearized simplified reference region model, which accounts for temporal perturbations in [^{18}F]fallypride displacement. Parametric voxel-based statistical maps, representing specific $D_{2/3}$ binding changes, were computed to subsequently localize areas within a binary mask of regions of interest with increased ligand displacement after the food reward task onset. Significant ligand displacement, representing food-induced DA release, was quantified as the number of voxels within each region exceeding a threshold of $T > 4.4$, which corresponds to $p_{FWE\text{-}corrected} < 0.05$. Data are presented as mean ± SEM.
Results: Food stimuli induced significant DA release in extra-striatal regions of the reward system (ventromedial prefrontal cortex (vmPFC, BA10), medial orbitofrontal cortex (mOFC, BA11), lateral orbitofrontal cortex (lOFC, BA47), anterior cingulate cortex (ACC, BA24 & BA32), and insula), with the largest amount of ligand displacement present in the ACC (BA24 = 28.6 ± 4.7%, BA32 = 33.5 ± 5.1%). Moreover, food-induced DA release in the left ACC and left insula strongly and significantly predicted the amount of milkshake consumed during an ad libitum drink test following the PET scan (respectively r = 0.84, p = 0.037 and r = 0.86, p = 0.027). The amount of significant food-induced ligand displacement in striatal regions was less pronounced compared to extra-striatal brain regions, with exception of the putamen (left = 24.4 ± 8.4%; right = 19.4 ± 7.0%). There was no significant DA release in the nucleus accumbens.
Conclusion: To the best of our knowledge, this study shows for the first time that food stimuli induce not only increased levels of endogenous DA in striatal regions, but also in extra-striatal brain regions of the reward system. Furthermore, this food-induced extra-striatal DA release predicted subsequent food intake. These results might be a first step towards a better understanding of the role of the brain DA system in food reward, which may facilitate the development of improved therapeutic approaches for disorders of food intake such as obesity.
Disclosure of Interest: N. Weltens: None declared, L. Cool: None declared, J. Ceccarini: None declared, J. Tack Financial support for research: Novartis, Shire, Zeria, Almirall, AstraZeneca, Janssen and Menarini, Lecture fee(s): Abbott, Almirall, AstraZeneca, Janssen, Menarini, Novartis, Shire, Takeda and Zeria, Consultancy: Almirall, AstraZeneca, Janssen, Menarini, Shire, Zeria, AlfaWassermann, Danone, GI Dynamics, GlaxoSmithKline, Ironwood, Novartis, Rhythm, Sucampo, Takeda, Theravance, Tsumura and Yuhan, K. Van Laere: None declared, L. Van Oudenhove: None declared

OP294 RNASEQ ANALYS REVEALS DYREGULATED EXPRESSION OF NOVEL GENES IN IDIOPATHIC ACHALASIA

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Introduction: Esophageal achalasia is a motility disorder characterized by the lack of esophageal peristalsis and failure of the lower esophageal sphincter to relax. The occurrence of genetic syndromic cases and data from mutant mouse models (Sprouty-2$^{-/-}$ and kit$^{-/-}$) suggest that genetic factors may play an important pathogenetic role.
Aims & Methods: This study was designed to identify novel molecular features of sporadic achalasia.
Methods: 16 (7 F; age range: 26-72 yrs) clinically, radiologically and manometrically characterized patients with sporadic achalasia were included. A group of 4 (2F; age range: 30-67 yrs) subjects undergoing surgery for uncomplicated esophageal cancer served as controls. During surgery, full-thickness tissue samples were obtained from achalasic patients and controls from immunohistochemical and molecular analysis. Total RNA (150 ng), extracted from tissues of 4 achalasia patients and 4 controls, was used for library preparation (TruSeq Stranded Total RNA Sample prep kit v2) and sequencing on HiScan SQ. Data analysis was performed with the 'edgeR' option of R-Bioconductor. Gene expression was validated by real-time qRT-PCR and immunohistochemical analysis. Variant calling analysis from transcriptome data was also performed using an internal pipeline for single nucleotide/small indels calling. Sanger sequencing was performed to validate the presence of the variants at the DNA level.
Results: Quantitative transcriptome evaluation and cluster analysis revealed 116 differentially expressed genes, with a $P = 10^{-3}$. 9 genes with a $P < 10^{-4}$ were chosen for validation and further analysis by qRT-PCR. Among the genes not previously associated to the achalasia phenotype in human samples *CYR61*,*CTGF*, *KIT, DUSP5*, *EGR1* were downregulated, whereas *AKAP6* and *INNP4B* were upregulated in patients vs. controls. Compared to control tissues immunohistochemical analysis revealed a clear increase in *AKAP6* and *INNP4B* immunostaining, whereas *KIT* immunolabeling resulted downregulated, thus confirming in humans previous data in mouse models.
Sequence analysis of the transcriptome data from the same achalasia patients revealed rare heterozygous missense variants for the type T calcium channel-encoding gene *CACNA1H*, which is expressed in murine ICC cells. The presence of the variants was confirmed in the corresponding genomic DNA.
Conclusion: Our study identified several novel genes dysregulated in achalasia patients, which provide a molecular basis to severe neuro-glial-ICC alterations. These findings may prove relevant for a better definition and identification of subsets of achalasic patients.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 14:00–15:30
TRAINING IN ENDOSCOPY – ROOM E3

OP295 DOES THE PRESENCE OF A TRAINEE COMPROMISE BILIARY CANNULATION RATES AT ECRP: RESULTS FROM A PROSPECTIVE AUDIT

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Introduction: A trainee endoscopist on the ERCP list prolongs procedure time and may increase risk of technical failure or procedural complications [1, 2]. Recent BSG guidance has identified a biliary cannulation rate of 90% as an ERCP performance indicator which may conflict with the need to train juniors. This prospective audit assessed the impact of an endoscopy trainee on the overall biliary cannulation rates.
Aims & Methods: We prospectively audited sequential ERCPs done on a ''virgin'' ampulla (no previous ERCP). Procedures were supervised by 2 experienced trainers ; trainees were present when possible(trainees were senior SpRs with limited ERCP experience) . A short-wire system was used for biliary cannulation and standard techniques used [1]. The trainee would have 6

minutes to achieve biliary cannulation, failing which the trainer would take over. Predicted ERCP difficulty was graded using accepted criteria [3]. The primary outcome was the biliary cannulation rate.
Results: One hundred and eight sequential ERCPs were prospectively audited over a period of 6 months [July 2014- Dec 2014]. Difficulty was graded as 1 (n = 69) or 2 [n = 39]. One of two trainee endoscopists was present during 61 [56%] ERCP cases; remaining cases were done by a consultant alone [n = 47, 44%]. Deep biliary cannulation was successful in 99 cases [91%]. The cannulation rate was 93% [57/61] with a trainee and 89% [42/47] without [p = 0.7229 Fishers exact test]. Median cannulation time was 6.6 minutes (range 1 – 25). There was no significant difference in cannulation times when a trainee was present [T test, p = 0.890]. Where a trainee was involved, 20/61 [32%] cannulations were achieved independently by the trainee. There were no major complications recorded in cases where a trainee was involved.
Conclusion: This audit suggested that acceptable biliary cannulation rates can be achieved on ERCP training lists, with involvement of experienced trainers and defined training parameters.

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Disclosure of Interest: None declared

OP296 STANDARDIZED TRAINING PROGRAM FOR DIAGNOSIS OF EARLY GASTROINTESTINAL CANCERS IN ASIA

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Introduction: Gastrointestinal (GI) cancers are diagnosed at advanced stage in most of the Asia Pacific countries. The development of NBI allowed endoscopists to improve recognition and characterization of early GI cancers through narrowing bandwidth of light with concentration on details of the mucosa. The Asian NBI group (ANBIG) was founded with an objective to conduct training in endoscopic diagnosis and treatment of early GI cancers in Asia using standardized training module. This is a prospective cohort study on the effectiveness of standardized training module for NBI on diagnosis of early GI cancers in Asia.
Aims & Methods: This is a prospectively collected database from workshops conducted in Asia on endoscopic diagnosis and treatment of early GI cancer by ANBIG. All the workshops were conducted in a standardized program, including pre-test, lectures on NBI diagnosis of early esophageal, gastric and colorectal cancers, case discussion, live demonstration or video presentation and hands-on training on EMR and ESD. After completion of the training course, a post-test was conducted to reassess the knowledge gained. The pre-training and post-training tests were standardized questions addressing 4 domain of knowledge, including basic knowledge of imaging, diagnosis of esophageal, gastric and colonic neoplasia.
Results: From Nov 2013 to April 2015, 15 ANBIG workshops were conducted in Asia, including China, Hong Kong, India, Indonesia, Malaysia, South Korea, Taiwan, Thailand, Mongolia and Myanmar. A total of 531 delegates had participated in these workshops and 279 of them completed the pre-test and the post-test. 26 faculties had contributed to the conduction of these training courses. Comparing the pre-training and the post-training test results, there was a significant overall improvement after the workshop training in the diagnosis of early gastric and colorectal neoplasia (Table 1). When the workshops were divided into those conducted in developed countries against those developing countries using GDP, there was generally a lower accuracy in pre-test knowledge for participants from developing countries than those in developed countries.

Table 1: - Comparison of accuracy in endoscopic diagnosis of early gastrointestinal neoplasia before and after standardized training workshops

Overall Accuracy	Pre-training	Post-training	p value
Basic NBI Knowledge	53.6%	64.6%	0.009∫
Endoscopic diagnosis of early esophageal neplasia	44.6%	52.6%	0.052
Endoscopic diagnosis of early gastric neoplasia	50.1%	65.5%	0.002∫
Endoscopic diagnosis of early colorectal neoplasia	50.8%	65.7%	0.020∫

∫ = $p < 0.05$

Conclusion: A standardized training module on image-enhanced endoscopy improved the diagnostic ability and quality for endoscopists in recognition of early gastrointestinal cancers.
Disclosure of Interest: None declared

OP297 NURSE PARTICIPATION COLONOSCOPY OBSERVATION VERSUS COLONOSCOPIST ALONE FOR POLYP AND ADENOMA DETECTION: A META-ANALYSIS

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Introduction: Colorectal cancer (CRC) is one of the most common cancers worldwide. Colonoscopy screening and removal of adenomas has been considered to be the most effective method reducing incidence and mortality of CRC [1,2].
Aims & Methods
Aims: This meta-analysis aimed to evaluate whether nurse participation (NP) colonoscopy improves polyp and adenoma detection, compared with colonoscopist alone (CA) colonoscopy.
Patients and methods: Literatures in English were searched for randomized controlled trials (RCTs) in the databases PUBMED, EMBASE, and Cochrane Library. Outcome measurements included: (1) polyp and adenoma detection rate (PDR and ADR); (2) advanced polyp detection rate; and (3) mean polyp and adenoma detection per colonoscopy.
Results: Three RCTs with a total of 1676 patients were included. Two RCTs compared NP colonoscopy versus CA colonoscopy on PDR and advanced PDR, and pooled data showed there was no significant difference in the PDR and advanced PDR between the two groups (RR: 0.95, 95% CI: 0.95-1.37; RR: 1.35, 95% CI: 0.92-1.97; respectively). Three RCTs compared NP colonoscopy versus CA colonoscopy on ADR, and pooled data showed a significant higher ADR on NP group (45.7% vs. 39.3%; RR 1.16; 95% CI, 1.04-1.30). Two trials compared NP colonoscopy versus CA colonoscopy on advanced PDR, and pooled data showed no statistical differences between the two groups (12.4% vs. 8.7%; RR 1.35; 95% CI, 0.92-1.97).
Conclusion: Nurse participation during colonoscopy can improve ADR, while no benefit for PDR and advance PDR.

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Disclosure of Interest: None declared

OP298 EXPERIENCE IN POLYPECTOMY TRAINING AND ASSESSMENT: AN INTERNATIONAL SURVEY

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Introduction: Colonoscopy is widely practised to reduce rates of colorectal cancer, although the protection it confers is not absolute. The most hazardous part of colonoscopy is polypectomy, accounting for the majority of serious complications. It is unclear whether countries around the world have highlighted polypectomy as a specific skill that needs to be taught.
Aims & Methods: The objective of the study was to assess both trainees' and trainers' experience of polypectomy training in countries around the world. Colonoscopy trainers from 19 countries worldwide were asked to provide access to local trainers and trainees who would be invited to participate in a survey. An online survey was created asking about trainees' experience of instruction and trainers' experience of teaching polypectomy skills.
Results: Data were obtained from 610 colonoscopists- 348 (57.0%) trainers and 262 (43.0%) trainees. Most (79.6%) of the trainers surveyed were involved in trainee polypectomy assessment weekly. 51.4% of those surveyed said that they used a specific framework when assessing polypectomy.
90.5% of trainees had a primary specialty of medical gastroenterology. The trainees had a breadth of colonoscopic experience, 31.7% having completed more than 500 colonoscopies and 38.2% fewer than 200 procedures. 51.1% stated that the principles of polypectomy had only been taught intermittently.

Most (64.1%, 168 respondents) trainees had never been taught the principles of endoscopic mucosal resection.
Only 53.1% of trainees had ever had their polypectomy technique formally assessed by any trainer. Of the 177 trainees who stated that they were competent at polypectomy, 70 (39.5%) had never had a formal evaluation of their polypectomy technique.
Conclusion: This study, the only in the literature, shows that polypectomy training is variable worldwide with low prevalence of formal competency assessment. There is a need to a) understand the learning curve for polypectomy, b) develop an international consensus defining optimal training methods and c) develop a framework of competency assessment. This should improve the safety of polypectomy and the effectiveness of colonoscopy in preventing colorectal cancer.
The authors would like to acknowledge the contribution of all 610 respondents and in particular the local training faculty who facilitated this study.
Disclosure of Interest: None declared

OP299 A LOCAL STRUCTURED TRAINING PROGRAM WITH IN-VIVO PIGS ALLOWS TO PERFORM RECTAL ESD WITH RESULTS CLOSE TO JAPANESE EXPERTS

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Introduction: Training in ESD requires numerous sessions to become efficient. A well-structured training program is essential, because the outcome of ESD is dependent of the experience of the endoscopist. European experts recommend such programs with animal models to overcome the initial learning curve. European experts recommended a minimum training of five ESD on animal model and observation of at least 15 live procedures before beginning ESD initially in the rectum before stomach and oesophagus. Afterwards, constant practicing of ESD is required to increase success and decrease the procedure time and complications. Despite the completion of these recommendations, first results published by european teams are far from those of Japanese experts in the rectal location.We thus decided to initiate a local training program with constant and regular exposure to gastric ESD in in vivo pigs.
Aims & Methods: Between March 2013 and April 2015, 52 pig gastric ESD were performed by two operators in a total of 14 anesthetized pigs, fasted for 48H prior to the procedure. After the 11 initial pig gastric ESD, operators felt able to begin human rectal ESD. 29 rectal human ESD for large LST were performed during the same period. The 41 next animals ESD were performed in parallel in order to keep a constant exposure to ESD cases. All procedures were performed with a hybridknife type T (Erbe medical, Germany). Glycerol mixture and physiologic serum were used for submucosal injection. In 25 human cases, the two operators took turns every hour to facilitate the procedures.
Results: Pig model: en bloc resection rate (EBRR): 98.07% (51/52); mean dissection time (DT): 47 min; mean speed of dissection (SOD): 23.3 mm^2/min; mean size of the resected specimen (SOS): 1046 mm^2.
The SOD of the 10 first ESD was significantly lower than each group of 10 next ESD: 15.7 vs 24.83-28.5-23.5-23.9 mm^2/min; $p < 0.05$).
Only 1 perforation (1.8%) occurred and 10 (19.2%) per procedure bleedings imposed the use of a coagulation forceps.
Human rectal ESD: EBRR: 100% (29/29); R0 resection rate: 93.1% (27/29); mean DT: 193.4 min; mean SOD: 12.70 mm^2/min; mean SOS: diameter 1: 56.57 mm, diameter 2: 43.85 mm, surface: 193.4 mm^2; perforation rate: 10.3% (3/29) all managed conservatively; post procedural bleeding 10.3% (3/29) all managed endoscopically. 0/24 and 0/8 had a residual or recurrent disease at 3 and 12 months respectively.
SOD increase linearly during the 8 first procedures to reach a plateau between 15 and 20 mm^2/min.
The SOD of the first 8 rectal ESD was significantly lower than the 10 next and the ten last ESD: 7.48 vs 15.68-15.93 mm^2/min ($p = 0.0035$).
Conclusion: Our prospective study of rectal ESD of large spreading tumors is one of the largest in a monocentric european center. A local training program with pig model allows starting human dissection with high safety and efficiency close to results published by japanese experts. Initial training accelerates the learning curve and the continuous practice in pig model allows maintaining constant training until the recruitment of patients becomes sufficient. The collaboration of two physicians during the long dissections probably helps improving the results.

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Disclosure of Interest: None declared

OP300 SURGICAL MARGIN NEGATIVE ENDOSCOPIC MUCOSAL RESECTION (SN-EMR) FOR ENDOSCOPY TRAINEE: A RANDOMIZED MULTICENTER PROSPECTIVE STUDY

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Introduction: As endoscopic mucosal resection (EMR) is an established colorectal polyp treatment, local recurrence occurs in 13% of cases due to inadequate snaring by endoscopy trainees.
Aims & Methods: A randomized multicenter prospective study was conducted whether surgical margin negative endoscopic mucosal resection (SN-EMR) with simple pre-clipping procedure enabled endoscopy trainees to perform complete resection. Of 159 polyps from 80 patients with colorectal polyps under 20 mm, we included 106 polyps from 51 patients. We randomly allocated polyps to the conventional injection group (CG) (55 polyps) or the pre-clipping injection group (PG) (51 polyps). The PG received three-point pre-clipping to ensure ample gripping to the muscle layer on the oral and both sides of the tumor with 4 mL local injection. Endoscopic ultrasonography was performed to measure the resulting bulge. Outcomes included the number of instances of thermal denaturation of the horizontal margin (HMX) or positive horizontal margins (HM+), the shortest distance from tumor margins to resected edges, and the maximum bulge distances from tumor surface to the muscularis propria.
Results: The numbers of HMX and HM+ in the CG and PG were 15 (27%) and 2 (3.6%) and 3 (5.8%) and 0 (0%), respectively ($P = 0.001$). The shortest distance from tumor margin to resected edge (±standard deviation, SD, mm) in polyps in the CG and PG were 0.673 ± 0.546 and 3.910 ± 1.271, respectively ($P = 0.017$). The maximum bulge distances were 4.740 ± 1.379 and 11.14 ± 2.924 ($P = 0.006$), respectively. In CG group, local saline injection extended horizontally to become larger and flatter, making the snare slippery resulting in HMX. In PG, pre-clipping from the mucosa to the muscularis propria allowed the snare to accurately strangulate the tumor without slippage by creating maximally vertical rather than horizontal bulges, resulting in resections with 3-4 mm of safety margin.
Conclusion: SN-EMR enabled endoscopy trainees to perform complete resection.

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Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 14:00–15:30

VISCERAL HYPERSENSITIVITY AND ALTERED GUT MOTILITY: MECHANISTIC INSIGHTS – ROOM E5

OP301 MODULATION OF MUCOSAL SENSITIVITY VIA THE EPITHELIAL GUANYLATE CYCLASE-C/CYCLIC GMP PATHWAY: LINACLOTIDE AS A REGULATOR OF VISCERAL SENSATION

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Introduction: Linaclotide, a guanylate cyclase-C (GC-C) agonist, effectively improves abdominal pain and constipation in patients with irritable bowel syndrome with constipation (IBS-C). Using a mouse model, we have previously shown that both linaclotide and exogenous extracellular cyclic guanosine monophosphate (cGMP) inhibit colonic nociceptor mechanosensitivity with greater efficacy during chronic visceral hypersensitivity (CVH) compared with healthy mice.[1]
Aims & Methods: To determine the effect of linaclotide and extracellular cGMP on other afferent classes, we investigated healthy C57BL/6 mice and mice with CVH (28 days after administration of 2,4,6-trinitrobenzenesulfonic acid).[1] Mechanosensory responses of colonic pelvic mucosal afferents were compared in the presence and absence of linaclotide (1–1000 nM) using *ex vivo* electrophysiological recordings. In addition, we assessed the ability of intracolonic linaclotide (1000 nM) to modulate mucosal signalling transmission *in vivo* by measuring the activation of dorsal horn neurons in the lumbosacral (LS:L6–S1) spinal cord in response to fine mechanical stimulation of the colorectal mucosa. Finally, we investigated the effects of exogenous extracellular cGMP (10–50 μM) on subpopulations of retrogradely traced colonic dorsal root ganglion

(DRG) neurons isolated from mice using whole-cell patch-clamp recordings in current clamp mode.
Results: Linaclotide caused a dose-dependent increase of low-threshold pelvic mucosal afferent mechanosensitivity in healthy mice ($P<0.001$; n = 7). This potentiating effect was completely lost in CVH mice ($P>0.05$; n = 7). *In vivo*, fine mechanical stimulation of the colorectal mucosa activated discrete populations of dorsal horn neurons within the LS spinal cord (n = 4). In healthy mice, intra-colonic administration of linaclotide increased the number of LS dorsal horn neurons activated by fine mucosal stimulation ($P<0.05$; n = 5), and the potentiating effect of linaclotide was lost in CVH mice ($P>0.05$; n = 5). In patch-clamp studies from healthy mice, application of cGMP, a known downstream mediator of GC-C activation, resulted in increased excitability of a subpopulation of colonic DRG neurons, as indicated by a reduced rheobase ($P<0.05$; n = 9) and increased firing frequency ($P<0.05$; n = 9). Notably, these potentiating effects of cGMP were not apparent in colonic DRG neurons from CVH mice.
Conclusion: Chronic oral administration of linaclotide reduces colonic nociceptor mechanosensitivity and reduces nociceptive signalling within the spinal cord in response to noxious CRD, with greater effect during CVH compared with healthy mice. Results complement our previous findings[1] and provide further mechanistic insight into how linaclotide, through GC-C agonism and the release of cGMP from mucosal epithelial cells, can reduce nociceptive signalling from the colon.

Reference

1. Castro J, Harrington AM and Hughes PA, et al. *Gastroenterology* 2013; 145: 1334–1346.

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OP302 ALUMINUM INGESTION PROMOTES THE DEVELOPMENT OF COLORECTAL HYPERSENSITIVITY IN RODENTS

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Introduction: Irritable bowel syndrome is a common disease characterized by chronic abdominal pain. Involvement of environmental factors is suspected in the development of this syndrome, especially because of the high prevalence in Western countries.
Aims & Methods: Our aim was to analyze the effect of aluminium ingestion on visceral sensitivity in rodent models.
Visceral pain threshold was assessed by colorectal distension in rats intoxicated with Aluminium Citrate (AlCi) at the environmentally relevant dosage of 1.5 mg/kg bw/day. Different doses and timings, gender specificity were evaluated. Effect of the co-administration of a well-known inhibitor of mast cells degranulation, cromolyn sodium, was assessed on visceral sensibility. Expression levels of 23 selected genes known to be involved in visceral pain were quantified in colons of rats intoxicated or not with AlCi. Visceral sensitivity and intestinal permeability assessed by FITC-dextran method were compared between PAR2 WT and KO mice treated with AlCi.
Results: A significant increase of response to colorectal distension was observed in AlCi treated rats from the day 8 of intoxication, which lasted at day 15 and even worsened at day 30, compared to non-intoxicated rats. This effect was time and dose dependent, and persists other time. A new administration of AlCi after discontinuation of intoxication led to a higher decrease of pain threshold. Females were more susceptible than males to AlCi induced visceral hypersensitivity. Although mast cells numbers did not vary, the percentage of degranulated mast cells was increased in AlCi treated rats compared to controls rats. The co-administration of cromolyn sodium reversed the decrease of pain threshold induced by 8 days intoxication with AlCi. Cannabinoid receptor 1 (*Cnr1*), the transient receptor potential cation channel (*Trpa1*), the proteinase activated receptor 2 and 4 (*Par2* and *Par4*), the vanilloid receptor 1 and 4 (*Trpv1* and *Trpv4*) genes showed significant mRNA expression alterations in Al intoxicated rats. Consistently, we observed in WT mice a significant increase of visceral motor response induced by AlCi intoxication. Notably, AlCi ingestion failed to induce significant variation on visceral motor response in PAR2 KO mice. Finally, the significant increase of intestinal permeability observed in PAR2 WT mice treated with AlCi compared to untreated mice was not found in PAR2 KO mice.
Conclusion: We have demonstrated that currently ingested amounts of Al in humans induced in mice and rats a dose dependent increase of colorectal sensitivity. Al-induced hypersensitivity persists over time so that intoxication was arrested, and appears again when Al intoxication resumes, dismissing any tolerance phenomenon. As for irritable bowel syndrome frequency, female gender was more affected by Al-induced hypersensitivity than male gender. The mechanisms involved a degranulation of masts cells and an increased permeability. Finally, the Al-induced visceral pain increase is PAR2 dependent.
Disclosure of Interest: None declared

OP303 LINACLOTIDE-INDUCED CHRONIC ACTIVATION OF THE GUANYLATE CYCLASE-C/CYCLIC GMP PATHWAY INHIBITS ASCENDING NOCICEPTIVE PATHWAYS AND RESTORES ABERRANT SPINAL CORD SIGNALLING

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Introduction: Linaclotide, a guanylate cyclase-C (GC-C) agonist, effectively improves abdominal pain and constipation in patients with irritable bowel syndrome with constipation (IBS-C). Recently, we have shown that in a mouse model acute application of linaclotide inhibits colonic nociceptor mechanosensitivity with greater efficacy during chronic visceral hypersensitivity (CVH) compared with healthy mice.[1]
Aims & Methods: To determine the effects of chronic linaclotide administration on nociceptor function, we investigated healthy C57BL/6 mice and mice with CVH (28 days post-2,4,6-trinitrobenzenesulfonic acid administration, when inflammation had resolved and nociceptors were mechanically hypersensitive).[1,2] Mice from each group were randomly assigned to either chronic linaclotide (3 μg/kg/day) or placebo (water) administered as a once-daily oral gavage for 2 weeks prior to experimentation. The effects of chronic oral linaclotide administration on colonic nociceptor function (stimulus response functions and activation thresholds to mechanical stimuli) from healthy and CVH mice were determined using *ex vivo* electrophysiological recordings. In addition, we assessed the ability of chronic oral linaclotide to alter nociceptive signalling transmission *in vivo* by measuring the activation of dorsal horn neurons in the thoracolumbar (TL:T10–L1) and lumbosacral (LS:L6–S1) spinal cord in response to noxious colorectal distention (CRD).
Results: In healthy mice, chronic linaclotide administration significantly reduced nociceptor mechanosensitivity compared with placebo ($P<0.05$; n = 10–12). Colonic nociceptors from CVH mice displayed mechanical hypersensitivity ($P<0.001$; n = 13) and reduced mechanical activation thresholds ($P<0.05$; n = 13) compared with healthy mice. In CHV mice, chronic linaclotide administration significantly reduced colonic nociceptor mechanosensitivity compared with placebo ($P<0.001$; n = 10–13). Furthermore, chronic linaclotide administration reversed the reduced mechanical activation thresholds of nociceptors from CVH mice compared with placebo. In separate *in vivo* experiments, chronic linaclotide administration to CVH mice significantly reduced the signalling of noxious CRD to the TL spinal cord ($P<0.01$; n = 4) compared with CVH mice administered placebo.
Conclusion: Chronic oral administration of linaclotide reduces colonic nociceptor mechanosensitivity and reduces nociceptive signalling within the spinal cord in response to noxious CRD, with greater effect during CVH compared with healthy mice. Results complement our previous findings[1] and provide further mechanistic insight into how linaclotide, through GC-C agonism and the release of cGMP from mucosal epithelial cells, can reduce nociceptive signalling from the colon.

References

1. Castro J, Harrington AM, Hughes PA, et al. *Gastroenterology* 2013; 145: 1334–1346.
2. de Araujo AD, Mobli M, Castro J, et al. *Nat Commun* 2014; 5: 3165.

Disclosure of Interest: J. Castro Financial support for research: Ironwood Pharmaceuticals/Forest Laboratories, A. M. Harrington Financial support for research: Ironwood Pharmaceuticals, S. Garcia-Caraballo Financial support for research: Ironwood Pharmaceuticals, J. Maddern Financial support for research: Ironwood Pharmaceuticals/Forest Laboratories, T. O'Donnell Financial support for research: Ironwood Pharmaceuticals, L. Grundy Financial support for research: Ironwood Pharmaceuticals/Forest Laboratories, C. Kurtz Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals, I. Silos-Santiago Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals, S. M. Brierley Financial support for research: Ironwood Pharmaceuticals/Forest Laboratories/Takeda Pharmaceuticals/Key Pharmaceuticals, Consultancy: Takeda Pharmaceuticals/Key Pharmaceuticals

Abstract number: OP304

	WT + DSS	WT + DSS + Nicotine	TLR2KO + DSS	TLR2KO + DSS + Nicotine
Body weight loss %	12	8*	16	14
IL-1β pg/ml	33 ± 6	12 ± 8*	93 ± 12	78 ± 10
MPO activity U/mg tissue	0.05 ± 0.1	0.02 ± 0.05*	0.08 ± 0.15	0.07 ± 0.2

*$p < 0.01$ vs WT + DSS

OP304 ENTERIC NEUROPATHY IMPAIRS EXPRESSION OF ALPHA7 NICOTINIC RECEPTOR IN INTESTINAL MUCOSAL MACROPHAGES: EVIDENCE FOR A NEURON-MACROPHAGE INTERPLAY TO MODULATE GUT INFLAMMATION

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Introduction: In inflammatory bowel diseases nicotine exhibits opposing effects on intestinal inflammation: it's beneficial in ulcerative colitis (UC) while it is detrimental in Crohn's disease (CD). We recently reported that expression of alpha7 nicotinic acetylcholine receptor (α7nAChR) is significantly lower in colonic macrophages (MΦc) of CD compared to UC and healthy subjects.

Aims & Methods: Since anomalies of the enteric nervous system (ENS) have been described mainly in CD patients we postulated that a diffuse gut neuropathy could influence the cholinergic counter-inflammatory mechanism in MΦc. To this goal we investigated the phenotype of MΦc in TLR2 knock-out (KO) mice, a well described animal model of ENS dysfunction resulting in severe colitis[1]. Mild colitis was induced in C57Bl/6J (WT) and TLR2KO mice by 3% dextran sulphate sodium (DSS) for 3 days. $CD11^+$ MΦc were isolated by magnetic beads separation and α7nAChR expression was evaluated by FACS analysis using α-Bungarotoxin (αBgt)-FITC. Otherwise, $CD11^+$ MΦc were cultured with ATP (1 mM)/LPS (100 ng/ml) with or without nicotine (10 mM) for 16 hrs. The inflammatory phenotype was evaluated investigating the activation of caspase-1 by FACS analysis. To assess the influence of enteric neuropathy on MΦc phenotype, anomalies of the ENS in TLR2KO mice were cured with recombinant murine (rm)GDNF (2 µg/g body weight) for 10 days. Colitis was induced by 3% DSS for 5 days with or without nicotine supplementation in drinking water (25 µg/ml). Colitis severity was assessed by evaluating body weight loss, IL-1β level and MPO activity.

Results: In basal conditions, α7nAchR expression and caspase-1 activity were comparable in MΦc from WT and TLR2KO mice. Following induction of mild colitis, expression of α7nAchR and activation of caspase-1 significantly increased in MΦc from WT but not from TLR2KO mice ($P<0.01$). Moreover, exposure of activated WT MΦc to nicotine significantly reduced LPS/ATP-induced caspase-1 activity (by 28%, $P<0.05$). Furthermore, *in vivo* nicotine administration significantly reduced the severity of DSS colitis in WT but not in TLR2KO mice (see table).

In TLR2KO mice pre-treatment with rmGDNF, able to rectify the anomalies of the ENS, corrected the inflammatory phenotype of MΦc. Indeed, in rmGDNF-treated TLR2KO mice the α7nAchR expression and caspase-1 activation levels following 3 days DSS exposure were comparable to WT mice.

Conclusion: In the gut, the integrity of the ENS is required to up-regulate α7nAchR expression and activate caspase-1 in MΦc, events mandatory in modulating mucosal inflammation. We speculate that in CD patients the severe and diffuse neuropathy of the ENS contributes to the inadequate expression of α7nAChR in MΦc thus accounting for the lack of the cholinergic counter-inflammatory mechanism during colitis.

Reference

1. Brun et al. *Gastroenterology* 2013; 145: 1323.

Disclosure of Interest: None declared

OP305 GUT MICROBIOTA DEPLETION ALTERS THE STRUCTURE AND FUNCTION OF THE ENTERIC NERVOUS SYSTEM IN ADOLESCENT MICE

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Introduction: Gut microbiota colonisation has a key role during the development of enteric nervous system (ENS) circuitries. Any change of its composition triggered by environmental factors or drugs could impact ENS homeostasis and determine the onset of functional bowel disorders.

Aims & Methods: The aim of the present study was to evaluate the effect of gut microbiota depletion on ENS integrity and intestinal motility during mouse adolescence. Depletion of gut microbiota was performed on male C57Bl/6 mice (age = 21 ± 5 days) by administering for 14 days an antibiotic cocktail (50 mg/kg vancomycin, 100 mg/kg neomycin, 100 mg/kg metronidazol and 100 mg/kg ampicillin) by oral gavage every 12 hours. In antibiotic–treated (ABX) and control (CNTR) animals we assessed: i) gastrointestinal transit 30 minutes after intragastric administration of nonabsorbable fluorescein isothiocyanate labeled dextran; ii) pellet frequency, measured as changes in stool output during a 60 minutes collection period; iii) stool water content; iv) contractile activity of isolated ileum segments, vertically mounted in organ baths, measured as changes in isometric muscle tension following carbachol (0.001-100 μM), KCl (60 mM), electric field stimulation (EFS, 1-40 Hz) or inhibition in non-adrenergic, non-cholinergic (NANC) conditions (EFS = 10 Hz, 1 μM atropine, 1 μM guanethidine, in the absence or presence of 0.1 mM L-NAME); v) distribution of the neuronal HuC/D and glial fibrillary acidic protein (GFAP) by double labelling confocal immunofluorescence in longitudinal muscle myenteric plexus preparations (LMMPs); vi) neurochemical coding integrity, evaluated by acetylcholinesterase biochemical staining, neuronal nitric oxide synthase (nNOS) immunohistochemistry and GluN1 mRNA levels in LMMPs.

Results: Antibiotic depletion determined a marked enlargement (+92 ± 0.1% $p < 0.01$) in cecum, associated with a three-fold increase in organ weight. ABX mice showed a significant reduction in the number/hour output of fecal pellets (-29.5 ± 0.5% $p < 0.01$) and increased stool water content (+35 ± 7% $p < 0.01$). Gastrointestinal transit was delayed in ABX mice compared to CNTR mice (GC 3.5 ± 0.2 vs 7.3 ± 0.2, $p < 0.01$, respectively). In vitro contractility studies showed altered receptor- and KCl-mediated responses and an overall modified neuronal excitability. NANC-mediated relaxations were significantly increased (+144 ± 30% at 10 Hz $p < 0.05$) in ileum segments from ABX mice. In the ENS of ABX mice HuC/D immunoreactivity decreased while acetylcholine-esterase$^+$ stained fibres increased (+37 ± 3%; $p < 0.01$). GFAP immunostaining showed distorted cellular processes as well as the distribution of $nNOS^+$ neurons was altered following gut microbiota depletion. A two-fold increase of GluN1 mRNA levels was also found in LMMPs of ABX mice.

Conclusion: Gut microbiota depletion determines complex anomalies in ENS architecture, neurochemical coding and function leading to intestinal dysmotility. On the whole such changes are highly indicative of the primary role played by the enteric microbiota in ensuring ENS integrity, consequently contributing to maintain the gut in a long-term healthy state.

Disclosure of Interest: None declared

OP306 IMPACT OF ADHERENT-INVASIVE E.COLI AND FAECALIBACTERIUM PRAUSNITZII ON COLONIC HYPERSENSITIVITY

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Introduction:
Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Diseases (IBD) are believed to result in part from breakdown of homeostasis between intestinal microbiota and the mucosal immune system and which may be associated with visceral pain.

Aims & Methods: The aim of this work was to study the impact of an intestinal dysbiosis on mouse model of colonic hypersensitivity (CHS) by determining if, (1) intestinal Crohn's disease-associated Adherent-Invasive *E.coli* (AIEC) colonization could spontaneously induce a CHS in mice, and (2) if *F. prausnitzii*, whose abundance is decreased in these gastrointestinal disorders, could have an impact on CHS, in a non-inflammatory CHS mouse model induced by Neonatal Maternal Separation (NMS). Visceral hypersensitivity was assessed using a technique based on measuring electromyographic abdominal contractions induced by colorectal distension for each models and inflammation and intestinal permeability was evaluated.

Results: Crohn's disease-associated AIEC (reference strain LF82) infection of transgenic mice overexpressing the human form of CEACAM6 protein dramatically and quickly (D4) increased levels of CHS, associated with a low-grade inflammation and increased intestinal permeability. In addition, such CHS persists in mice, even after AIEC clearance and a restoration of the colon homeostasis (inflammation and permeability) to a normal level.

NMS treatment induced an increased visceromotor response (VMR) in the absence of alteration in gut wall macroscopic integrity or colonic mucosa inflammation status. However, a slight increase of intestinal permeability has been measured. *F. prausnitzii* treatment (reference strain A2-165) significantly decreased VMR and restored intestinal permeability in NMS model.

Conclusion: These results suggested a direct involvement of CD-associated AIEC LF82 infection in CHS and a protective role of *F. prausnitzii* A2-165 on CHS in a non-inflammatory model. Thus, intestinal dysbiosis could impact on CHS, suggesting that targeting intestinal microbiota could be a new therapeutic approach to modulate CHS and associated abdominal pain in patients.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 14:00–15:30
MOLECULAR MECHANISMS OF PROGRESSION AND THERAPY RESISTANCE IN PANCREATIC CANCER – ROOM E6

OP307 LYMPHOTOXIN ACCELERATES PRE-NEOPLASTIC CONVERSION IN PANCREATIC TUMORIGENESIS BY PROMOTING ACINAR CELL REPROGRAMMING

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Introduction: Despite the availability of multimodal therapies, patients with pancreatic cancer have less than 5% 5-year survival rate after diagnosis. For developing early detection methods and treatments, it is essential to understand the primary events leading to tumor initiation. The most common oncogenic mutations associated with all stages of pancreatic cancer (PDAC) are found in the *KRAS* gene; however signaling pathways that drive progression of pre-neoplastic PanIN lesions need to be investigated. Recent studies using genetically engineered mice propose a stepwise process starting from acinar cells undergoing ductal reprogramming (acinar-to-ductal metaplasia, ADM) throughout premalignant PanIN (pancreatic intraepithelial neoplasia) lesions leading to tumor formation in mice harboring a mutated Kras allele. Inflammation has been described as a risk factor for PDAC development. Still, little is known about the cellular and molecular mechanisms how inflammation promotes ADM and PanIN progression. The pro-inflammatory cytokines TNFa, Lymphotoxin (LT) and Light and their downstream master transcription factor NF-κB emerged as critical regulators linking inflammation to cancer.
Aims & Methods: The aim of the study is to explore the inflammatory mechanisms promoting ADM and PanIN development. Therefore, we established a new genetic model (LTKC) by crossing $p48^{+/Cre};Kras^{+/G12D}$ (KC) model for pancreatic tumorigenesis, with a transgenic mouse developing spontaneous pancreatitis, due to Lymphotoxin (LT) overexpression. Immunohistochemistry and qPCR were used to obtain an inflammatory signature. Ras activity and activation of pathways downstream of EGFR and LTbR were compared in LT, LTKC and KC models. *In-vitro* experiments were performed to investigate the direct role of LT in ADM development.
Results: Overexpression of Lymphotoxin in mice harbouring an activating Kras mutation in the pancreas (LTKC) dramatically accelerates the development of premalignant PanIN lesions compared to KC animals. Already after 8 weeks extensive ADMs and PanIN lesions up to PanIN3 are observed in LTKC mice. This coincides with significant upregulation of inflammatory genes and increased Ras activity. Similar molecular and phenotypic changes were observed around 16 weeks in Kras animals. LT overexpression alone could transiently increase Ras activity and phosphorylation of EGFR in early time points. *In vitro* experiments show that LT overexpression in wt acinar cells is sufficient to initiate spontaneous transdifferentiation. Furthermore, acinar cells derived from LTKC animals form ADMs significantly faster than acini from KC animals. Pharmacological inhibition of LTbR signalling mitigated inflammatory environment but could not significantly moderate PanIN development in both KC and LTKC models.
Conclusion: We conclude that Lymphotoxin may contribute to the initiation of PDAC precursor formation: By (1) inducing inflammatory environment and by (2) regulating cell autonomous acinar transdifferentiation, leading to accelerated PanIN development. LTbR inhibition was not sufficient to influence PanIN formation which could imply that LTbR activation results in a secondary activation of EGFR and Ras.
Disclosure of Interest: None declared

OP308 THE INNER PLASMA MEMBRANE PROTEIN PLAC8 REGULATES CELL CYCLE PROGRESSION IN PANCREATIC DUCTAL ADENOCARCINOMA (PDAC)

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Introduction: Pancreatic ductal adenocarcinoma (PDA) is the most aggressive pancreatic cancer with an overall 5-year survival rate of $<5\%$. Despite significant advances in treatment of the disease, the median survival rate ($\sim$6 months) remains unchanged, warranting the need to identify new targets for therapeutic approaches. Our previous transcriptomic analyses as well as parallelised cell-based assays indicated a previously unknown role for Plac8 in pancreatic cancer. Plac8 is a small protein whose physiological functions remain largely unclear. The main aim of this project is to characterise the cellular localisation as well as the molecular function of Plac8 PDAC cells.
Aims & Methods: Tissue microarrays, RNAi, FLIP-, FRAP-, and TIRF microscopy, cell proliferation and viability assays, FACS analysis, Western blot, transgenic mouse models.
Results: qRT-PCR as well as tissue microarray data confirmed strong ectopic expression of Plac8 in pancreatic cancer tissues. High Plac8 expression is also retained in the majority of pancreatic tumour cell lines *in vitro*, with negligible expression in non-transformed cell lines. Using TIRF microscopy and FLIP/FRAP experiments, we show for the first time that Plac8 locates to the inner face of the plasma membrane and stably interacts with distinct membrane structures. Functionally, proliferation and viability were strongly impaired by Plac8 down-regulation, achieved by transient RNAi-mediated knockdown. Western blot and flow cytometry did not show any involvement of classical apoptosis pathways (Caspase-3 and PARP cleavage). Flow cytometry analyses and time course experiments with cell cycle inhibitors demonstrated strong attenuation of cell cycle progression after loss of Plac8 expression. *In vivo*, genetic Plac8 deficiency selectively prolonged survival in *Kras*-driven, but not *Kras*/*p53*-driven PDAC mouse models.
Conclusion: Our experimental data show that ectopic expression of Plac8 is indispensable for proliferation, viability and cell cycle progression in pancreatic cancer cells and suggests Plac8 as a potential new therapeutic target in pancreatic ductal adenocarcinoma.
Disclosure of Interest: None declared

OP309 TRAIL-INDUCED NF-KB/RELA ACTIVATION TARGETS A CCL20-DEPENDENT PATHWAY MEDIATING IMMUNE CELL RECRUITMENT CONFERRING APOPTOSIS RESISTANCE OF PANCREATIC CANCER CELLS

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) represents one of the deadliest malignancies with an overall life expectancy of up to one year despite palliative chemotherapy. The transcription factor NF-κB has been shown to be a critical component of molecular mechanism conferring profound apoptosis resistance in PDAC. Despite extensive data on the role of the most abundant NF-κB subunit p65/RelA in PDAC apoptosis control, there is only little knowledge of the downstream targets and their functional relevance in PDAC.
Aims & Methods: In the present study, a panel of pancreatic carcinoma cell lines (Panc1, PancTu1, Capan-1, Patu8988t, MiaPaca2) were analyzed for the role of RelA target genes in the resistance against TRAIL induced apoptosis.
Results: Resistant PDAC cell lines exhibit a high basal NF-κB activity that was further strongly induced by TRAIL. In contrast, sensitive MiaPaca2 cells displayed only little basal NF-κB activity and only weak induction of the transcription factor by TRAIL. Transfection with siRNA against the RelA subunit of NF-κB sensitized the TRAIL-resistant PDAC cells. Gel shift analysis revealed that the p65/RelA subunit is critical component of the TRAIL-inducible and the basal expressed NF-κB complex in PDAC. By analysis of genome-wide expression patterns of RelA dependent gene expression we were able to show that CCL20 represents the strongest TRAIL-inducible RelA target gene in resistant PDAC cells. Using Chip and luciferase assay we were able to describe the RelA responsive element in the CCl20 promoter. ELISA confirmed that RelA dependent upregulation of CCL20 mRNA after TRAIL treatment leads to a strongly increased secretion of CCL20. Surprisingly targeting CCL20 by siRNA, blocking antibodies or by downregulation of the CCL20 receptor CCR6 had no effect on PDAC cell death or cancer cell migration. However by using an *ex vivo* coculture system with PBMC of healthy donors we were able to show that CCL20 secreted by the TRAIL-treated resistant PDAC cells strongly induces migration of PBMC. Furthermore these PBMC showed a CCL20/RelA-dependent TH17-like differentiation. Finally these cocultured PBMC conferred apoptotic protection of PDAC cells against TRAIL-induced apoptosis.
Conclusion: In conclusion we were able to establish a RelA-CCL20 pathway in TRAIL-resistant PDAC cells which does not confer direct apoptotic protection or migration of the tumor cells but instead leads to the recruitment and TH17-like differentiation of immune cells which in turn mediate apoptosis resistance of PDAC cells.
Disclosure of Interest: None declared

OP310 CANCER-CELL-DERIVED CXCL12 ACTIVATES SCHWANN CELLS AND SUPPRESSES PAIN SENSATION IN PANCREATIC CANCER

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Introduction: Neural invasion (NI) is an independent prognostic factor for overall and progression-free survival in pancreatic cancer (PCa). Recently, we showed that peripheral glia, i.e. Schwann cells (SC), specifically migrate toward PanIN lesions and initiate NI in PCa, but the mediators of this glia-cancer crosstalk are unknown. Here, we aimed to analyze the role of the CXCL12-CXCR4-CXCR7 chemokine-receptor axis in the glial attraction to pancreatic cancer.
Aims & Methods: Here, we aimed to analyze the role of the CXCL12-CXCR4-CXCR7 chemokine-receptor axis in the glial attraction to pancreatic cancer. Expression of CXCL12, CXCR4 and CXCR7 was analyzed in human SC, in SC-PCa-cell-co-cultures, in human PCa tissues and correlated to pain sensation of PCa patients. In novel 3D-SC-migration/outgrowth-assays, native SC and SC derived from glia-specific CXCR4-knockout mice ($GFAP\text{-}Cre^{ERT2};CXCR4^{lox/lox}$) were tracked for their migration to PCa cells via digital-time-lapse-microscopy. Mice with PCa and simultaneous pancreas-specific depletion of CXCL12 ($Ptf1a\text{-}Cre;LSL\text{-}Kras^{G12D};CXCL12^{lox/lox}$, termed "KC12") were generated and analyzed for the frequency of SC around PanINs, and for their abdominal mechanosensitivity via von-Frey-filaments.
Results: PCa cells were major producers of CXCL12, which strongly chemoattracted human SC via CXCR4 and CXCR7. SC constitutively expressed CXCR4 and CXCR7 which they upregulated in co-culture with PCa cells. Glia-specific depletion of CXCR4 in mice abrogated the glial chemoattraction to tumor cells in the 3D-SC-migration-/outgrowth-assays. In KC12 mice, SC-chemoattraction

to PanINs was suppressed, and KC12 mice had increased abdominal hypersensitivity, which was in accordance with the reduced intrapancreatic expression of CXCR4 and CXCR7 among PCa-patients with pain.
Conclusion: Cancer-cell-derived CXCL12 chemoattracts CXCR4- and CXCR7-expressing SC and results in analgesia. These findings propose a novel explanation for the lack of symptoms like pain in early stages of PCa.
Disclosure of Interest: None declared

OP311 IEX-1 KNOCKOUT IN AN EX VIVO MOUSE MODEL OF PANCREATIC CANCER INHIBITS DNA DAMAGE INDUCED NF-KAPPAB ACTIVITY AND MCL-1 NUCLEAR TRANSLOCATION LEADING TO ENHANCED APOPTOSIS

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) represents one of the deadliest malignancies with an overall life expectancy of up to one year despite palliative chemotherapy. The transcription factor NF-κB has been shown to be a critical component of apoptosis and therapeutic resistance in PDAC. Recently we showed in an in vitro model that the immediate early response NF-kB target gene regulates apoptosis of PDAC cells by interfering with NF-kB activation.
Aims & Methods: In the present study, we investigated the role of IEX-1 in murine $Kras^{G12D}$-driven models of PDAC. We isolated primary cancer cell lines from murine PDACs, IEX-1 proficient or deficient. These cell lines were treated with chemotherapeutics and analyzed for responsiveness, NF-kB acitivity and expression of death limiting BCL2 family members.
Results: IEX-1 deficiency is associated with decreased gemcitabine and etoposid responsiveness. Apoptosis, measured by sub-G1 analysis and caspase-3/-7 assay upon treatment with either etoposid or gemcitabine was significantly reduced in IEX-1-deficient murine PDAC cells. Mechanistically, both drugs induce NF-kB and activation of this signaling pathway was enhanced in IEX-1-deficient cells. In addition, DNA damage induced nuclear translocation of Mcl1, was reduced in IEX-1 knock out cell lines. Finally, a genetic rescue experiment, by stably transfection of IEX-1, proved IEX-1 specificity.
Conclusion: In conclusion we were able to confirm a central role of IEX-1 in regulation of apoptosis, NF-kB activity and MCL1 localization in novel PDAC models. Furthermore, such data point to an IEX-1 specific stratification strategy to select for patients benefit from DNA-damage inducing therapies
Disclosure of Interest: None declared

OP312 ACTIVATED GLIA IN PANCREATIC CANCER DECREASES PAIN VIA INHIBITION OF SPINAL ASTROCYTIC ACTIVITY

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Introduction: Pancreatic cancer (PCa) is characterized by a pronounced neuropathy and neuropathic pain, but the role of glia cells in PCa-associated neuropathy and pain is unknown.
Aims & Methods: In the present study, we aimed to analyze the impact of PCa-associated activated Schwann cells (SC) on pain sensation and spinal activity in vivo. Human SC were cultured under hypoxia, or in co-culture with PCa cells or T-lymphocytes and assessed for glial-fibrillary-acidic-protein (GFAP) expression, viability and cell size. Expression of glial-activation-markers and of hypoxia-inducible-factor-1alpha in human PCa nerves was correlated to pain severity. In conditional PCa mouse models, SC activation, abdominal mechanosensitivity, pain-related behavior, astroglial, microglial and neuronal activity in the spinal cord were assessed after *in vivo* blockade of interleukin-6/IL-6 signaling.
Results: SC upregulated GFAP expression and became "stellated "under hypoxia, or in co-culture with PCa cells and T-lymphocytes, and this SC activation was reversible upon inhibition of IL-6 *in vitro*. Correspondingly, inhibition of the classical IL-6-signaling suppressed SC activation around the PanIN lesions in Ptf1a-Cre;$Kras^{G12D}$;$IL6^{-/-}$ mice. Activated, GFAP- and p75NTR-upregulating SC were associated with diminished pain in human PCa and with decreased abdominal mechanosensitivity and increased locomotor activity in mice with PCa. In the spinal cord, the proportion of activated astrocytes was significantly less among mice with increased pancreatic SC activation during PCa.
Conclusion: Activated SC in PCa undergo "reactive gliosis" and attenuate pain sensation via suppression of spinal astroglia. These findings point out a novel mechanism for how and why cancer may not evoke pain during cancer progression.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 15:45–17:15
ENDOSCOPY MEETS PATHOLOGY: ADENOCARCINOMA OF THE OESOPHAGOGASTRIC JUNCTION – ROOM A3

OP313 EXPLORING DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS OF ENDOSCOPIC MUCOSAL RESECTION IN EUS-STAGED T2 OESOPHAGEAL ADENOCARCINOMA

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Introduction: Most oesophageal cancers are assessed by endoscopic ultrasound (EUS). EUS is accurate in staging clinical (c)T3-4 tumours and loco-regional lymph node metastases but the accuracy is lower when it comes to differentiating cT1 from cT2 tumours with a tendency to 'overstage'. Endoscopic mucosal resection (EMR) allows for a histological diagnosis and staging and is emerging as a treatment option for early oesophageal adenocarcinoma (EAC). Because of the possible overstaged cT2 tumours, in recent years we have adopted the policy to be suspicious of cT2 tumours with a low threshold tendency to endoscopic reassessment. The aim of this study is to evaluate the final histological diagnosis in patients with a cT2 EAC as determined by EUS and also to assess the value of endoscopic reassessment followed by EMR if deemed possible.
Aims & Methods: Patients with cT2 EAC were identified from 2 institutional databases: a surgical cohort of patients who underwent oesophagectomy between January 1990 and October 2014, and a gastroenterological cohort where endoscopic reassessment was done between November 2010 and April 2014. Main outcome measures were final pathological (p) T-stage after oesophageal resection without preoperative therapy, and the final pT-stage of patients that underwent endoscopic reassessment with or without subsequent EMR.
Results: A total of 158 patients with T2-staged EAC by EUS were identified retrospectively. 87 Patients underwent oesophagectomy without neoadjuvant therapy for a cT2-tumor. In 46 patients (53%) the pT-stage was less than T2. In 21 (24%) of these patients the resection specimen showed tumour characteristics that fulfil current criteria for endoscopic resection.
In 11 prospectively identified patients with cT2 EAC and no evidence of lymph node or distant metastasis, an endoscopic reassessment was done to evaluate endoscopic resectability. In 10 patients (91%) a complete EMR was successfully performed by multiband mucosectomy and histological evaluation demonstrated a pT1 tumour in all 10 patients. In 3 patients (30%), the resection specimen showed tumour characteristics that fulfil current criteria for endoscopic resection and were successfully treated with EMR. Poor tumour characteristics were present in 7 patients (70%); 3 patients were referred for oesophagectomy, 1 for definitive chemoradiotherapy, and 3 patients receive ongoing endoscopic surveillance.
Conclusion: This study demonstrates that 53% of cT2 EAC are pT1 tumours after histological examination of the oesophagectomy specimen. Curative treatment by EMR is possible in 24-30% of these patients avoiding the need for oesophagectomy. Endoscopic reassessment seems to be justified for all cT2 staged oesophageal adenocarcinomas followed by EMR if deemed possible.
Disclosure of Interest: None declared

OP314 BURIED BARRETT'S DYSPLASIA: RFA IS NOT THE ONLY CULPRIT

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Introduction: Buried Barrett's' or Subsquamous Intestinal Metaplasia (SSIM) refers to glands which are 'buried' underneath the squamous epithelium. Buried Barrett's can pose significant diagnostic and surveillance challenges. Buried Barrett's has mainly been reported in the post ablation context (APC, RFA, PDT).
Aims & Methods: We aim to evaluate its prevalence in patients who are ablation naïve, and understand the reasons behind it. This is a prospective cohort study. We investigated our Barrett's database for patients who were referred for endoscopic treatment (EMR) of Barrett's neoplasia between June 2006 to June 2014. We assessed histology reports before and after endoscopic therapy (EMR), specifically looking for evidence of buried Barrett's.
Biopsy: Biopsies were first obtained from any suspicious-looking area. Following this, biopsies were then obtained from the neosquamous area. Finally, random biopsies were obtained. These were sent in separate cassettes. Histopathology was reported by two independent GI pathologists and was prospectively recorded on a central pathology database.
Buried Barrett's was defined as any metaplastic or glandular tissue beneath the squamous epithelium. Pathology specimens were reported by 2 independent, accredited GI pathologists.
Results: Our study shows that in the pre-EMR cohort, there was an overall prevalence of 12.2% of buried Barrett's and a 9.1% prevalence of buried Barrett's with high grade neoplasia (HGD or IMC) (see Table 1). Our results in the post-EMR cohort shows an overall prevalence of 16.8% of buried

Barrett's with 6.1% prevalence of buried high-grade neoplasia (HGD or IMC). This has significant implications for post EMR endoscopic assessment and surveillance.

Table 1: Buried Barrett's with and without dysplasia

	Buried Barrett's diagnosed in endoscopic therapy naïve patients	Buried Barrett's diagnosed in patients post EMR procedure
Total	16/131 (12.2%)	22/131 (16.8%)
Buried Barrett's with no dysplasia	2/131 (1.5%)	10/131 (7.6%)
Buried Barrett's dysplasia	14/131 (10.7%)	13/131 (9.9%)
HGD	9/131 (6.9%)	4/131 (3.0%)
IMC	3/131 (2.3%)	4/131 (3.0%)
HGD + IMC	12/131 (9.1%)	8/131 (6.1%)
LGD	2/131 (1.5%)	5/131 (3.8%)

Conclusion: 1) Buried Barrett's and Barrett's cancer are seen in endotherapy naïve patients. This is likely to be related to intensive biopsies.
2) EMR, despite being a non ablation technique, still results in buried Barrett's and Barrett's cancer.
3) The overall prevalence of buried Barrett's is higher than previously reported. We need to be aware of this while assessing Barrett's patients.
Buried Barrett's glands after ablation (APC/RFA/PDT) are well reported.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 15:45–17:15

WHAT'S NEW IN BARRETT'S OESOPHAGUS? – ROOM 7.1

OP315 THE IMPACT OF ENDOSCOPIC ERADICATION FOR BARRETT'S ESOPHAGUS ON ESOPHAGEAL ADENOCARCINOMA INCIDENCE AND MORTALITY: A COMPARATIVE MODELING ANALYSIS

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Introduction: Esophageal adenocarcinoma (EAC) incidence increased dramatically over the past 40 years in Western countries and neither EAC incidence nor mortality has plateaued. New techniques for endoscopic eradication of the EAC precursor Barrett's esophagus (BE) such as radiofrequency ablation (RFA) are utilized to prevent progression to EAC. The efficacy and durability of endoscopic eradication are reported, but the long-term impact of eradicative treatment and recurrent disease on EAC incidence and overall mortality reduction has not been analyzed with comprehensive and robust simulation models using this recently updated clinical data. In this study we analyzed the impact of RFA for endoscopic eradication of BE with or without dysplasia on EAC incidence and mortality using a comparative simulation modeling approach.
Aims & Methods: This study includes the predictive modeling of endoscopic eradicative treatment (EET) using three previously established population-based EAC models calibrated to NCI-SEER data. The modeling of clinical aspects of EET was based on available clinical data for RFA and endoscopic mucosal resection (EMR). We simulated a hypothetical cohort of 60 year old patients with BE for whom multiple management strategies were tested, selected on initial dysplasia status and evaluated the simulation outcomes for EAC incidence and mortality reduction; required surveillance endoscopies and treatments including RFA and EMR and numbers of treatments needed to avert one EAC death (NNT/death).
Results: A strategy to endoscopically eradicate BE with high-grade dysplasia will decrease EAC incidence by 50% (range 44% > 58%) and EAC mortality by 46% (41% > 53%) with NNT/death of 30 (26-34). If all BE (dysplastic and non-dysplastic) were eradicated, EAC incidence would incrementally decrease by 83% (81% > 86%) and mortality by 80% (75% > 85%). However, this reduction in EAC was associated with a four-fold increase in the number of treatments with an incremental NNT/death of 209 (132-316). Halting post-treatment surveillance after a recurrence-free period of 5-10 years has a negligible influence on NNT/death when eradicating only patients with HGD.
Conclusion: The resources needed to achieve EAC mortality reduction increase substantially as patients with lower severity of disease are selected for treatment. From a resource efficiency perspective, the large NNT/death suggests that treatment benefits justify endoscopic eradication only among BE patients with HGD.
Disclosure of Interest: None declared

OP316 ACETIC ACID GUIDED FOCAL ENDOSCOPIC RESECTION WITHOUT RFA REMAINS AN EFFECTIVE TREATMENT FOR BARRETT'S NEOPLASIA: TIME TO REASSESS THE ROLE OF RFA?

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Introduction: Endoscopic resection (ER) is an established effective treatment for Barrett's neoplasia. ER can lead to recurrence due to residual neoplasia left behind, so it is suggested that all patients should undergo radiofrequency ablation (RFA) after ER. Acetic acid chromoendoscopy has been shown to be an effective method of localising and delineating dysplastic areas of Barrett's oesophagus.
Aims & Methods: We aim to review the outcome of Acetic Acid-guided focal ER without RFA in our patients. All ER procedures between January 2005 and November 2014 were recorded in a prospective database which was analysed. Acetic acid guided focal ER was the treatment strategy with the aim of removing all neoplasia visible with acetic acid chromoendoscopy. RFA was not used in this group.
Results: 112 patients were treated for dysplastic Barrett's oesophagus or early Barrett's cancer by ER. The mean age at first procedure was 68 years and 82% of the patients were male. Mean initial Barrett's length was 5.1cm. 35 of 112 patients had advanced histological features on the initial ER specimen and were referred for radical cure. The remaining 77 cases showed; intramucosal cancer (IMC) in 46, high-grade dysplasia (HGD) in 28 and low-grade dysplasia in 3. All 77 cases have follow-up data with a mean duration of 5.4 years. 67 of 77 cases (87%) have sustained eradication of HGIN/IMC after focal ER. 10 patients (13%) developed further neoplasia during follow up. 5/10 patients (6.5%) developed invasive cancer in the residual Barrett's, all were diagnosed endoscopically and successfully managed with radical curative treatment. Focal ER was successful in a mean of 1.3 procedures per patient (range 1-3). Complication rate was 4% (4 bleeds, 2 strictures). No additional RFA was performed in this patient group. Table 1 compares our outcomes with UK HALO registry outcomes where all patients receive RFA.

	AA guided EMR	UK RFA Data[1]
Clearance of neoplasia	87%	77%
Progression to Cancer	6.5%	6.7%
Mean Follow up	5.4 Years	2.6 Years
Stricturing	2.6%	9.4%
Mean number of therapeutic procedures	1.3	ER + 2.6 RFA

Conclusion: Acetic acid-guided ER is an effective and safe treatment for dysplastic Barrett's oesophagus. Progression to cancer after acetic acid guided ER is equivalent to the reported rate of progression after EMR + RFA[1]. Equal rates of sustained eradication of HGIN/IMC are achieved. An acetic acid + ER strategy is potentially much cheaper than an ER + RFA strategy. This data calls for a better stratification of patients who require RFA after ER.

Reference

1. Haidry et al *Gastroenterology* 2013; 145: 87–95.

Disclosure of Interest: None declared

OP317 INCREASED DETECTION OF BARRETT'S ESOPHAGUS AND ESOPHAGEAL DYSPLASIA USING TRANSEPITHELIAL BRUSH BIOPSY WITH THREE DIMENSIONAL COMPUTER-ASSISTED TISSUE ANALYSIS: A PROSPECTIVE MULTI-SITE COMMUNITY-BASED STUDY

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Introduction: Barrett's esophagus (BE) is a known precursor to esophageal adenocarcinoma. Endoscopic guidelines for BE and esophageal dysplasia (ED), rely on random four-quadrant forceps biopsies (FB) obtained every 1-2 cm in the BE segment, and are subject to sampling error. Wide area transepithelial brush biopsy combined with 3 dimensional computer image analysis of the sample ($WATS^{3D}$) previously has been shown to provide incremental value as an adjunct to FB in the detection of both BE and ED.
Aims & Methods: A prospective multi-center, community-based trial utilizing $WATS^{3D}$ testing was conducted during the period 2012-2014. Patents with symptoms of reflux, suspected BE, and known BE undergoing surveillance for ED were enrolled. A specially designed transepithelial $WATS^{3D}$ biopsy brushes for

tissue sampling in addition to forceps biopsies (FB) during the same endoscopy. WATS^{3D} and FB samples were sent to a central laboratory for analysis. In contrast to the standard 2 micron cut tissue slice, WATS^{3D} biopsy specimens also include an uncut direct smear of up to 150 microns in thickness to better capture the natural three dimensional appearance of the glandular tissue. Laboratory analysis of this uniquely thick tissue sample is aided by a computer based image processing system that integrates into a single three dimensional image information taken from up to 150 separate one micron focal planes. This information is then automatically reviewed by the systems image processing algorithms and neural networks which select and display to the pathologist the most suspicious cells that are found in every focal plane of the entire WATS^{3D} specimen.

Results: There were 4203 patients enrolled in the study with adequate FB and WATS^{3D} specimens. The medianage was 59 yr with 43% being males. BE was diagnosed in 594 patients by FB and in 799 patients byWATS^{3D}. Of these 799 patients, 493 had no BE seen on FB. Thus, the addition WATS^{3D} tothe standard forceps biopsy protocol increased the detection of BE by 83.0% (493/594; 95%confidence interval 74% > 93%), This added detection of BE in 12% (493/4203) of all patients testedwith WATS^{3D} results in a number of patients needed to test (NNT) to obtain one additional BEpatient of 8.53. Esophageal dysplasia was diagnosed in 26 patients by FB and in 33 patients byWATS^{3D}. Of these 33 patients, 23 had no ED on FB. Thus, the addition of WATS^{3D} to the standardforceps biopsy protocol increased ED detection by 88.5% (23/26; 95% confidenceinterval 48% > 160%). This augmented ED detection in 0.5% (23/4203) of all screening patients testedwith WATS^{3D}, results in an NNT to obtain one additional ED case of 182.7. There were no adverse events which resulted from use of WATS^{3D}.

Increased detection of BE Increased detection of ED

	WATS^{3D} Neg	WATS^{3D} BE		WATS^{3D} Neg	WATS^{3D} Dysplasia
FB Neg	3116	493	**FB Neg**	4154	23
FB BE	288	306	**FB Dysplasia**	16	10

Conclusion: This multi-center trial demonstrates the benefit of WATS^{3D} use in daily community-based endoscopic practice. These results underscore previous data demonstrating the adjunctive benefit of adding WATS^{3D} to FB for augmented detection of both Barrett's metaplasia and dysplasia.

Disclosure of Interest: S. Gross Consultancy: CDx Diagnostics, M. Smith: None declared, R. Ali: None declared, V. Kaul: None declared

OP318 PERSISTENT LOW-GRADE DYSPLASIA IN BARRETT'S ESOPHAGUS IDENTIFIES PATIENTS AT HIGHER RISK FOR ESOPHAGEAL ADENOCARCINOMA: A DUTCH NATIONWIDE COHORT STUDY

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Introduction: Confirmation of low-grade dysplasia (LGD) in Barrett's esophagus (BE) by an expert pathologist has been suggested to increase the risk of progression to esophageal adenocarcinoma (EAC). However, even after a confirmed LGD diagnosis, non-dysplastic (ND) BE is found in follow-up biopsies of 28-39% of patients. To avoid unnecessary risks and costs associated with ablative treatment, further risk stratification of patients with confirmed LGD is therefore required.

Aims & Methods: To determine whether persistence of LGD in BE could be used for risk stratification in identifying the subgroup of patients actually benefiting from ablative treatment.

Patients with a first diagnosis of LGD in BE were selected from PALGA, a registry of histopathology diagnoses in the Netherlands, in the period 2005-2010. Exclusion criteria were a diagnosis of high-grade dysplasia (HGD)/EAC prior to or simultaneously with the initial LGD diagnosis, or within 1 year after LGD diagnosis, a diagnosis of indefinite for dysplasia and patients with a follow-up less than 1 year. Persistent LGD was defined as LGD at the index and the first follow-up endoscopy.

Results: A total of 1582 LGD patients were identified, of whom 161(10%) had confirmed and 1351(85%) unconfirmed LGD at the index endoscopy. Patients were followed-up for a median of 4.2 years (IQR 2.76-5.96). The overall incidence rate of developing HGD/EAC and EAC in patients with LGD at the index endoscopy was 2.10(95% CI 1.78-2.46) and 1.19(95% CI 0.96-1.48) per 100 person years, respectively. In the subgroup of patients with confirmed LGD, the incidence rate significantly increased to 5.18(95% CI 4.32-8.10) and 2.51(95% CI 1.46-3.99) per 100 person years, respectively. Of patients with a confirmed LGD diagnosis, 51% (n = 82) regressed to ND and 30% (n = 49) had persistent LGD. For patients with confirmed and persistent LGD (median follow-up 3.72 years, IQR 1.78-5.38), the incidence rate of developing HGD/EAC and EAC was 7.65(95% CI 4.45-12.34) and 2.04 (95% CI 0.65-4.92) per 100 person years, respectively. The incidence rate for patients with ND at follow-up endoscopy after initial confirmed LGD was significantly lower, 2.32(95% CI 1.08-4.40) and 1.45(95% CI 0.53-3.21) per 100 person years, respectively. Patients with 2 consecutive endoscopies showing ND BE (29%, n = 46) after a confirmed LGD diagnosis developed no HGD/EAC during follow-up.

Conclusion: In this large population-based cohort of patients with LGD in BE, confirmed and persistent LGD identifies patients at an increased risk of developing of HGD/EAC. Ablative treatment should therefore be considered in patients with confirmed and persistent LGD in BE.

Disclosure of Interest: None declared

OP319 IDENTIFICATION OF METHYLATED TISSUE FACTOR PATHWAY INHIBITOR 2 (TFPI2) AS A DIAGNOSTIC BIOMARKER FOR BARRETT'S ESOPHAGUS USING THE CYTOSPONGE™

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Introduction: Barrett's Esophagus (BE), a known precursor to Esophageal Adenocarcinoma (EAC), commonly remains undiagnosed. Whilst routine endoscopic screening is not recommended, the advent of non-invasive techniques may allow for screening of individuals at risk for BE as a strategy to reduce the rising mortality from EAC. A minimally invasive cell sampling device, the Cytosponge™, coupled to an immunohistochemical marker, Trefoil Factor 3 (TFF3), has good sensitivity and specificity for diagnosing BE.[1] Aberrant DNA methylation of several genes has been shown to occur in BE and these genes have the potential to be utilised as biomarkers.

Aims & Methods: The aim of this study was to validate methylation of a tumour suppressor gene, Tissue Factor Pathway Inhibitor 2 (*TFPI2*), as a diagnostic biomarker for BE using Cytosponge™ samples and investigate whether it can further improve the accuracy of TFF3.

Previous methylation data from our laboratory was examined for differential methylation of *TFPI2* in BE (n = 22) and controls (n = 2). For validation, Cytosponge™ samples from a randomly selected cohort of 150 non-dysplastic Barrett's cases and 134 controls without BE from the Barrett's Esophagus Study Trial 2 (BEST2) were included. DNA was extracted, bisulphite converted and analysed for methylation from the samples. *TFPI2* methylation was compared between the two groups and sensitivity and specificity for diagnosing BE were determined using Receiver Operating Characteristic analysis. The accuracy of methylated *TFPI2* for diagnosing BE was compared to TFF3.

Results: We observed a significant difference in methylation of *TFPI2* CpG islands between BE and controls ($p = 0.03$) in the discovery cohort. We confirmed that the levels of *TFPI2* methylation are significantly different between the cases and controls ($p = < 0.0001$) in the validation cohort. The sensitivity of methylated *TFPI2* for diagnosing BE was 78.7% [95% CI, 71.4%–84.5%] and the specificity was 97.0% [95% CI, 92.2%–99.1%]. When the same cases were analysed for TFF3 the sensitivity was 94.0% [95% CI, 88.8%–96.9%] and the specificity was 99.3% [95% CI, 95.4%–100%], with more false positives with *TFPI2* (4 versus 1) and more false negatives (32 versus 9).

Conclusion: We have identified that *TFPI2* in Cytosponge™ samples is significantly deferentially methylated in BE patients compared to healthy controls. Whilst the sensitivity and specificity data are encouraging, comparison with the sensitivity of the established TFF3 marker in the same cohort revealed that methylated *TFPI2* is not as accurate, putting its use as a potential diagnostic marker in question. Further work to determine the functional role of *TFPI2* in this disease is warranted.

Reference

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Disclosure of Interest: N. Bezawada: None declared, H. Chettouh: None declared, N. Galeano-Dalmau: None declared, I. Debiram-Beecham: None declared, M. O'Donovan: None declared, P. Lao-Sirieix: None declared, R. Fitzgerald Conflict with: Rebecca Fitzgerald is named on patents related to the Cytosponge. The Cytosponge technology has been licensed by the Medical Research Council to Covidien (now Medtronic).

OP320 TAILORED PROTON PUMP INHIBITOR THERAPY, BASED ON ACID REFLUX PARAMETERS, IN LONG-SEGMENT BARRETT'S ESOPHAGUS PATIENTS: THE SIGNIFICANCE OF THE LEVEL OF SYMPTOM CONTROL

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Introduction: In clinical practice the management Barretts esophagus (BE), is based on a symptom control approach where the dose of proton pump inhibitors (PPI) is adjusted until symptoms are controlled. But few data are available

on the correlation between symptoms relieve, decrease in acidic reflux and PPI dosing, using taylored PPI dosing.
Aims & Methods: The objectives of the present study were threefold. First to determine whether the acid reflux variables co-varied with the symptom scores, throughout the upwards titration of the respective PPI doses. Second to ascertain whether it is possible to eradicate acid reflux in these patients. Finally to determine if tailored medical therapy can reach the same level of reflux and symptom control as a successful total fundoplication does. A consecutive series of patients with long-segment BE (LSBE) were invited. Esophageal manometry, ambulatory 24h pH recording, symptoms assessment and endoscopy were performed at baseline. Thereafter patients were given pantoprazole in a daily dose of 40mg for 8 weeks, and then re-evaluated with ambulatory 24h pH recording, endoscopy and symptoms assessment. Dose escalation then ensued and the respective investigations repeated after each 8 weeks until normalization of intraesophageal pH. The second study group (group 2), included patients with LSBE that had previously undergone ARS.
Results: Group 1 included 24 patients, 18 male, median age 64.7 years-old, with BE median length of 5 cm (range 3-15cm). In 14 of these, we were able to normalize acid reflux into the esophagus already by a daily dose of 40mg of pantoprazole. Doubling the dose for another 8 weeks left still 8 with abnormal acid reflux. Only one patient did not reach normalization of pH. The acid suppression was associated with a significant reduction in GERD/HRQL symptoms ($p = 0.001$). However, when considering individual steps of the PPI titration process, it was only possible to statistically confirm the connection between acid reflux and symptom relief during the initial 8 weeks of therapy with the lowest PPI dose ($p < 0.001$). When symptoms were objectively assessed in BE patients in clinical remission after ARS, using the same GERD-HRQL questionnaire, complete absence of acidic reflux was associated with somewhat but statistically lower symptoms scores ($p = 0.030$) than in those with remaining reflux. Globally, non-operated patients with reflux normalization under PPI treatment achieved the same GERD/HRQL scores as BE patients after successful ARS ($p = 0.51$).
Conclusion: Most BE patients can reach complete acid suppression under tailored PPI therapy. Acid reflux normalization is associated with a significant improvement in symptoms score similar to that seen after effective ARS. The symptom relief PPI dose response curve seemed to be extremely steep with a predominant and close association between the level of acid reflux control and symptom control only for the first dose of PPI. Patients with no acidic reflux under PPI treatment have the same level of symptoms control as patients after ARS with all reflux eradicated.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 15:45–17:15
IMPROVED CLASSIFICATION OF COLORECTAL LESIONS – ROOM E1

OP321 CLINICOPATHOLOGICAL STUDY OF LATERALLY SPREADING TUMORS OF THE COLORECTUM

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Introduction: Laterally spreading tumors (LSTs) of the colorectum are classified into the following four subtypes according to their morphology ; granular homogeneous type (LST-GH), granular nodular mixed type (LST-GM), non-granular flat-elevated type (LST-NGF), and non-granular pseudo-depressed type (LST-NGPD). Clinical features of each subtype of LSTs have not been fully evaluated.
Aims & Methods: The aims of this study was to clarify the clinicopathological features of colorectal LSTs focusing on their subtypes. We reviewed clinical charts and pathology files of 3591 endoscopically resected specimens during January 2007 and December 2014 at our institution. A total of 286 LSTs were detected. We examined the clinical features (mean age, male to female ratio, size, location, Incidence of concomitant carcinoma) according to their subtypes.
Results: Of these 286 lesions, a total of 95 (33.2%) were LST-GH, 24 (8.4%) LST-GM, 146 (51.1%) LST-NGF, and 21 (7.3%) LST-NGPD. Mean age of patients with each subtype was 69.0 years old for LST-GH, 65.9 for LST-GM, 68.4 for LST-NGF, and 69.3 for LST-NGPD. Male to female ratio (M/F) was 1.07 for LST-GH, 2.0 for LST-GM, 1.92 for LST-NF, and 1.33 for LST-NGPD. Mean size of LST-GM (21.9mm) was significantly larger than that of LST-NGF (15.2mm) and LST-NGPD (13.7mm). All subtypes were located predominantly in the proximal colon. Incidences of concomitant carcinomas in LST-GH, LST-GM, LST-NGF, and LST-NGPD were 20% (19 out of 95), 70.8% (17 out of 24), 15.8% (23 out of 146), and 61.9% (13 out of 21), respectively. Incidences of concomitant submucosal carcinomas in LST-GH, LST-GM, LST-NGF, and LST-NGPD were 0% (0 out of 95), 12.5% (3 out of 24), 1.4% (2 out of 146), and 23.8% (5 out of 21), respectively.
Conclusion: Each subtype of LSTs has distinct clinical features. LST-GM and LST-NGPD have higher malignant potentials than other subtypes. Especially LST-NGPD has the highest risk of invasive carcinoma regardless of its size. Therefore we should carefully detect these lesions and choose appropriate treatment according to the subtypes.
Disclosure of Interest: None declared

OP322 ENDOSCOPIC CHARACTERIZATION OF SESSILE SERRATED ADENOMAS/POLYPS; BOTTLENECK FOR THE IMPLEMENTATION OF A "RESECT AND DISCARD" POLICY?

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Introduction: Sessile serrated adenomas/polyps (SSA/P) are the main precursors in the serrated neoplasia pathway, responsible for up to 15-30% of colorectal cancer (CRC). Optical diagnosis of SSA/P is difficult and the common classification models do not enable the differentiation of SSA/P. Inaccurate characterization of SSA/P might have major implications for a ''Resect and Discard'' policy. To date, no studies have assessed this issue in a prospective cohort setting.
Aims & Methods: We aimed to assess the performance of optical diagnosis of SSA/P among endoscopists in routine practice and to evaluate its impact for the implementation of a ''Resect and Discard'' policy. Colonoscopy data were retrieved from a colonoscopy center, specialized in surveillance and screening, between 2011 and 2014 using a structured reporting system, enabling prospective data collection and automatic quality assessment.[1] Endoscopists were instructed to resect all lesions, irrespective of predicted polyp histology. Size, location, morphology and predicted histology were recorded for every polyp in a structured manner.[1] All endoscopists were familiar with the NICE- and KUDO-classification for optical diagnosis of polyps. All lesions were assessed by gastrointestinal pathologists in routine practice. Patients with a known hereditary CRC syndrome were excluded from analysis. Performance of optical diagnosis of SSA/P was analyzed, stratified for polyp size and morphology.
Results: In total 3360 colonoscopies were included for analysis in which 373 SSA/P were detected. The prevalence of at least one detected SSA/P was 8%. Of all detected lesions, 10% was a SSA/P (7% for lesions 1-5mm and 19% for lesions 6-9mm). In total 76% of SSA/P were located in the proximal colon. The median size of SSA/P was 5mm (IQR 3-8). Overall, 54% of SSA/P were sessile and 46% were flat or flat-elevated. Of all SSA/P with an optical diagnosis ($n = 360$), 36% were accurately characterized, while 37% were diagnosed as hyperplastic polyps and 27% as adenomas (Table). The optical diagnosis was accurate for 25% of diminutive SSA/P, 51% of small SSA/P and 53% of large SSA/P ($p < 0.001$). The optical diagnosis was accurate for 56% of flat SSA/P and 21% of sessile SSA/P ($p < 0.001$).

Optical diagnosis of SSA/P

Predicted histology	Overall ($n = 360$); n (%)	SSA/P 1-5mm ($n = 200$); n (%)	SSA/P 6-9mm ($n = 113$); n (%)	SSA/P ≥10mm ($n = 45$); n (%)
Adenoma	97 (27)	70 (35)	20 (18)	7 (16)
Hyperplastic polyp	132 (37)	81 (41)	35 (31)	14 (31)
Sessile serrated adenoma/polyp	131 (36)	49 (25)	58 (51)	24 (53)

Conclusion: This study demonstrates the performance of optical diagnosis of SSA/P in routine practice. Our results show that overall only 36% of SSA/P were accurately characterized, decreasing to 25% for polyps 1-5mm in size. These results may impede the implementation of a ''Resect and Discard'' policy, since the proportion of both diminutive as well as small SSA/P seems to be larger than assumed in literature. To increase the performance of optical diagnosis and enable a safe implementation of a ''Resect and Discard'' policy, classification systems that facilitate the endoscopic differentiation of adenomas, hyperplastic polyps and SSA/P should be introduced and validated in clinical practice.

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Disclosure of Interest: None declared

OP323 APPLICATION OF KUDO PIT PATTERN CLASSIFICATION IN ENDOMICROSCOPIC DESCRIPTION OF COLONIC NEOPLASTIC CHANGES

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Introduction: Confocal laser endomicroscopy is a novel and "high-tech'' imagistic approach of colonic neoplastic lesion. Comparing the images with a normal control image of colonic mucosa and accordingly to endomicroscopic Mainz and Sanduleanu classification there are glandular opening characteristics that are specific to neoplastic changes. This can be improved by using as a tool Kudo pit-pattern clasiffication in establishing the morphological criteria.
Aims & Methods: In this study were examined more than 4200 endomicroscopic images from 40 colonic neoplastic lesions. Were included 29 patients patients aged > 18,mean age 63.7, with colonic polyps. The lesions were examined with Pentax integrated endomicroscope after injection of Fluoresceince as a contrast agent, and described characteristics of colonic glandular openings, using the following features: regularity, shape (round, star shaped, elongated with or witout branching, distorted), and sizes raported to a normal endomiscroscopic

image of normal colonic mucosa and compared with histological findings and diagnostic. The histological diagnostic was made by to experienced pathologists and the neoplasia grading was made accordingly to Vienna classification.
Results: We found that the shape of glandular opening as seen in endomicroscopic examination is statistical significant associated with the grade of neoplasia (Cramer's V = 0.666, $p < 0.0001$). According to the results the star shape is associated with absence of neoplasia (PPV = 83.33% for absence of neoplasia) and low-grade dysplasia, and the distorted-anarchic appereance is associated with adenocarcinoma with PPV = 85%.
The size and regularity of the crypts openings also had a high corellation with neoplasia grade: the increased size had VPP = 84% for high grade dysplasia and adenocarcinoma ($p < 0.0001$ Cramer'sV = 0.672) and the regular preserved aspect is strongly associated ($p < 0.0001$ Cramer's V = 0.784) with the absence of neoplasia and low-grade dysplasia, while irregularity and lost of pattern is correlated with high-grade dysplasia and adenocarcinoma.
Conclusion: Since 1994 Kudo has described the 5 types of cryptal opening patterns that suggest the neoplasic characteristic of a colon polyp. This classification has still a place in high performance endoscopy and it can be well adapted to the newest elaborated classification to describe endomicroscopic features of colonic neoplastic lesions, alongside to description of vascular changes and the nuclear ones that should be achieved.

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Disclosure of Interest: None declared

OP324 DISTINCT CLINICOPATHOLOGICAL AND MOLECULAR FEATURES BETWEEN LATERALLY SPREADING TUMORS AND POLYPOID NEOPLASMS IN THE COLORECTUM

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Introduction: Laterally spreading tumors (LSTs) were defined as large flat tumors of the colorectum. LSTs are subcategorized into granular-type LST (LST-G) and nongranular-type LST (LST-NG). LSTs tend to extend laterally and circumferentially rather than vertically along the colonic wall and seem be found at an early stage tumor such as adenoma. These characteristics suggest that there may be biological differences between LSTs and polypoid neoplasms (PNs).
Aims & Methods: We examined the clinicopathological and molecular features of 156 colorectal neoplasms including 54 LST-Gs, 52 LST-NGs and 50 PNs that were endoscopically resected at Showa University Hospital from July 2007 through December 2014. We evaluated the frequency of *KRAS* and *BRAF* mutations by pyrosequencing and DNA methylation of nine genes or sequences (*MINT1, MINT2, MINT31, CDKN2A, MLH1, SFRP1, HPP1, ESR1* and *LINE1*) by bisulfite-pyrosequencing. We also investigated the methylation level of *SFRP1, HPP1, ESR1* and *LINE1* in adjacent normal mucosa. A tumor was considered to be CpG island methylator phenotype (CIMP) -positive if 2 or more CIMP markers (*MINT1*, *MINT2*, *MINT31*, *CDKN2A* and *MLH1*) were methylated.
Results: We observed significant differences in age (71 yrs. vs. 62 yrs.), and tumor size (27 mm vs. 14 mm) between LSTs and PNs ($P < 0.001$). The frequency of *KRAS* mutation of LST-Gs was significantly higher than the other groups (LST-Gs, 65%; LST-NGs, 12%; PNs, 23%, $P < 0.001$). The frequency of CIMP tended to be higher in LST-Gs than LST-NGs or PNs (16% vs. 9% or 0%, respectively). No *BRAF* mutation was detected in any tumor samples. On the other hands, we observed methylation densities of *SFRP1, HPP1* and *ESR1* in adjacent normal mucosae as well as tumor tissues of LST-Gs, LST-NGs and PNs (*SFRP1*, 20%, 21% and 22%; *ESR1*, 18%, 17% and 19%; *HPP1*, 10%, 11% and 11%, respectively). There were no significant differences in the methylation densities of *SFRP1, HPP1* and *ESR1* between any groups. For elderly patients who were more than 70 years old, however, *SFRP1, HPP1* and *ESR1* methylation densities of adjacent normal mucosae were significantly higher in PNs than LSTs ($P < 0.05$). Furthermore, the methylation level of *LINE1* was significantly lower in LST-Gs than LST-NGs or PNs (67% vs. 70% or 69%, respectively; $P < 0.01$).
Conclusion: Our results suggest that different molecular mechanisms may exist in these subtypes of colorectal tumors and that DNA methylation of adjacent normal mucosa might be associated with field effects defined by epigenetic changes.
Disclosure of Interest: None declared

OP325 KID: A CAPSULE ENDOSCOPY DATABASE FOR MEDICAL DECISION SUPPORT

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Introduction: Computer-based systems support medical decision-making by integrating expert knowledge with machine learning algorithms. The use of such systems in capsule endoscopy (CE) is limited[1]. Therefore, a database to be used as source of data for the development of automated medical-decision support, as well as educational resource for physicians, was created[2].
Aims & Methods: The database, named KID, is publicly available at **http://is-innovation.eu/kid/**. It accommodates anonymized CE images & video files. Lesion categorisation follows the Capsule Endoscopy Structured Terminology (CEST)[3]. Contributions should be of high quality (original resolution) & not distorted by compression. For image contributions, the recommended standard is ISO/IEC 15948 PNG (Portable Network Graphics); popular, platform-independent & with lossless compression. However, acceptable standards include popular near-lossless coding; ISO/IEC 14496-10 MPEG-4 AVC (Advanced Video Coding) H.264. Supported container formats for synchronized videostreams through the web include F4V & FLV (Flash video). Furthermore, KID delivers knowledge through image annotations. Semantic & graphic annotations are supported by an open access & platform-independent annotation tool (**Ratsnake**)[4]. Semantic annotation is based on standard web ontology language description logics (OWL DL). The quality of data & annotations submitted to KID is scrutinized by an international scientific committee; contributions not conforming with the afore-mentioned standards & objectives are rejected.
Results: More than 1,500 annotated CE images, 47 videoclips & full videos have been registered in KID during its first 6 months of operation (Sept. 2014-Feb. 2015). These include normal images & images of the following lesion categories: a) vascular: angiectasias and/or intraluminal bleeding; b) inflammatory: mucosal aphthae & ulcers, erythema, cobblestone, and luminal stenosis; c) lymphangiectasias: chylous cysts, nodular lymphangiectasias, punctuate lymphangiectasias, and d) polypoid lesions. Datasets submitted to KID have already been used for lesion detection by machine learning algorithms[4]. Direct comparisons with results of developing automated lesion detection/recognition algorithms can be made. In this context, we applied a novel algorithm for blood detection in KID (*dataset 1*). The algorithm is capable of identifying salient image regions[2], from which color features are extracted & classified by a support vector machine[4]. The average sensitivity & specificity obtained are 96% & 91%, respectively.
Conclusion: KID provides a platform for data & knowledge exchange between medical & IT researchers. It enables direct comparisons between methods for medical-decision support in CE, thus leading to essential progress in the field.

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Disclosure of Interest: None declared

OP326 AUTOMATED DIAGNOSIS SYSTEM USING ENDOCYTOSCOPY CAN BE A POWERFUL TOOL FOR ON-SITE CHARACTERIZATION OF COLORECTAL POLYPS: A PILOT STUDY EVALUATING A "SECOND-GENERATION" MODEL

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Introduction: Endocytoscopy (EC) enables *in vivo* observation of nuclei at 380-fold magnification during gastrointestinal endoscopy, thus allowing precise prediction of lesion pathology; however, it requires training and experience.[1] Therefore, for untrained endoscopists, we have developed a computer-aided diagnosis system for EC imaging (EC-CAD) that provides fully-automated classification of colorectal polyps.[2]
Aims & Methods: The aim of the present study was to evaluate the efficacy of a second-generation model of EC-CAD. The EC-CAD comprises image acquisition, nuclear segmentation, feature extraction, and classification into three pathological groups (neoplastic, adenoma, and invasive cancer). The classification algorithm was programmed based on 350 features of each image (e.g., area, circularity, diameter, and perimeter of nuclei, and over 300 variables calculated by texture analysis of a whole image). We used a support vector machine to help classify these many features; 4880 EC images were used for machine

learning in the process of construction of the model. As a pilot study to validate the EC-CAD, we evaluated its diagnostic ability, speed, and reproducibility for prediction of neoplastic change on a test set of 476 randomly selected EC images (234 neoplastic and 242 non-neoplastic lesions that had not been used for machine learning).
Results: The EC-CAD automatically output pathological predictions with "high confidence" (over 90% probability calculated by support vector machine) in 63% (302/476) of the subject images, providing sensitivity of 98%, specificity of 96%, and accuracy of 97%. On the other hand, the overall diagnostic abilities for the total of 476 subjects were sensitivity of 92%, specificity of 87%, and accuracy of 89%. The EC-CAD also enabled instant diagnosis, taking only 0.2 seconds for each lesion with perfect reproducibility (Kappa = 1).
Conclusion: The EC-CAD achieved almost perfect diagnostic performance in classification of colorectal polyps with "high confidence" mode. It can be a powerful tool for supporting endoscopists' decisions during colonoscopy.
Acknowledgement: We express great gratitude to Prof. Kensaku Mori and Yukitaka Nimura (Nagoya University, Information and Communications Headquarters) for their invaluable support as co-researchers.

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Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 15:45–17:15
IMPACT OF ENDOSCOPIC OESOPHAGEAL INTERVENTIONS ON CLINICAL OUTCOME – ROOM E3

OP327 PERSISTENT OR RECURRENT INTESTINAL METAPLASIA IN PATIENTS WITH NORMAL NEO-Z-LINE AFTER RFA IS NOT A RISK FACTOR FOR RECURRENCE OF NEOPLASIA

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Introduction: It is not known whether persistent or recurrent intestinal metaplasia (IM) within a normal neo-Z-line represent a risk factor for recurrence of Barrett's esophagus related neoplasia (BORN) in patients undergoing radiofrequency ablation (RFA).
Aims & Methods: Aims of this study were: 1. To assess the long-term efficacy of endoscopic treatment (RFA with or without endoscopic resection - ER) for BORN; 2. To assess the clinical relevance of persistent or recurrent IM in patients with macroscopically normal neo-Z-line after RFA; 3. To investigate the origin of persistent/recurrent IM at the level of neo-Z-line.
A single center, prospective cohort study with consecutive patients undergoing RFA for BORN. After treatment, the patients undergo regular endoscopic surveillance with multiple biopsies (neo-Z-line and esophagus). The median follow-up was 36 months (range 3-74). Conover one-way analysis was used to calculate the risk factors for recurrence of IM and neoplasia. All specimens obtained from patients with persistent/recurrent IM were examined with regard to expression of cytokeratins 7 and 20 (CK7, CK20).
Results: The study involved 76 consecutive patients (mean age 62, range 20-86) undergoing endoscopic treatment for BORN (early adenocarcinoma: 30 (40%), high-grade dysplasia (HGD): 23 (30%), low-grade dysplasia (LGD): 23 (30%); during 2009-3/2015. In 24 patients (32%), RFA was a single treatment modality while in 56 patients (68%) RFA was combined with ER or ESD. At present, 62 patients completed the treatment.
Complete remission of IM (CR-IM) and complete remission of neoplasia (CR-N) were achieved in 71% (95% CI 69-81%) and 98% (95% CI 95-99%), respectively. Among 18 patients without CR-IM (29%), 17 (94%) had macroscopically normal neo-Z-line.
During the follow-up, there were 18 recurrences (41%) of IM and all occurred at the level of neo-Z-line. In 14 of these patients (78%), the neo-Z-line was macroscopically normal. There were 3 patients (5%) with recurrent neoplasia (2x LGD, 1x HGD), 1 of them occurred at the macroscopically normal neo-Z-line but this patient has had no CR-N (persistent LGD). The risk factors for recurrence of IM were male sex, younger age and diagnosis of cancer. The presence of IM at the level of macroscopically normal neo-Z-line has not been found as a risk factor for BORN recurrence.
Among 31 patients with persistent/recurrent IM with normal neo-Z-line, 90% had typical Barrett's esophagus expression pattern (CK7+, CK20+).
Conclusion: A majority of patients without CR-IM or with a recurrence of IM have macroscopically normal neo-Z-line. Persistent or recurrent IM in patients with normal neo-Z-line is mostly of Barrett's esophagus origin but is not a risk factor for BORN recurrence.
Disclosure of Interest: None declared

OP328 ENDOSCOPIC RESECTION AND RADIOFREQUENCY IN MANAGEMENT OF BARRETT'S ESOPHAGUS WITH HIGH-GRADE DYSPLASIA

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Introduction: High-grade dysplasia (HGD) and intramucosal carcinoma (IMC) developed on Barrett's esophagus (BE) are now well-established indications for endoscopic resection (ER) as first line treatment. Radiofrequency (RF) is also a recognized treatment for BE with dysplasia and is actually associated with ER for complicated BE ablation.
Aims & Methods: Aim of this study was to evaluate the efficiency of combined ER and RF compare to ER alone for management of BE with HGD. We retrospectively reviewed computerized data from 89 patients who had endotherapy for HGD on BE, between 2006 and 2013. 2 subgroups were created corresponding to patients treated by ER alone (group 1) or by combination of ER and RF (group 2).
Results: 55 patients were included in group 1 (7F/48M, mean age 68). 53/55 (96%) had HGD on preoperative sample histological analysis. Surgical specimen confirm HGD in 30/53 (57%), low-grade dysplasia (LGD) in 16/53 (30%) and metaplasia in 7/53 (13%). 2/55 (4%) patients had HGD on surgical specimen and LGD on preoperative sample. With an average of 1.8 sessions of ER per patient, the respective complete eradication rate of HGD, DBG and metaplasia was 100% (32/32), 94% (15/16) and 16% (9/55). Median Prague classification of BE was C3M5. HGD recurrence rate was 9% within an average of 22 months.
34 patients were included in group 2 (3F/31M, mean age 67). 32/34 (96%) had HGD on preoperative sample histological analysis. Surgical specimen confirm HGD in 25/32 (78%), low-grade dysplasia (LGD) in 5/32 (16%), metaplasia in 1/32 (3%) and normal stratified squamous epithelium in 1/32 (3%). 2/34 (6%) patients had HGD on surgical specimen and metaplasia on preoperative sample. With an average of 2 sessions of ER and 1.6 sessions of RF per patient, the respective complete eradication rate of HGD, DBG and metaplasia was 93% (25/27), 100% (5/5) and 59% (20/34). Median Prague classification of BE was C4M7. HGD recurrence rate was 15% within an average of 18 months.
HDG or LGD relapse rates were not significantly different between the 2 groups ($P = 0.13$ for group 1 and 0.42 for group 2). Initial length of BE was significantly superior for group 2 ($P < 0.015$). Complication rate in group 1 was 16% (9/55) with perforation in 1/55 (1.8%) and stenosis in 8/55 (15%), always treated endoscopically. Complication rate in group 2 was 24% (8/34) with haematemesis in 1/34 (3%), intraperitoneal hemorrhage without perforation in 1/34 (3%) and stenosis in 6/34 (18%), always treated conservatively or endoscopically. No death has been observed during all the follow-up.
Conclusion: Combined treatment of ER and RF can treat significantly longer BE with HGD than ER alone, with the same efficiency and safety. The long-term recurrence has not been studied.
Disclosure of Interest: None declared

OP329 EFFECTS OF RADIAL AND AXIAL FORCE OF ESOPHAGEAL STENTS ON OCCURRENCE OF SEVERE ADVERSE EVENTS AND RECURRENT DYSPHAGIA IN PATIENTS WITH MALIGNANT DYSPHAGIA

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Introduction: Self-expanding stent placement is an effective palliative treatment for malignant dysphagia. However, serious adverse events (SAEs) and recurrent dysphagia are frequently encountered. Stent-related forces, i.e. radial force (RF) and axial force (AF), are thought to play a causative role in these events, with a high RF being associated with migration risk and pain, and AF with stent-induced complications to the esophageal wall, such as perforation, hemorrhage and fistula formation. Furthermore, knitted esophageal stents elongate when compressed, depending on the braiding angle, which may also be of clinical relevance.
Aims & Methods: The aim of this study was to evaluate whether RF, AF and the degree of elongation of esophageal stents is associated with the occurrence of SAEs and recurrent dysphagia in clinical practice. Follow-up data of seven types of esophageal stents, placed for malignant dysphagia between January 2006 and December 2013, were collected in two academic centers. Stent types included the Ultraflex (n = 50, 20%, high RF, low AF), fully covered (FC) Wallflex (n = 32, 13%, low RF, high AF), partially covered (PC) Wallflex (n = 45, 18%, low RF, high AF), PC Evolution (n = 40, 16%, low RF, moderate AF), Hanaro (n = 40, 16%, moderate RF, moderate AF), Polyflex (n = 11, 5%, high RF, high AF) and SX-Ella (n = 27, 11%, low RF, moderate AF). Multivariate Cox regression analysis was performed to assess the effect of RF, AF and elongation on SAEs.
Results: In total, 245 patients (178 male [73%], mean age 67 ± 11 years) were included. SAE's were observed in 59 patients (24%, after a median of 14 days, IQR 2-45) and included hemorrhage (n = 14, 24%), fistula formation (n = 14, 24%), pneumonia (n = 11, 19%), severe pain (n = 11, 19%), perforation (n = 3, 5%) and other (n = 6, 10%). Recurrent dysphagia was seen in 74 patients (30%, after a median of 52 days, IQR 18-122), mainly due to migration (n = 20, 27%) and tumor in-/overgrowth (n = 31, 42%). After correction for patient, tumor, treatment and stent characteristics, multivariable analysis showed no association between RF, AF or elongation and SAEs ($P = 0.23$, $P = 0.30$, $P = 0.32$, respectively), recurrent dysphagia ($P = 0.07$, $P = 0.39$, $P = 0.18$, respectively) and stent migration in particular ($P = 0.22$, $P = 0.48$, $P = 0.40$, respectively). Furthermore,

no association was found between stent forces and the occurrence of pain, perforation, hemorrhage or fistula formation.
Conclusion: Both SAEs and recurrence of dysphagia following esophageal stent placement were not associated with RF, AF or degree of elongation. It can be speculated that their occurrence is a multifactorial process determined by a combination of stent-, tumor- and patient-related characteristics.
Disclosure of Interest: None declared

OP330 CLINICAL OUTCOMES FOLLOWING STENT PLACEMENT IN REFRACTORY BENIGN ESOPHAGEAL STRICTURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: The management of benign esophageal strictures is challenging. Common causes are represented by peptic injury, caustic ingestion, radiation treatment and anastomotic ischemia after esophageal resection. The first management strategy includes endoscopic dilation using bougies or balloons. Although the immediate success rate is up to 90%, about 30% to 40% of patients experience recurrent dysphagia within the first year of follow-up. The management of such relapsing refractory cases consists of repeat dilations. To provide alternative and more definitive treatment option, self-expandable stents have been proposed. Three different types of stents have been used: metallic (SEMS), plastic (SEPS) and biodegradable stents (BD).
Aims & Methods: We performed a systematic review and meta-analysis to examine the efficacy of stent placement in the long-term resolution of dysphagia in patients with refractory benign esophageal stricture (RBES). PubMed, SCOPUS, Google Scholar were searched (up to January 2015). Studies recruiting adults with RBES treated with stent placement were eligible. The success, complication and migration rates were pooled by means of a random effect model to obtain an odds with a 95% confidence interval (CI).Statistical heterogeneity was tested using the Q^2 test (significance level: 0.05) and I^2 statistic. If high levels of heterogeneity among the trials occurred ($I^2 >= 50\%$ or $P < 0.05$), the sources of heterogeneity were explored by sensitivity analysis and meta-regression analysis.
Results: Eighteen studies (444 patients) were eligible for inclusion. The pooled clinical success rate was 40.5% (95%CI, 31.5%>49.5%), yielding an odds of 0.68 (95%CI 0.46-0.98) with high heterogeneity ($I^2 = 65.0\%$). The meta-regression analysis showed stricture etiology as the only influencing factor. Patients treated with plastic (SEPS) and metallic stents (SEMS) reported not significantly higher success rates than patients treated with biodegradable (BD) stent [SEPS > SEMS > BD: 46.2% (95%CI 27-66.3%) > 40.1% (95%CI 28.1-54.1%) > 32.9% (95%CI 23.1-44.1%)]. The migration rate was 28.6% (95%CI 21.9-37.1%) yielding an odds of 0.40 (95%CI 0.28-0.59), with SEPS and SEMS reporting not significantly higher migration rates than BD stent [SEPS > SEMS > BD: 33.3% (95%CI 19.4-51.5%) > 31.5% (95%CI 22.5-42.2%) > 15.3% (95%CI 8.3-25.4%)]. The complication rate was 20.6% (95%CI 15.3-28.1%) yielding an odds of 0.26 (95%CI 0.18-0.39) without significant difference between stents [SEMS = BD > SEPS: 21.9% (95%CI 11.5-37.5%) = 21.9% (95%CI 13.8-32.9%) > 19.4% (95%CI 12.3-30.1%)].
Conclusion: Stent placement for the treatment of RBES is effective in about 40% of cases. Since patients with RBES have only two possible treatment options, i.e. life-long dilations or surgery, the overall success rate reported by stent placement should not be considered negligible. Furthermore, the success rates might be even higher in subgroups of patients, according to the stricture etiology (i.e. post-surgery or post-radiotherapy strictures). Further studies should investigate whether the clinical success rate varies according to the stricture etiology.
Disclosure of Interest: None declared

OP331 PREDICTORS OF PARTIAL VS. COMPLETE SYMPTOMATIC RESPONSE IN PATIENTS WITH ESOPHAGEAL ACHALASIA TREATED BY PER ORAL ENDOSCOPIC MYOTOMY (POEM)

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Introduction: POEM results in treatment success in more than 90% of operated patients. Treatment success is usually defined as an Eckardt score (ES) 0-2 (or 0-3). The aim of our study was to assess whether there are any predictive factors for only partial symptomatic improvement with residual symptoms (ES 1 or 2) vs. complete symptomatic response (ES = 0).
Aims & Methods: Since 2012, we performed 87 POEM procedures in 86 patients with achalasia. The overall treatment success at 12 months was 98%. We analyzed clinical outcomes of 59 patients who have had a treatment success (ES= 0, 1 or 2) and completed at least 6 months follow up (27 female, 32 male, mean age 48 years). We performed multivariate logistic regression with stepwise selection of predictors and tested equality of means for continuous variables for the two target levels and Fisher's exact test for independence of the target level and factor variables.
Results: Among 59 analyzed patients, 36 (61%) had a complete symptomatic response (post-POEM ES = 0) while 23 patients (39%) had partial symptomatic response (post-POEM ES 1 or 2). The mean age of patients with a complete response was lower(51 vs. 42 years) as well as the frequency of pre-POEM treatments (botulinum toxin injection or pneumatic dilatation; 11% vs. 35%). The patients with a complete symptomatic response had higher both the pre-POEM IRP (mean 30.1 vs. 23 mmHg) and the mean basal LES tonus (44 vs. 32 mmHg). The frequency of type II achalasia was higher in patients with a complete symptomatic response (83% vs. 61%). Both groups did not differ with regard to the procedure related data (length of the procedure, length of myotomy, etc.). The stage of the disease (duration of symptoms, esophageal width) and the frequency of partial recovery of esophageal peristalsis after POEM (33% vs. 30%) were similar in both groups. Post-POEM esophagitis was more frequent in patients with a complete symptomatic response (36% vs. 26%). In multivariate logistic regression analysis, only age (under 40, p = 0.03), pre-POEM basal LES-tonus (under 40 mmHg, p = 0.04) and any prior treatment for achalasia (p = 0.04) have been found as independent predictors of partial symptomatic response.
Conclusion: Among the patients with treatment success, approx. 40% do not have a complete symptomatic response. Younger age, lower pre-POEM basal LES tonus and previous treatment attempts with botulinum toxin or balloon dilatation are independently associated, despite the overall treatment success, with an incomplete symptomatic response.
Disclosure of Interest: None declared

OP332 PERORAL ENDOSCOPIC REMYOTOMY (RE-POEM): A SALVAGE OPTION FOR PERSISTENT/RECURRENT SYMPTOMS AFTER PREVIOUS POEM

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Introduction: Peroral endoscopic myotomy (POEM) has been described with high success rates for the treatment of achalasia. However, persistence/recurrence of symptoms can occasionally occur after POEM.
Aims & Methods: Our purpose was to evaluate the feasibility, safety and efficacy of salvage peroral endoscopic remyotomy (Re-POEM) for patients after failed POEM. Fifteen patients with persistence/recurrence of symptoms (Eckardt symptom score ≥4) after previous POEM were identified from a prospectively maintained database that included a total of 1454 consecutive achalasia patients. The primary outcome was symptom relief during follow-up, defined as an Eckardt score of ≤3. Secondary outcomes were procedure-related adverse events, lower esophageal sphincter (LES) pressure on manometry, and reflux symptoms before and after Re-POEM.
Results: All patients underwent successful Re-POEM after a mean of 13.5 months (range 4–37 months) from the time of the primary POEM. The mean operation time was 41.5 minutes (range 28–62 minutes). Submucosal tunnel infection occurred in one case and was successfully managed with conservative treatments. During a mean follow-up period of 11.3 months (range 3–18 months), treatment success was achieved in all patients. The mean symptom score pre-treatment was 5.6 (range 4–8) compared with a mean post-treatment score of 1.2 (range 0–3; $P < 0.001$). Mean LES pressure also decreased from a mean of 25.0 mmHg to 9.5 mmHg after Re-POEM ($P < 0.001$). The overall clinical reflux complication rate of Re-POEM was 33.3%.
Conclusion: Re-POEM seems to be a safe and effective salvage option for failed POEM, resulting in short-term symptom relief in all patients and without serious complications.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 15:45–17:15
BASIC ASPECTS OF HEPATOCARCINOGENESIS AND REGENERATION – ROOM E5

OP333 CONTRIBUTION OF NATIVE AND ACTIVATED HEPATIC STELLATE CELLS IN LIVER REGENERATION AFTER PARTIAL HEPATECTOMY AND 2-ACETYLAMINOFLUOREN INJECTION

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Introduction: Actual problem of modern hepatology is to find new and athogenetic treatment of liver diseases. One of these methods could be cell therapy with using hepatic stellate cells (HSC), that are thought to be regional stem cell of the liver. Experiments on freshly isolated rat HSC transplantation confirmed their participation in liver regeneration after partial hepatectomy (PH). However, the role of freshly isolated and activated in vivo HSC transplantation to rats undergoing PH and the injection of 2-acetylaminofluoren (AAF) is still unknown.
Aims & Methods: To study the influence of transplanted HSC on activity of liver regeneration after PH and AAF injection.
Before transplantation HSC were labeled by the gene of Enhanced Green Fluorescent Protein (GFP). We selected the classical model of acute liver damage – partial hepatectomy. In one case, we transplanted native HSC, in the other – in vivo activated HSC. Activation was carried out by lead nitrate injection into the tail vein of rats donor, HSC were isolated 2 days thereafter.

To inhibit hepatocyte proliferation in the recipient rats, animals were administered intraperitoneally AAF 5 days before and after surgery. The animals were sacrificed after 1, 2, 3, 5, 7 and 14 days after the transplantation of HSC. Paraffin slices were stained by immunohistochemistry with antibodies to desmin – marker of HSC and è-SMA - myofibroblast marker.
Results: GFP + hepatocytes were detected (found, stained) in liver parenchyma even at the first days after transplantation. All groups showed an increase in the number of desmin - positive cells in the parenchyma. After transplantation of freshly isolated and activated HSC to rats after PH and AAF administration, the maximum number of such cells was found 2 days after surgery, then their number gradually decreased. Desmin-positive HSC in animals after PH without AAF injection retained in the liver longer: in case of freshly isolated HSC transplantation – till the 5th day, after in vivo activated HSC transplantation - till the 7th day. In all the groups è-SMA positive myofibroblasts were not detected.
Conclusion: Transplantation of native and activated HSC stimulates liver regeneration and contributes to hepatocytes repopulation without the risk of liver fibrosis.
Disclosure of Interest: None declared

OP334 O-GLCNAC TRANSFERASE PROMOTES FATTY LIVER-ASSOCIATED LIVER CANCER THROUGH ACTIVATING JNK AND NF-KB PATHWAYS

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Introduction: O-GlcNAc transferase (OGT), a unique glycosyltransferase, is involved in metabolic reprogramming. Using transcriptome sequencing, OGT was identified to be highly expressed in non-alcoholic steatohepatitis (NASH)-associated hepatocellular carcinoma (NASH-HCC) compared to their adjacent non-tumor tissues of 18 patients. However, the role of OGT in NASH-HCC is still unclear.
Aims & Methods: We aim to investigate the functional role of OGT in NASH-HCC and its potential clinical implication. The biological function of OGT was determined by proliferation, clonogenicity, migration and invasion experiments through gain- or loss- of OGT functional assays *in vitro* and in nude mice. OGT target factors and pathways were identified by promoter luciferase assay, DNA binding activity assay and Western blot. The effects of OGT on oxidative stress, reactive oxygen species (ROS), lipid peroxide and endoplasmic reticulum (ER) stress and ER stress-related cascades were also investigated. The clinical impact of OGT was evaluated in 209 serum samples of 137 NAFLD patients and 72 control subjects by ELISA.
Results: OGT was upregulated in 12 out of 18 (66.7%) NASH-HCC tumor tissues compared with their adjacent non-tumor tissues by transcriptome sequencing. Enhanced OGT expression was further confirmed in an independent set of 9 pairs of human NASH-HCC tissues (66.7%) by Western blot and in six HCC cell lines and two NASH-HCC cell lines, but silenced in normal livers and weak in immortalized normal hepatocyte cell lines MIHA and LO2. OGT production was significantly induced in MIHA cells treated with insulin ($P<0.01$) or cholesterol ($P<0.01$). Ectopic expression of OGT in MIHA and LO2 cells promoted cell growth, clonogenicity, migration and invasion ability; whereas stable knockdown of endogenous OGT in two NASH-HCC cell lines had opposite effects. Moreover, subcutaneous tumor xenografts of LO2 cells with stable OGT expression in nude mice exhibited an increased tumor growth compared with the control cells ($P<0.01$). Mechanistically, OGT induced ROS production, increased lipid peroxide levels and enhanced the protein expression of ER stress markers GRP78 and IRE1α in LO2 and MIHA cells. In this connection, OGT significantly activated JNK cascade as evidenced by increased protein expression of p-JNK, p-c-Jun and activation of AP-1; induced NF-κB pathway through enhancing the protein levels of p-IKKα/ p-IKKβ, p-p65, p-p50 and the NF-κB DNA binding activity in OGT-transfected LO2 cells compared to the control cells. Moreover, the serum levels of OGT were significantly higher in patients with steatosis (3.30 ng/ml vs 1.83 ng/ml, $P<0.0001$) or NASH (3.49 ng/ml vs 1.83 ng/ml, $P<0.001$) compared with control subjects. The AUROC of diagnosing NAFLD was 0.741 (95% CI: 0.671-0.812) and diagnosing NASH was 0.749 (95% CI: 0.681-0.816). Multivariate analysis showed that OGT was an independent risk factor for NASH patients.
Conclusion: OGT plays an oncogenic role in NASH-associated HCC through inducing ER stress and ROS production and consequently activating oncogenic JNK and NF-κB pathways. Serum detection of OGT may serve as a potential diagnostic marker for NASH patient.
Disclosure of Interest: None declared

OP335 ANTI-ANGIOGENIC TREATMENT WITH OCTREOTIDE ATTENUATES PORTAL HYPERTENSION OF THE CIRRHOTIC RATS THROUGH SOMATOSTATIN RECEPTOR 2

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Introduction: Angiogenesis is pivotal for the devolvement of portal hypertension in cirrhosis. Somatostatin (SST) and its analogue octreotide are widely used for the management of gastroesophageal varices bleeding. However, the molecular and cellular mechanism of SST and octreotide on portal hypertension remains unclear.
Aims & Methods
Aims: To investigate the mechanism of octreotide on regulation of portal hypertension.
Methods: Peritoneal injection of thiacetamide (TAA) was employed to induce liver cirrhosis (200 mg/kg every 3 days for 16 weeks). 36 male Sprague-Dawley rats were randomized into control, TAA and TAA + octreotide with 12 animals in each group. TAA + octreotide group received TAA plus octreotide (50 mg/kg/day) from the initiation of TAA administration. TAA group received TAA plus placebo and control group received injections of normal saline. Scanning electron microscope of vascular casting, hematoxylin-eosin staining (HE), Masson trichrome staining (MT) were applied to evaluation of cirrhosis and angiogenesis. Portal pressure was also measured. Immunohistochemistry (IHC), quantitative real-time PCR (qRT-PCR) and Western blot for alpha-smooth muscle actin (a-SMA), collagen III, CD31, vascular endothelial growth factor (VEGF), phosphorylated extracellular signal-regulated kinase (p-ERK) and somatostatin receptors (SSTRs) were determined. *In vitro*, human umbilical vein endothelial cell line (HUVEC) was treatment with vehicle, octreotide, octreotide plus SSTR-2 antagonist (CYN154806) or octreotide plus SSTR-5 antagonist (BIM23056) for 24 hours. Afterwards, wound-healing assay for cell migration, tube formation assay for angiogenesis, immunocytofluorescence and Western blot for VEGF and p-ERK were carried out.
Results: *In vivo*, compared with TAA group, liver fibrosis and portal pressure in TAA + octreotide group were remarkably decreased by 40.4% and 17.1%, respectively. And the mRNA levels of a-SMA and collagen III in TAA + octreotide group were also reduced. Histological sections, vascular casts of hepatic portal vein, IHC and qRT-PCR for CD31 showed that angiogenesis in TAA + octreotide group were dramatically reduced when compared with TAA group. The up-regulation of VEGF, p-ERK and SSTR-2, SSTR-5 induced by TAA administration were significantly inhibited after treatment with octreotide. *In vitro*, compared with vehicle treated cells, the migration rate, tube length, VEGF and p-ERK protein were obviously substantially decreased in octreotide treated cells. However, these inhibitory effects afford by octreotide were remarkably restored by SSTR-2 antagonist but not SSTR-5 antagonist.
Conclusion: Octreotide could ameliorate portal hypertension in cirrhotic rat through inhibition of intrahepatic angiogenesis. The anti-angiogenesis effect afford by octreotide may attribute to regulation of integrated signal pathways involving SSTR-2 - p-ERK – VEGF.
Disclosure of Interest: None declared

OP336 GENOMIC MUTATIONS AND PATHWAYS IDENTIFIED BY WHOLE-EXOME SEQUENCING IN NAFLD-ASSOCIATED HEPATOCELLULAR CARCINOMA

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Introduction: Epidemiological studies have shown that obesity and its related non-alcoholic fatty liver disease (NAFLD) promotes the development of hepatocellular carcinoma (HCC). However, the underlying genetic mechanism of obese-related HCC is still largely unknown.
Aims & Methods: We aimed to uncover the genetic alterations of obesity-associated HCC using cross-species oncogenomics and whole-exome sequencing. HCC development in genetic obese (*db*/*db*) mice and dietary obese mice kept on high-fat diet was monitored in comparison with wild-type lean mice kept on normal diet treated with diethylnitrosamine (DEN). Paired HCC tumor and adjacent normal samples from obese mice and lean mice were subjected to whole-exome sequencing and cross-species oncogenomics to reveal genetic alteration landscapes. Candidate mutation genes were further validated in HCC tumor and adjacent normal samples from 16 genetic and 13 dietary obese mice and 16 control lean mice by PCR Sanger sequencing. The bio-functional significance and molecular pathways of the candidate mutation genes was evaluated.
Results: Significantly higher tumor incidence, multiplicity and larger tumor size of NAFLD-HCCs were found in both genetic and dietary obese mice compared with those of lean HCCs in wild-type mice. Totally 277 and 268 genes were found to be mutated in liver tumors from obese mice and control lean mice, respectively, with only 8 genes overlapped by whole-exome sequencing. Eight important metabolic or cancer-related pathways were significantly enriched in mutated genes found in obese HCC, whereas only two pathways were enriched in mutated genes found in lean HCC. Mutation frequency of *Cel* was significantly higher in obese HCC than in lean HCC (34.5% *vs.* 6.3%, $P < 0.05$). Mutations in *hRas* were detected in 10.3% of obese HCCs, all located at codon 61, but not in lean HCCs. *CEL* inactivating mutation and *hras* activating mutation promote liver cell growth. Inactivating mutation in CEL (D454E and D555N) led to the accumulation of cholesteryl ester, which activated ER stress and consequent IRE1α/JNK/c-Jun/AP-1 signalling cascade; whist activating mutations in hRas (Q61R and Q61K) activated MAPK and PI3K/PDK1/Akt signaling cascades to promote cell growth.
Conclusion: The genetic alterations of NAFLD-associated HCC are distinguished from that of lean HCC. Mutations in *CEL* and *hRas* play important roles in NAFLD-associated hepatocellular carcinogenesis.
Disclosure of Interest: None declared

OP337 EX VIVO-EXPANSION OF CD34+ CELLS FROM PATIENTS WITH LIVER CIRRHOSIS UP-REGULATES THERAPEUTIC EFFICACY OF CELL TRANSPLANTATION FOR LIVER CIRRHOSIS RAT

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Introduction: We demonstrated that the transplantation of human peripheral blood-CD34$^+$ cells into an immunodeficient rat liver fibrosis model reduced liver fibrosis by suppressing activated hepatic stellate cells and increasing matrix metalloproteinase (MMP) activity, and led to hepatic regeneration[1]. Recently, we reported that autologous granulocyte-colony stimulating factor (G-CSF)-mobilized peripheral blood-CD34$^+$ cell transplantation for patients with decompensated liver cirrhosis (LC) had therapeutic potential, but the colony-forming ability of CD34$^+$ cells from patients with decompensated LC was reduced[2]. So, recovery of CD34$^+$ cell function is indispensable for cell transplantation therapy of patients with decompensated LC.

Aims & Methods: The aim of this study was to investigate the efficacy of cell transplantation therapy with ex vivo-expanded human CD34$^+$ cells for carbon tetrachloride (CCl_4)-induced liver fibrosis model. Human G-CSF-mobilized peripheral CD34$^+$ cells of patients with LC were isolated by magnetic cell sorting system. Recipient nude rats were injected intraperitoneally with CCl_4 twice weekly for 3 weeks before initial treatment. Then, saline, 5×10^4, 2×10^5, or 1×10^6 non-expanded and expanded CD34$^+$ cells/kg body weight were transplanted via spleen, respectively. The administration of CCl_4 was continued for three more weeks until the rats were sacrificed. Examination items were as follows. 1) FACS and RT-PCR analysis of freshly isolated and expanded CD34$^+$ cells, 2) morphometry of fibrotic areas of Azan-Mallory stained liver, and 3) immunohistochemistry using anti-CD31, smooth muscle myosin heavy chain-1 (SM1), αSMA, Ki67, and PCNA antibodies.

Results: Seven days in culture, G-CSF-mobilized CD34$^+$ cells were effectively expanded in the serum-free culture medium. Expanded CD34$^+$ cells were also increasingly characterized as positive for cell surface markers of VE-cadherin, KDR and Tie-2, whereas they were down-regulated for CD34, CD133 and CD117. The expression of pro-angiogenic growth factors in expanded CD34$^+$ cells increased compared with non-expanded CD34$^+$ cells. The transplanted cells differentiated into CD31$^+$and SM1$^+$ cells. Expanded CD34$^+$ cell transplantation had dose-dependently reduced liver fibrosis, with the decrease of collagen type-I and αSMA positive cells. Assessments of hepatocytes and sinusoidal endothelial cells proliferative activity indicated the superior potency of expanded CD34$^+$ cells over non-expanded CD34$^+$cells.

Conclusion: These findings strongly suggest that expanded CD34$^+$ cell transplantation induces better therapeutic effects for LC.

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Disclosure of Interest: None declared

OP338 TRANSPLANTATION OF HEMATOPOIETIC STEM CELLS CAN CHANGE THE INTENSITY OF LIVER CELLS' APOPTOSIS IN PATIENTS WITH ALCOHOLIC LIVER CIRRHOSIS

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Introduction: Stem cell therapy is a promising technology for treating liver cirrhosis. Main source of these cells is bone marrow. The current method of aspiration of bone marrow under general anesthesia is inadvisable in patients with liver failure. Hematopoietic stem cells (HSCs) can be collected from blood stream with a non-invasive harvesting technique.

Aims & Methods: In this clinical trial we checked safety and efficacy of autologous HSCs from peripheral blood in patients with alcoholic liver cirrhosis and their influence to apoptosis intensity of liver cells. We examined liver biopsy specimens of 11 alcoholic cirrhosis patients (Child-Pugh class A and B). Biopsies were taken before the injection of autologous HSCs mobilized by granulocyte-colony-stimulating factor (G-CSF) into celiac trunk, 3 and 12 months after the procedure. Formalin-fixed, paraffin-embedded liver biopsy preparations were stained immunohistochemically with antibodies against Bcl-2, the anti-apoptotic protein.

Results: In the biopsies that were taken before the transplantation of HSCs we have seen many Bcl-2 positive cells in portal tracts. They were localized in liver parenchyma and in inflammatory infiltrates around the portal tracts. Positive cells could be divided into 3 types of cells: inflammatory cells with round or oval nucleus, cells with processes (sinusoidal cells) and single hepatocytes. We also observed weak expression of Bcl-2 in cholangiocytes. Three months after transplantation the number of positively stained cells significantly decreased. Nevertheless, twelve months after transplantation the amount of cells expressing anti-apoptotic protein grew up again, but didn't reach the level of first biopsies.

Conclusion: The analysis showed that the HSC treatment had no side effects. These results might indicate an intensification of inflammatory cells' apoptosis as a result of HSCs therapy. However, the effect of treatment remains only a few months and it is necessary to repeat the procedure.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 15:45–17:15
HOT TOPICS IN THE MANAGEMENT OF COLORECTAL PATHOLOGY – ROOM E6

OP339 LAPAROSCOPIC COLON RESECTION: TO PREP OR NOT TO PREP? ANALYSIS OF 1,535 PATIENTS

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Introduction: Recent systematic reviews and metanalyses of randomized controlled trials have shown that mechanical bowel preparation (MBP) should be omitted before elective open colon resection. However, there are very few data regarding the utility of preoperative MBP in patients undergoing laparoscopic colon resection (LCR).

Aims & Methods: The aim of this study was to challenge the use of MPB before elective LCR. It is a retrospective analysis of a prospectively collected database. All patients undergoing elective LCR with primary anastomosis were included. Preoperative MBP with polyethylene glycol solution was used routinely between April 1992 and December 2004, then it was abandoned. The early postoperative outcomes in patients who had preoperative MBP (MBP group) and in patients who underwent LCR without preoperative MBP (No-MBP group) were compared.

Results: From April 1992 to December 2014, 1,535 patients underwent LCR: 706 MBP patients and 829 No-MBP patients. There were no differences in demographic data, indication for surgery and type of procedure performed between MBP and No-MBP group patients. The incidence of anastomotic leakage was similar between the two groups (3.4% vs. 3.6%, $P = 0.925$). No differences were observed in intra-abdominal abscesses (0.6% vs. 0.8%, $P = 0.734$), wound infections (0.6% vs. 1.4%, $P = 0.149$), infectious extra-abdominal complications (1.8% vs. 3%, $P = 0.190$), and non-infectious complications (6.1% vs. 6.8%, $P = 0.672$). The overall reoperation rate was 4.6% for MBP patients and 5% for No-MBP patients ($P = 0.813$).

Conclusion: The use of preoperative MBP does not lead to lower incidence of intra-abdominal septic complications after LCR and therefore it should be abandoned.

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Disclosure of Interest: None declared

OP340 NORMAL MUCUS COMPOSITION IS ESSENTIAL IN COLONIC ANASTOMOTIC HEALING IN MICE

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Introduction: Anastomotic leakage (AL) is one of the most dreaded complications after colorectal surgery causing high morbidity and mortality. Despite extensive research, it is unclear why the incidence of AL remains approximately 10%. We hypothesize that mucus plays a pivotal role in the healing of colorectal anastomoses, since the mucus layer forms the first line of defense in the gastrointestinal tract. Previous research showed that Prostaglandin E2 (PGE2) supplementation in $COX2^{-/-}$ mice reduced the anastomotic leakage rate and ex vivo stimulation of the colon with PGE2 showed significant increase in mucus thickness. Therefore, we investigated if MUC2 (mucin 2, main component of mucus) depletion is associated with AL.
Aims & Methods: Twenty-two male and 22 female mice of different Muc2 genotypes were subjected to a model of colonic AL. Mice were matched for age, gender and when possible littermates were used as controls. Half of the mice received daily administration of dmPGE2 to potentially stimulate mucus secretion, starting a day prior to surgery and follow-up was 3 days. Mucus thickness measurements were performed ex vivo by measuring the distance between the epithelial surface and the mucus surface by a micropipette to ascertain presence of mucus at the anastomosis. Bacterial translocation into mesenterial lymph node (MLN) and spleen was determined by qPCR of bacterial 16S rDNA. Histological scoring of anastomosis, control proximal and distal colon was performed according to van der Ham et al. Intestinal Fatty Acid Binding Protein (I-FABP) levels were determined by ELISA as a marker of enterocyte damage.
Results: Of $Muc2^{-/-}$ mice, 91% developed AL, compared to 32% of control animals ($p < 0.001$). An evident mucus layer could be found at the anastomotic site of control animals, but not in colon of $Muc2^{-/-}$ mice. DmPGE2 did not reduce the anastomotic leakage rate, neither in $Muc2^{-/-}$ nor in control mice. Histologically, normal healing could be found in control animals, while $Muc2^{-/-}$ showed more inflammation with granulocyte influx and less fibroblast activity and neoangiogenesis at the anastomotic site, although not significant. Of $Muc2^{-/-}$ 90% had bacterial 16S rDNA in their MLN and 27% in their spleen at day 3 after surgery, while only 61% of the control animals had bacterial 16S rDNA in their MLN and no bacterial 16S rDNA could be found in spleens of these animals. I-FABP levels were significantly higher in $Muc2^{-/-}$ mice (3.89 ± 0.6ng/mL) compared to control mice (1.82 ± 0.4ng/mL, $p < 0.01$).
Conclusion: Normal mucus composition is essential in the healing process of colonic anastomosis in mice. DmPGE2 cannot stimulate mucus secretion in vivo in order to promote anastomotic healing, at least not in this model. Further research on anastomotic healing should focus on ways to positively influence the mucus layer as a way to promote better postoperative recovery.
Disclosure of Interest: None declared

OP341 LONG-TERM RESULTS OF INTERSPHINCTERIC RESECTION FOR VERY LOW RECTAL CANCER WITHOUT PREOPERATIVE CHEMORADIOTHERAPY

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Introduction: In Japan, the standard treatment of advanced rectal carcinoma is surgery with adjuvant chemotherapy. Intersphincteric resection has recently been considered as an alternative option to avoid permanent colostomy for selected patients with very low rectal carcinoma. However, with intersphincteric resection, there is a potential risk of increasing short- and long-term morbidity and mortality.
Aims & Methods: To evaluate the morbidity, mortality, and short-term, long-term results of intersphincteric resection for patients with very low rectal cancer, retrospective clinicopathologic analysis of prospective data registry was done. Between 1997 and 2012, 181 patients with cT1-to-cT3 rectal cancer below 5 cm from the anal verge underwent total mesorectal excision with intersphincteric resection. All patients did not receive preoperative chemotherapy and chemoradiotherapy.
Results: There were 134 men and 47 women with a median age of 58 (range 22-79) years. Median distance between tumor and the anal verge was 3 (range 1-5) cm. There were 50 pT1, 64 pT2, and 67 pT3 tumors. Eighty-four patients had disease categorized as stage I, 31 as stage II, 61 as stage III, and 5 as stage IV. Radial and distal margins were negative for 178 patients, but 3 patients had positive margins. Short-term morbidity and mortality were 26% and 0.6%, respectively. 11 patients underwent emergency operation and 5 patients had permanent stoma due to complication. Fifteen patients (8%) developed anastomotic leakage.Median follow-up was 61 months. Five-year overall and relapse-free survival rates of the 181 patients were 91% and 77%, respectively. The rates of local and distant recurrence of the 181 patients were 6% and 17%, respectively. One patient with T1 and 10 patients with T3 tumor developed local recurrence. Positive surgical resection margin and T3 tumor were significantly associated with local recurrence.
Conclusion: This study suggested that intersphincteric resection without neoadjuvant therapy is safe procedure for selected patients with cT1-to-cT3 rectal cancer below 5 cm from the anal verge in terms of short- and long-term morbidity and mortality.
Disclosure of Interest: None declared

OP342 WAITING TIME TO TREATMENT FOR PATIENTS WITH COLORECTAL CANCER IN FRANCE FROM MEDICO-ADMINISTRATIVE DATABASES

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Introduction: Time to treatment of cancer is becoming a social and political issue. In France one of the objectives of cancer plan is to ''better understand the timing of cancers'' care in order to reduce inequalities on access to care due to any delays''
Aims & Methods: We aim to study time elapsed from the colonoscopy to various first treatments such as surgery, and adjuvant treatments before and after surgery.
Based on International classification on diseases 10th revision and French medical procedures codes, we selected patients newly diagnosed for colorectal cancer in 2009 or 2010, who underwent to surgery or adjuvant treatment, from national hospital discharge and long term illness databases. We analyzed time to first treatment after colonoscopy according to the patient's pathway, the therapy's combination and the region of the patient's residence.
Results: We included in our study 15 694 and 6 623 patients suffering from colon and rectum cancers respectively. The median waiting time from colonoscopy to surgery was 22 (Q1: 14; Q3: 34) and 97 (Q1: 34; Q3: 141) days for colon and rectum cancers respectively. It was 36 (Q1: 21; Q3: 59) and 40 (Q1: 27; Q3: 59) days from colonoscopy to first chemotherapy, for colon and rectum cancers respectively and 53 (Q1: 39; Q3: 78) days from colonoscopy to first radiation for rectum cancer.
Median waiting times were longer in most of north regions (Picardie, Basse-Normandie) and overseas departments (Guadeloupe, Martinique, La Réunion, Guyane), and shorter in south regions (Languedoc-Roussillon, Limousin, Provence-Alpes-Côte-d'Azur) in France for both Colon and rectum cancer.
Conclusion: This original study is the first performed at national and regional level including overseas departments in France. Waiting times to treatment were longer for rectum cancer compared to colon cancer. There was heterogeneity on waiting times between regions of patient's residence.
Disclosure of Interest: None declared

OP343 CONSIDERATIONS FROM THE FIRST DELAYED BLEEDING RISK SCORE FOR ENDOSCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL LESIONS: TO CLIP OR NOT TO CLIP?

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Introduction: Delayed bleeding (DB) is the main complication after endoscopic mucosal resection (EMR) of large colorectal lesions. Many of the risk factors of DB described remain controversial.
Aims & Methods: The aims of this study were to create a DB risk score for EMR of large colorectal lesions (≥2 cm) and to consider the cost-effectiveness of prophylactic clipping in the high-risk group.
EMR of non-pedunculated large colorectal lesions were prospectively registered in an ongoing Spanish multicenter study from February 2013 to February 2015. A score for DB was developed by assigning a weight from 0 to 3 to each risk factor category found based on the β parameter from the multivariate logistic regression. We evaluated the cost-effectiveness of the prophylactic complete closure of the mucosal gaps in the high-risk group.
Results: A total of 1255 EMR were performed. There were 46 (3.7%, 95%CI: 2.7% > 4.9%) cases of DB.
Factors associated to DB in the multivariate analysis ($p \leq 0.05$) were age ≥75 years, ASA classification III-IV, lesion size ≥40 mm, location proximal to transverse colon, aspirin use during EMR and not fully clipped mucosal gaps after EMR. Taking the continuous score (ROC = 0.79, 0.72-0.85), we classified patients into three DB risk categories: low (score 0-3, risk 0.6% [CI 0.2% > 1.8%]), average (score 4-7, risk 5.5% [CI3.8% > 7.9%]) and high (score 8-10, risk 40% [CI 21.8%, 61.1%]).

In the high-risk group (n = 25, 2%) DB occured in 40%. None of the mucosal gaps were clipped. The patients with DB needed 33 hospitalization days (medium 3.3 days/patient) and 5 (20%) required transfusion. This implies a hospitalization cost of 19800 €whereas the cost of the complete closure of these 25 mucosal defects (medium size 40.8 mm) would be around 7500 €.
Conclusion: DB rate after EMR of large colorectal lesions was 3.7% (95%CI: 2.7% > 4.9%).
Six easily available predictors can be used to calculate a simple and novel DB risk score that allows endoscopists to stratify patients and colonic lesions.
In the high-risk group DB rate reaches 40%. Complete clip closure of the mucosal gap after EMR appears to be a cost-effective preventive method when used in high-risk patients.
Disclosure of Interest: None declared

OP344 AN AUDIT OF COLONIC STENTING IN ACUTE LARGE BOWEL OBSTRUCTION IN A UK GENERAL HOSPITAL

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Introduction: The objective of this study was to audit practice in colonic stenting in acute presentations of malignant bowel obstruction in a London Hospital (UK) against the UK's National Institute of Health and Care Excellence (NICE) recommendations.
Aims & Methods: Patients were retrospectively identified using the hospital's endoscopy database ('Scorpio') and by using the hospital's data warehouse to identify all patients who presented with acute large bowel obstruction. Data were captured between May 2009 and December 2012 by two independent doctors. A notes check was performed 6 months after the data capture period closed to check for: stent complications; progression to colorectal surgery; length of time to colorectal surgery where applicable; and stoma rate where applicable. The following endpoints were used to determine the gold standard: 1) The use of CT chest, abdomen and pelvis prior to stent deployment 2) The exclusion of self-expanding metallic stents in low rectal lesions or to relieve right-sided colonic obstruction or if clinical or radiological evidence of colonic perforation or peritonitis 3) Deployment of self expanding stents within 24 hours of presentation 4) Enrolment into an RCT.
Results: During the audit period 363 patients presented with acute large bowel obstruction. Of these 36 patients (9.9%) had stents deployed within the audit period. Median age of those who had stents was 77 years (range 50-98 years) and 55.5% were male. The stent was intended as a palliative measure in 53% and as bridge to colorectal surgery in 47% of cases. In 2 instances the stent could not be deployed for technical reasons: in one instance due to patient hypoxia, and in a second due to an impassable stricture. 100% of patients had a CT abdomen and pelvis and 83% also had a CT chest. No stents were placed where there was evidence of perforation or peritonism. One right sided stent and one rectal stent were placed. Only 44% of stent procedures were carried out within 24 hours of hospital admission for obstruction. Patients were not offered the opportunity to take part in an RCT as none was available. The stent failure rate was 8.8% at 6 weeks. In two cases the stent became blocked with faecal matter and in one case the stent was occluded by tumour growth. There were no cases of stent migration or perforation. 15 patients (41.2%) went on to have colorectal surgery. Mean time to surgery after stenting was 51 days (range 1-256 days). The primary anastomosis rate was 66.6%; 33.3% had a stoma. Of these 15 patients there were two surgical deaths, both of whom died in ITU on the third post-operative day; one following a cardiac arrest, the second in which ITU withdrew care as multi-organ failure led to an unsustainable inotrope requirement.
Conclusion: Colonic stenting can be deployed safely in a district general hospital and it is effective. However a stent was placed in fewer than 10% of admissions for acute large bowel obstruction and of those who had a colonic stent insertion fewer than half had the procedure within 24 hours of hospital admission. This suggests that greater awareness is still required amongst clinicians.

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Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 15:45–17:15
MOTILITY, MECHANISMS AND THE UPPER GI TRACT – ROOM B3

OP345 INCREASED RISK OF OVERWEIGHT, OBESITY AND MOOD DISORDERS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS (FGID)

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Introduction: Functional gastrointestinal disorders (FGIDs) are common clinical conditions of unknown etiology. Around 30% of North American adults are obese, and the prevalence of obesity is increasing. Although some reports have suggested that obesity may be more prevalent in FGIDs, the data on adult patients are scarce and contradictory.
Aims & Methods: Thus our objective was to evaluate the association between obesity and FGIDs and to determine the factors contributing to this association.
This is an observational study conducted between January 2008 and January 2015. New patients referred to the Gastroenterology outpatient clinic at McMaster University completed questionnaires evaluating FGIDs (Rome III), anxiety and depression (HAD score) and basic demographic data. A chart review was then performed in a random sample of the total population to collect further clinical and demographic data, and to rule out organic diseases. Continuous variables were expressed as mean ± SD and categorical variables as percentages. $\chi 2$, and logistic regression analyses were performed and adjusted by age, gender, lifestyle habits, psychiatric medication and mood.
Results: Three thousand and thirty four patients out of 4965 were included in the analysis. From them, 71% of patients fulfilled the Rome III criteria for FGIDs but only 53% were confirmed as FGIDs after organic diseases were ruled out. 53% of all the patients were overweight or obese (BMI ≥25 and ≥30, respectively). An increased risk for overweight and obesity was observed in patients with FGIDs compared to those who did not meet the Rome III criteria for FGIDs (aOR1.2, 95% CI 1.01-1.42). The highest risk for overweight/obesity was observed in patients with functional dyspepsia (FD; aOR 2.55, 95% CI 1.70-3.80) followed by irritable bowel syndrome (IBS; aOR 1.67, 95% CI 1.62-2.20). The use of antidepressants contributed to the association between FGIDs and overweight/obesity (OR 1.46, 95% CI 1.17-1.82). An increased risk for depression (OR 1.28, 95% CI 1.10-1.46) but not for anxiety was found in the overall overweight/obesity population. However, both anxiety and depression were significantly increased in population with both overweight/obesity and FGIDs (OR 1.33, 95% CI 1.14-1.56 and OR 1.51, 95% CI 1.26-1.80 for anxiety and depression, respectively).
Conclusion: Overweight and obesity are frequently found in patients with FGIDS, mainly in patients with IBS and FD, and in those patients using antidepressants. The patients with concomitant obesity/overweight and FGIDs have increased risk for anxiety and depression.

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Disclosure of Interest: None declared

OP346 GAS SWALLOW DURING MEALS IN PATIENTS WITH UPPER ABDOMINAL SYMPTOMS

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Introduction: Previous studies using ultrafast CT-scans have shown that in each swallow of a 10 ml liquid bolus, 8-32 ml of gas can be ingested. In patients with aerophagia, the association between swallowed gas and belching have been addressed under laboratory conditions. However, and despite gas-related digestive symptoms are common, our knowledge of volume and number of meal-related gas swallows in humans performed during a normal day is unknown.
Aims & Methods
Aim: To characterize the number of meal-related swallows and the proportion of gas containing swallows during a 24-h period in a group of patients with excessive belching and a group of patients without abdominal symptoms.
Methods: A 24-h pH-impedance monitoring was performed in 6 patients complaining of excessive belching. As control group, 11 patients studied for chronic cough and without digestive symptoms or reflux in the pH-impedance study were included. In each patient we counted the number of liquid swallows, gas swallows and mixed gas/liquid swallows during meals, as oro-caudal drops and increments of impedance over 50% from baseline, respectively. During the study, patients were asked to follow with their daily routine and customary meals, without any specific limitation. Data is expressed as mean ± standard desviation.
Results: Control patients expended 75 ± 26 min to eat along the 24-h study period, distributed in 4 ± 1 meals. During this time, a total of 74 ± 28 swallows were detected by impedance, with the majority of them being mixed gas/liquid swallows (94 ± 10%). Pure liquid swallows or pure gaseous swallows were rarely detected (2 ± 1% and 4 ± 5%, respectively). Patients with frequent belching expended a similar length of the day to eat (83 ± 24 min; p = 0.514 vs. controls), distributed in a somewhat greater number of meals (5 ± 1 meals; p = 0.038 vs. controls). In contrast to controls, and despite a similar length of time expended to eat, patients with frequent belching performed a significantly greater number of swallows during meals along the day (124 ± 37 swallows; p = 0.004 vs controls), due to a greater frequency of swallows while eating (15 ± 4 swallows vs 10 ± 3 swallows/10 min, belchers vs controls, respectively; p = 0.006). Similar to the control group, most swallows were mixed gas/liquid swallows (89 ± 6%), with only a minority of pure liquid or gaseous swallows (5 ± 4% and 6 ± 2% swallows, respectively). Consequently, patients with frequent belching performed during meals a significantly greater number of gas-containing swallows during 24 h (116 ± 34 swallows) than the control group (69 ± 26 gaseous swallows; p = 0.003 vs controls).
Conclusion: Under normal customary conditions, relevant volumes of gas can be ingested during meals along the day. In patients complaining of excessive belching, gas ingestion is greater, due to a different pattern of food swallow,

with a greater rate of swallows per time. This specific eating behaviour could play a pathophysiological role in gas-related symptoms, and opens the possibility to new therapeutic approaches in patients with gas-related symptoms.
Disclosure of Interest: E. N. Caballero: None declared, C. Julia: None declared, J. Serra Financial support for research: ALMIRALL, Lecture fee(s): NORGINE, Consultancy: RECKITT BENCKISER

OP347 DISTENSIBILITY OF THE ESOPHAGO-GASTRIC JUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS: A STUDY WITH THE FUNCTIONAL LUMEN IMAGING PROBE

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Introduction: Manometry is widely used for evaluating the function of the esophagus, including the esophago-gastric junction (EGJ). However, studies suggest that distensibility is a better parameter than pressure for assessment of EGJ function. The functional lumen imaging probe (FLIP) is a novel method that provides detailed information on geometric properties of the gastrointestinal sphincter function during distension. Systemic sclerosis (SSc) is a connective tissue disease which causes fibrosis and atrophy of smooth muscle cells. In 90% of patients with SSc the esophagus is affected often resulting in severe gastro-esophageal reflux and dysphagia.
Aims & Methods
Aim: To provide comprehensive evaluation of EGJ function by means of FLIP in a well characterized group of patients with smooth muscle dysfunction caused by SSc.
Method: We included 11 patients with SSc (10 women, median age 58, [range 35-72], duration of disease 1- 20 years) referred because of upper GI symptoms. After doing upper endoscopy the EGJ was distended with FLIP. Standard esophageal manometry had been performed in all patients. Patients were compared to 9 healthy volunteers (HVs) with no gastrointestinal symptoms. The FLIP recorded pressure and minimum diameter along the EGJ, which were used for the distensibility analysis.
Results: The FLIP procedure was successful in all patients. The pressure and diameter increased during the inflation in both groups. At the maximum distension volume 50ml, the pressure in the HVs was higher than in the SSc (49.5 ± 18.8 mmHg for HVs and 38.2 ± 16.1 mmHg for SSc, $p = 0.02$) whereas the diameter was largest in the SSc group (14.8 ± 4.5 mm for HVs and 21.9 ± 4.8 mm for SSc, $p = 0.004$) (Figure 1). The pressure strain elastic modulus (*Ep = (Pressure at volume 50ml - Pressure at volume 0ml)/ (Diameter at volume 50ml -Diameter at volume 0ml) * Diameter at volume 50ml*) was significantly reduced in SSc (3.4 ± 1.7 kPa in HVs and 1.7 ± 1.1 kPa, $p = 0.006$), indicating a more distensible EGJ in SSc patients. There was no correlation between duration of disease and Ep (rho = 0.32 and $p = 0.33$).
Conclusion: FLIP is an easy-to-perform method for assessment of EGJ function. Patients with SSc and dysphagia or reflux have significantly higher distensibility of the EGJ than healthy volunteers. Distensible of the EGJ is, however, not associated with duration of the disease.
Disclosure of Interest: L. Fynne: None declared, D. Liao: None declared, C. Lottrup: None declared, K. Aksglaede: None declared, H. Gregersen Consultancy: Consultancy with the manufacture of FLIP, Crospon, N. C. Bjerregaard: None declared, A. Drewes: None declared, K. Krogh: None declared

OP348 VELUSETRAG IMPROVES GASTRIC EMPTYING TIME IN SUBJECTS WITH DIABETIC OR IDIOPATHIC GASTROPARESIS

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Introduction: Patients with diabetic or idiopathic gastroparesis have delayed gastric emptying (GE) time. Velusetrag (VEL) is an oral, once-daily, investigational, highly-selective 5-HT4 agonist that has demonstrated prokinetic effects in the lower gastrointestinal tract in subjects with chronic idiopathic constipation. The current study evaluated VEL prokinetic effects in the upper gastrointestinal tract by assessing GE time in both diabetic and idiopathic gastroparesis subjects.
Aims & Methods: Subjects with gastroparesis were screened for increased GE time ($t_{1/2} > 160$ mins), symptoms consistent with gastroparesis for ≥ 3 months, Gastroparesis Cardinal Symptom Index score between 2 and 4 inclusive, and HbA1c $< 10\%$ (diabetics). Subjects were randomised in an incomplete block, 3-period, cross-over design to 3 of 4 treatments, VEL 5-, 15- and 30-mg and placebo stratified for diabetic or idiopathic gastroparesis. In all 3 treatment periods, subjects performed a 6-hr ^{13}C-octanoate breath test of GE time on Day -1 (baseline) and after the 7th dose. Efficacy was assessed by the change from baseline in GE $t_{1/2}$. All efficacy endpoints were evaluated using mixed-effect models with a covariate for baseline GE.
Results: 34 subjects were randomised; n = 26 (placebo), 26 (VEL 5-mg), 25 (VEL 15-mg), and 25 (VEL 30-mg). The study population was 68% female, 82% Caucasian, and 53% diabetic, with mean (SD) age of 46 (10.3) yrs and baseline GE $t_{1/2}$ mean (SD) [range]: 206 min (91.1) [107-640]. The proportion of subjects with at least a 20% reduction in GE $t_{1/2}$ was 5% for placebo and 26%, 20%, 52% for VEL 5-, 15-, and 30-mg, respectively. Statistical significance was observed in the 30-mg dose group ($p = 0.002$). The mean (SD) change from baseline of GE $t_{1/2}$ was -13 (14.9) mins for placebo and -35 (14.6), -34 (15.5), and -52 (15.2) mins for VEL 5-, 15-, and 30-mg, respectively. Similar treatment effects were observed with VEL in both diabetic and idiopathic subjects. A pre-specified analysis of subjects with delayed GE time at baseline (GE between 180-350 mins excluding relatively normal and extremely abnormal GE times) revealed a placebo-adjusted mean (SD) reduction [% improvement] from baseline in VEL-treated subjects of -76 (41.9) [-33%], -73 (50.4) [-28%] and -85 (40.9) [-37%] mins for VEL 5-, 15- and 30-mg, respectively. All doses of VEL were generally well tolerated. The most common adverse events were diarrhoea (n = 16) and headache (n = 6). No on-treatment serious adverse events were observed.
Conclusion: Velusetrag treatment was generally well tolerated and resulted in a statistically significant improvement in GE time at the 30mg dose in subjects with diabetic or idiopathic gastroparesis. Future studies will assess the translation of these pharmacodynamics effects into symptomatic improvement.
Disclosure of Interest: A. Ahn Shareholder: Stocks received, Conflict with: Employee, C. Barnes: None declared, D. Shaywitz Shareholder: Received stock, Conflict with: Employee at time of conduct, M. Grimaldi Conflict with: Employee, D. Canafax Shareholder: Received stocks, Conflict with: Employee

OP349 COMPARATIVE QUANTITATIVE ASSESSMENT OF GLOBAL SMALL BOWEL MOTILITY USING MAGNETIC RESONANCE IMAGING IN CHRONIC INTESTINAL PSEUDO-OBSTRUCTION AND HEALTHY CONTROLS

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Introduction: Chronic Intestinal Pseudo-Obstruction (CIPO) is a rare but life-threatening disorder characterised by failure of the intestinal tract to propel its contents. In this study, we compare resting and stimulated global small bowel motility in Chronic Intestinal Pseudo-Obstruction (CIPO) patients and normal controls using software quantification of cine MRI.
Aims & Methods: Twenty healthy volunteers (mean age 28, range 22-48, 14 Male) and 11 CIPO patients (7 male, mean age 47, range 19-90) were recruited prospectively and underwent 3T MRI enterography including a dedicated motility sequence (3D Balanced Turbo Field Echo, 2.5x2.5x10mm voxel size, FA 20, TE = 1.7ms, TR = 3.5ms) to capture global small bowel motility over a 20 second breath-hold. All CIPO patients stopped taking motility influencing medication (laxatives, antiemetics, opioids etc.) for 5 days prior to their scan.
11 controls and 7 CIPO patients in addition underwent a randomized placebo-controlled crossover study of either IV 0.5 mg neostigmine (Mercury Pharma, UK) or saline with motility MR imaging repeated at a mean of 3 weeks. Motility was quantified in regions of interest (placed by an experienced radiologist blind to the motility data) to encompass the whole small bowel volume using a validated, post-processing technique to give a global motility index in arbitrary units (AU)[1,2]. Baseline and stimulated motility was compared using Wilcoxon rank sum paired T-tests.
Results: Baseline small bowel motility was significantly lower in CIPO patients (0.25AU) compared to controls (0.35AU), $p < 0.001$. Motility in both groups significantly increased after neostigmine against placebo although compared to baseline, response was greater in the CIPO group (mean 38%) than controls (mean 13.5%) $p = 0.0015$.
Conclusion: Global small bowel motility in CIPO patients is significantly lower than in controls and the relative response to the pro-kinetic agent neostigmine appears exaggerated. Software quantified bowel motility using cine MRI appears to be a useful tool and, in combination with a pharmacological probe, could represent a safe and cost-effective approach for the investigation of enteric dysmotility.

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Disclosure of Interest: A. Menys Shareholder: Motilent Ltd, Directorship(s): Motilent Ltd, S. Butt: None declared, A. Emmanuel : None declared, A. Plumb : None declared, A. Fikree: None declared, C. Knowles: None declared, D. Atkinson: None declared, N. Zarate: None declared, S. Taylor: None declared

OP350 EFFECT OF AMINO ACIDS ON GASTRIC EMPTYING AND SATIATION HORMONES IN LEAN AND OBESE SUBJECTS

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Introduction: Changes in gut motor and hormonal function contribute to the eating-inhibitory and glucose-lowering effects of protein. The effect of amino acids, the digestive products of protein, on gastrointestinal function, hormone

release, and glycemia has not been investigated comprehensively. The aim of this study was to investigate the effect of L-tryptophan (L-trp) and L-leucine (L-leu) on gastric emptying, gastrointestinal satiation hormones and appetite perceptions in lean and obese subjects.
Aims & Methods: The study was conducted as a randomized, placebo-controlled, parallel-group trial. A total of 10 lean (5 men and 5 women) and 10 obese (BMI > 30), non-diabetic participants (5 men and 5 women) took part in the study. Subjects received intragastric infusions of different physiological concentrations of L-trp (0.52 g and 1.56 g) and L-leu (1.56 g). Control treatment was tap water infusion. The test solutions were labelled with ^{13}C-sodium acetate for determination of gastric emptying rates. To investigate a second gut motor function in response to the amino acids, gallbladder contraction was measured by ultrasound. Plasma samples were collected for glucagon-like peptide-1 (GLP-1), peptide tyrosine tyrosine (PYY) and cholecystokinin (CCK), insulin and glucose analysis. Visual analogue scales (VAS) were used for appetite measurements.
Results: L-trp dose-dependently stimulated gallbladder contraction and CCK release ($p < 0.01$). L-leu did neither stimulate CCK release nor gallbladder contraction. Of note, the high dose of L-trp slowed gastric emptying ($p < 0.05$) in lean subjects. In obese subjects, gastric emptying rates were significantly ($p < 0.01$) delayed compared to lean controls. Both amino acids stimulated insulin release ($p < 0.01$, respectively) in obese, but not in lean subjects; fasting insulin was increased in obese documenting insulin resistance. Appetite ratings were not changed by the amino acid infusions in both subject groups. GLP-1 and PYY measurements are in process.
Conclusion: Low caloric intragastric loads of L-trp affect gastric emptying and CCK release. The increase in CCK may play a role in the observed delay of gastric emptying rates, but was not sufficient to modulate appetite sensations. Both L-trp and L-leu didn't stimulate insulin release in lean subjects confirming that amino acids can only stimulate insulin secretion in the presence of glucose. In contrast, in obese both L-trp and L-leu induced insulin secretion suggesting a disturbed metabolic pathway.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 15:45–17:15

ABSTRACTS ON FIRE: ESD IN 2015 – EAST-WEST PERSPECTIVES – HOTSPOT

OP351 TECHNICAL FEASIBILITY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECTAL TUMOR WITH INVOLVEMENT TO THE ANORECTAL JUNCTION, COMPARE WITH THE RECTAL TUMOR WITHOUT INVOLVEMENT TO THE ANORECTAL JUNCTION

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Introduction: Endoscopic submucosal dissection (ESD) has been developed for en-bloc resection of mucosal gastric neoplasms. ESD for colorectal lesions is more difficult than for the gastric lesions because of anatomical feature of the colon and rectum. Especially, ESD for rectal lesions with involvement to the anorectal junction is more difficult than rectal lesion without involvement to the anorectal junction because of narrower lumen, comorbidity of hemorrhoid, fibrosis of submucosal layer, longer procedure time, and increased risk of bleeding. The curability by ESD brings large benefit because preservation of an anal function is closely related to quality of life.
Aims & Methods: The aim of this retrospective study was to investigate the clinical outcome and feasibility of ESD with involvement to the anorectal junction compare with ESD without involvement to the anorectal junction. ESD of 153 lower rectal lesion were performed under conscious sedation in our institute from January 2004 to December 2014. A total 37 lesions with involvement to the anorectal junction (with ARJ) and 116 lesions without involvement to the anorectal junction (without ARJ) treated with ESD. ESD procedure for rectal lesions with involvement to the anorectal junction: at first we inject lidocaine to squamous epithelium of anorectal junction for local anesthesia, next inject sodium hyarulonate acid to the submucosal layer of rectun. Circumferential incision and submucosal dissection was performed by Dual knife with CO2 insufflation.
Results: No statistically significant differences were noted between with ARJ and without ARJ for median age (70years old with ARJ, 67years old without ARJ), male/female ratio (19/18 with ARJ, 60/56 without ARJ), en-block resection rate (100% with ARJ, 98% witout ARJ), median hospital days (4days with ARJ, 4days without ARJ), perforation (0%with ARJ, 0% without ARJ) and local recurrence and residual tumor (0% with ARJ, 0% without ARJ). Statistically significant differences between the two groups were observed for mean tumor size (45.8mm with ARJ versus 28.7mm without ARJ; $p < 0.05$), mean time of procedure (86.5minutes with ARJ versus 33.8minutes without ARJ; $p < 0.05$), postoperative bleeding (27% with ARJ versus 8% without ARJ; $p < 0.05$) and postoperative pain (27% with ARJ versus 0% without ARJ; $p < 0.01$). The pain could be controled with NSAIDS or acetaminophen administration. We suppose that reasons for difficulty of ESD with ARJ are past history of treatment for hemorrhoid, fibrosis of submucosal layer due to prolapse of tumors and others. In both group, anal function of patients is preserved.
Conclusion: ESD of rectal lesions with ARJ appears to be a feasible and curative treatment, even though it is associated with a higher adverse event rate, higher degree of technical difficulty, and longer procedure time. Considering the potential poor quality-of-life after anorectal surgery, ESD for anorectal lesions becomes an attractive alternative.
Disclosure of Interest: None declared

OP353 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR EARLY GASTRIC CANCE(EGC): A PROSPECTIVE STUDY OF ITS EXPANDED INDICATION

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Introduction: ESD has been widely used as a minimally invasive treatment for EGC. Long-term outcomes such as survival rate would be the final endpoints, however it is not fully reported prospectively. The aim of this study was to investigate long-term outcomes of ESD for EGC in a study of its expanded criteria.
Aims & Methods: We designed a prospective study in which ESD was applied in patients with differentiated-type EGC up to 30 mm in diameter regardless of ulceration or above 30 mm without ulceration, but definite signs of submucosal invasion. According to final diagnosis after ESD, EGC below considered to have hardly metastasis, were enrolled and follow up and otherwise were advised to be operated on additionally; differentiated-type mucosal EGC above 30 mm in diameter without ulceration, and EGC up to 30 mm with ulceration and/or minute submucosal invasion. The protocol was approved by the ethics committee of our hospital. Followed-up endoscopic examinations are performed 6 months later, and then every six months.
Results: From April 2006 to March 2013, ESD was performed in 1070 lesions. En bloc resection was achieved in 1060 lesions (99%). Among them 950 were enrolled (guideline (less than 2cm without ulceration) group; 642, expanded criteria group; 308) and were followed up (median 45months (range 15 to 96)). R0 (margin-free) resection was achieved in 629 (98%), and 287 (93%) cases, respectively. Perforation and bleeding were encountered in 59 (5.6%) and 40 (3.8%) lesions, but there was no ESD-related death. During the follow-up, one patient (0.13%) in the expanded criteria group died from distant metastasis of the EGC and 55 patients (7%) died of some causes unrelated to EGC. Five-year overall survival rates were 97.9% and 94.7%, respectively. Metachronous multiple cancers were detected in 126 (16%) patients. Among the 120 patients with lesions not fulfilled the expanded criteria, 65 were underwent additional surgery, and 7 (11%) had LN metastasis and 7 residual lesions were found. The remaining 55 patients refused additional surgery and were followed up; 9 (16%) had local recurrence and 2 (4%) died from gastric cancer.
Conclusion: This study indicates favorable long-term outcomes of ESD for patients of not only guideline group but also of expanded group. The expanded criteria would be useful in clinical settings.
Disclosure of Interest: None declared

OP354 LONG-TERM OUTCOME AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER: ACCORDING TO FINAL PATHOLOGICAL RESULTS

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Introduction: Endoscopic submucosal dissection (ESD) is an effective treatment for selected patients with early gastric cancer (EGC). The purpose of this study was to examine the short-term and long-term outcomes after ESD in patients EGC according to the pathological extent.
Aims & Methods: ESD were performed in 599 patients with 611 EGC from January 2005 to January 2015. We performed a retrospective analysis of the medical records of these patients. The tumors were classified by pathological severity based on absolute indication (AI), expanded indication (EI), expanded indication with undifferentiated histology (EI(U), mucosal cancer, ulcer(-), 20mm) or beyond expanded indication (BEI). The therapeutic outcomes among the four groups were analyzed. After ESD, 40 patients underwent surgery immediately and 135 patients followed up less than 6 months. These 175 patients were excluded for the long-term outcome study.
Results: Number of patients was 447, 91, 19 and 54 in the AI-EGC, EI-EGC, EI(U)-EGC and BEI-EGC groups. The complete resection rates of EGC were 97.8%, 86.4%, 89.5% and 46.3% in the AI-EGC, EI-EGC, EI(U)-EGC and BEI-EGC groups, respectively ($P = 0.000$). *En bloc* resection rates were 99.1%, 98.9%, 100% and 98.1% in the AI-EGC, EI-EGC, EI(U)-EGC and BEI-EGC groups ($P = 0.833$). The 5-year tumor recurrence rates were 4%, 8.1%, 28.6% and 6.7% in the AI-EGC, EI-EGC, EI(U)-EGC and BEI-EGC groups ($P = 0.000$). The 5-year disease-free survival rates were 93.2%, 87.0%, 53.3% and 88.9% in the AI-EGC, EI-EGC, EI(U)-EGC and BEI-EGC groups ($P =$

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Characteristics, n (%)	Total(n = 611)	AI-EGC(n = 447)	EI(n = 91)	BEI(n = 54)	EI(U)(n = 19)	p
Age (year)	67.9 9.6	67.5	69.7	69.3	68.6	0.146
Male	432 (75.7%)	326 (77.4%)	60 (73.2%)	35 (68.6%)	11 (64.7%)	0.325
Location						0.001
Upper	17 (2.8%)	10 (2.2%)	1 (1.2%)	6 (11.1%)	0	
Middle	176 (28.8%)	119 (26.6%)	29 (31.9%)	22 (40.7%)	6 (31.6%)	
Lower	418 (68.2%)	318 (71.1%)	61 (67%)	26 (48.1%)	13 (68.4%)	
Tumor size > 30mm	12 (2.0%)	0	8 (8.8%)	4 (7.4%)	0	0.000
ulcer	35 (5.7%)	0	26 (28.6%)	9 (16.6%)	0	0.000
Pathologic type						0.000
WD	402 (65.8%)	326 (78.9%)	54 (59.3%)	22 (40.7%)	0	
MD	178 (29.1%)	121 (27.1%)	37 (40.7%)	20 (37.0%)	0	
PD	25 (4.1%)	0	0	8 (14.8%)	17 (89.5%)	
SRC	5 (0.8%)	0	0	3 (5.6%)	2 (10.5%)	
Lymphovascular invastion	24 (3.9%)	0	6 (6.6%)	17 (31.5%)	1 (5.3%)	0.000
Depth of invasion						0.000
SM1	33 (5.4%)	0	28 (30.8%)	5 (9.3%)	0	
SM2	40 (6.5%)	0	0	40 (74.1%)	0	
Cancer recurrence in 5yrears	22 (5.0%)	14(63.6%)	5 (22.7%)	1 (4.5%)	2 (9.0%)	

0.082). The risk factors related to recurrence were undifferentiated histology (p = 0.048) and tumor size (> 3cm, p = 0.01).
Conclusion: ESD was effective and safe in treating AI-EGC and EI-EGC. But, EI(U)-ECG after ESD should be considered surgical treatment because of high recurrence rate.
Disclosure of Interest: None declared

OP355 HIGH-PRESSURE INJECTION OF GLYCEROL WITH HYBRIDKNIFE FOR ESD INCREASES THE EASE AND SPEED OF THE PROCEDURE: A RANDOMIZED STUDY IN PIGS AND FIRST USE IN HUMAN

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Introduction: The HybridKnife water-jet system (ERBE, Germany) has shown to increase dissection speed and decrease the risk of perforation during endoscopic submucosal dissection (ESD). Glycerol is a viscous, long-lasting solution preferentially used by Japanese experts and has shown an increase of the speed of dissection in a non-randomized control trial in pigs. We report here the results of a randomized control trial of ESD with HybridKnife injecting of either a glycerol mixture or normal saline and the first results of human use.
Aims & Methods: 20 gastric dissections of a virtual lesion (10 per group) with hybridknife were performed by 2 operators blinded of the injected solution (Glycerol or NaCl 0.9%) on 7 anaesthetised domestic mini-pigs. Dissection speed (mm^2/min), size of the specimen (mm^2), duration (min), en bloc resection rate, bleeding and perforation rates were prospectively recorded. An evaluation of operator comfort and perception of safety (dissection score) was performed using a visual analogue scale (0 = the worst, 10 = the best). In parallel; we performed a total of 36 ESD for precancerous or superficial cancerous lesions in humans. The setting of the Erbejet 2 varied from 12 to 15 bars in humans and between 30 to 35 bars in pigs due to the thickness of the pig gastric mucosae. In our experience we always chose the minimum pressure that allowed a good lifting of the lesion to avoid bleeding during the injection phase.
Results: In the randomized study in pigs, high-pressure injection of the glycerol mixture and dissection with the HybridKnife was feasible without complication. Dissection was significantly more rapid (1,38-fold) with glycerol injection than normal saline injection (28.94 vs. 20.91 mm^2/min; p = 0.035). The dissection score was significantly higher in the glycerol group than in the normal saline group (7.3 vs. 4.7; p = 0.006). No difference was observed in the rates of en bloc resection (100%), bleeding (20%) and perforation (0%); in the size of specimen (1166 vs 1080 mm^2 p = 0.55) and the duration of the procedure (42.6 vs 53.6 min p = 0.07). The injection system has failed several times due to the carbonization of the knife but with the same frequency in the 2 groups.
In parallel between September 2013 and March 2015 we performed 36 ESD for precancerous or superficial cancerous lesions: 8 oesophageal, 5 gastric and 23 rectal lesions. The en bloc resection rate, R0 resection rate and curative resection rate were respectively 100% (36/36) and 91.7% (33/36) and 86.1% (31/36). High-pressure injection of glycerol with hybridknife was always feasible with a pression between 12 and 15 bars. The injection system failed several times due to the carbonization and close regular cleaning of the knife allowed a longer life of the device. No complication or pathological damage occurred with high-pressure glycerol injection.
Conclusion: High-pressure jet injection of glycerol with HybridKnife for ESD is feasible and increases the speed and ease of the procedure compared with use of normal saline. This is the first study confirming the feasibility of injecting a viscous solution (glycerol) using the ERBE HybridKnife system in human ESD.

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Disclosure of Interest: None declared

OP356 ESD VERSUS EMR IN ESOPHAGEAL ADENOCARCINOMA (EAC) - REPORT OF A GERMAN CENTER

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Introduction: Endoscopic mucosal resection (EMR) is the standard treatment for superficial esophageal cancer but in larger lesions it may lead to piecemeal or incomplete resection. Endoscopic submucosal dissection (ESD) allows the en-bloc resection of a lesion regardless of its size, which enables histopathological assessment of R0 resection and may reduce the risk of recurrence. Studies from Asia have demonstrated the superiority of ESD in ESCC but in EAC data on ESD is rare.
Aims & Methods
Aim: To evaluate ESD and EMR in EAC.
Methods: Between 02/2003 and 12/2014 162 early esophageal adenocarcinomas were treated with EMR or ESD in a German tertiary referral center. ESD data was recorded prospectively, EMR results were analysed retrospectively.
Results: EMR: 54 resections in 37 patients, en-bloc-resections 16/54 (29.6%), R0 resections 13/54 (24.1%), R1 resections 30/54 (55.5%; R1 horizontal margin = 24, R1vertical margin = 2, R1 horizontal and vertical margin = 4), Rx 11/54 (20.4%). Residual or recurrent tumor in 17/54 (31.5%). Subgroup Barrett esophagus > M3: 35 EMRs in 23 patients, en-bloc-resections 9/35 (25.7%), R0 resections 9/35 (25.7%). Subgroup Barrett esophagus ≤ M3: 19 EMRs in 14 patients, en-bloc-resections 7/19 (36.8%), R0 resections 4/19 (21.1%). Complications: Stenosis 5/54 (9.3%), bleeding 3/54 (5.5%).
ESD: 108 resections in 107 patients, en-bloc resections 104/108 (96.3%), R0 resections 90/108 (83.3%), R1 resections 18/108 (16.7%, horizontal margin = 11, vertical margin = 3, dissection stopped = 4). No recurrent disease after curative resection so far (in 2 patients with R1 resection at the horizontal margin operation was recommended but not performed and local recurrence occurred 3

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	EMR			ESD		
	n	en-bloc-resections	R0-resections	n	en-bloc-resections	R0-resections
EAC total	54	16/54 (29,6%)	13/54 (24,1%)	108	104/108 (96,3%)	90/108 (83,3%)
EAC withinBarrett's > M3	35	9/35(25,7%)	9/35(25,7%)	31	28/31 (90.3%)	21/31 (67,7%)
EAC within Barrett's ≤ M3	19	7/19(36,8%)	4/19(21,1%)	77	76/77 (98,7%)	69/77(89,6%)

months after ESD). Subgroup Barrett esophagus > M3: n = 31, en-bloc-resections 28/31 (90.3%), R0 resections 21/31(67.7%). Subgroup Barrett esophagus ≤ M3: n = 77, en-bloc resections 76/77 (98.7%), R0-resections 69/77 (89.6%). Complications: Stenosis in 12/108 (11.1%) (patients with ESD > 75% circumference), bleeding 1/108 (0.9%).
Conclusion: Our results show the advantage of ESD in terms of en-bloc and R0-resection rate and risk of recurrence. ESD should be considered the treatment of choice in early EAC when en bloc resection seems impossible with other resection techniques.
Disclosure of Interest: None declared

OP357 ENDOSCOPIC SUBMUCOSAL DISSECTION VERSUS LAPAROSCOPIC COLECTOMY FOR EARLY COLONIC NEOPLASM: AN INTERIM ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: Laparoscopic colectomy (LC) is a widely accepted treatment option for early colorectal neoplasms that are not amenable to *en bloc* endoscopic resection with conventional polypectomy. Endoscopic submucosal dissection (ESD) has emerged as a novel endoscopic procedure that enables resection of large colorectal tumors *en bloc* with low reported complication rate. To date, no randomized controlled trial (RCT) can be found in the literature comparing LC and ESD for early colorectal neoplasms. We report interim analysis of a RCT comparing the short-term clinical outcomes of the two approaches.
Aims & Methods: Consecutive patients diagnosed with early colorectal neoplasms > 2 and < 5 cm in size in the colon without endoscopic signs of massive submucosal invasion were randomized to receive either ESD or LC. Patients in the LC arm were managed using an enhanced recovery protocol. The primary endpoint of this study was short-term morbidity within 30 days after ESD/LC. Secondary outcomes included procedure time, post-ESD/LC recovery, analgesic requirement, hospital stay, and serial C-reactive protein (CRP) levels. Data were analyzed according to the intention-to-treat principle. This study was registered with the ClinicalTrials.gov, number NCT01112046.
Results: Between June 2010 and May 2015, 40 patients were randomized (20 to ESD, 20 to LC). Baseline characteristics did not differ between the two groups. The mean size of the lesions was 3.0 ± 0.9 cm in the ESD group and 2.9 ± 1.0 cm in the LC group ($P = 0.545$). Two lesions in the ESD group and one lesion in the LC group were early T1 adenocarcinoma, while the rest were adenomas. Nineteen out of twenty patients (95%) in the ESD group could achieve an *en bloc* resection. The short-term morbidity was lower in the ESD group than in the LC group (5% *vs.* 20%), but the difference did not reach a statistical significance ($P = 0.342$). The only morbidity in the ESD group was an intraprocedural perforation, which was successfully managed with endoscopic clipping. Comparing with the LC group, the ESD group had significantly shorter procedure time (97.5 *vs.* 162.5 min; $P < 0.001$), earlier time to resume full diet (2 *vs.* 3 days; $P < 0.001$), earlier time to full ambulation (0 *vs.* 2 days; $P < 0.001$), and shorter median hospital stay (3 *vs.* 4 days; $P = 0.001$). No patient in the ESD group required any analgesia, while the LC group required a median dose of 200 mg (range, 0-750 mg) of tramadol as postoperative analgesia. Median CRP level was significantly lower in the ESD group than in the LC group at 2 hours (1.0 *vs.* 2.4 mg/L; $P = 0.040$), 8 hours (3.3 *vs.* 12.9 mg/L; $P = 0.006$), 24 hours (4.2 *vs.* 72.8 mg/L; $P < 0.001$), and 48 hours (5.1 *vs.* 73.9 mg/L; $P < 0.001$) after the procedure. The median follow-up duration in the ESD group was 10 months (range, 4-43 months), and no recurrence was detected on regular endoscopic surveillance.
Conclusion: This interim analysis suggested that ESD was associated with better short-term clinical outcomes in terms of earlier recovery, lower analgesic requirement, shorter hospital stay, and less stress response when compared with LC for early colorectal neoplasms. Short-term morbidity was lower in the ESD group than in the LC group, but the difference did not reach a statistical significance. A larger trial size is required.
Disclosure of Interest: None declared

OP358 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION IN A EUROPEAN CENTER

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Introduction: Endoscopic submucosal dissection (ESD) is an effective method for en bloc removal of large colorectal tumors in Japan but this technique is not yet widely established in western countries.
Aims & Methods: The aim herein was to report the experience of implementing colorectal ESD in a European center.
Between January 2014 and April 2015 were 287 patients with colorectal lesions larger than 2 cm referred to our center. All patients underwent colonoscopy and 101 patients were judged to be suitable for ESD (colon 48 and rectum 53 cases). The ESD procedures were standardized including consistent use of hood and flush knife. 10 patients had advanced macroscopic cancer and five cases were considered too difficult for ESD and these 15 patients were sent for surgery. The remaining 171 patients underwent endoscopic mucosa resection. Four cases of invasive cancer underwent ESD due to high co-morbidity excluding surgical intervention or as an unexpected finding. 53% of all ESD cases of which 83% and 17% were located in the rectum and sigmoid colon, respectively, were performed as outpatient procedures without hospitalization.
Results: The median age of patients undergoing ESD was 72 years (range 20-95). The median tumor size was 40 mm (range 21-105 mm). En bloc resection rate was 73% and a snare was used after starting the ESD procedure due difficulties or to time-limitation in 23%. In only four cases were the ESD resections incomplete. R0 resection rate was 61% and in 33% was it difficult for the pathologist to judge the resection margins and the remaining 6% were determined R1 resections. All four invasive carcinomas were R0 resections. Five perforations occurred amounting to a perforation rate of 6.1%. Two patients with perforation could be managed conservatively. Three patients with perforation underwent emergency surgery followed by an uneventful recovery. No peroperativ bleeding occurred having any impact on the treatment. Two cases (2%) of postoperative bleeding were managed conservatively but prolonged hospital stay.
Conclusion: This study represents the largest material on colorectal ESD in western countries in the literature and our results confirm that ESD is an effective method for en bloc resection of large colorectal adenomas and early cancers. This study demonstrates that implementation of colorectal ESD is feasible in Europe after proper training, careful patient selection and standardization of the ESD procedure.
Disclosure of Interest: None declared

OP359 ENDOSCOPIC SUBMUCOSAL DISSECTION OF COLORECTAL EPITHELIAL NEOPLASMS USING THE CLUTCH CUTTER IN 220 CONSECUTIVE CASES

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Introduction: The Clutch Cutter (CC) was developed to reduce the risk of complications related to endoscopic submucosal dissection (ESD) using conventional knives. The CC is able to grasp and coagulate and/or incise the targeted tissue using electrosurgical current, like a biopsy technique.
Aims & Methods: The aim of this study was to evaluate the efficacy and safety of ESD using the CC for colorectal epithelial neoplasms. From June 2007 to April 2015, 220 consecutive patients (121 men, 99 women; mean age 69 years, range 42-89) with a diagnosis of adenoma or intramucosal or superficial submucosal cancer without lymph node involvement, that had been confirmed by preliminary endoscopy, EUS, and endoscopic biopsies, were enrolled in this prospective study. The CC was used for all steps of ESD (mucosal incision, submucosal dissection, and hemostatic treatment). The therapeutic efficacy and safety were assessed.
Results: The mean size of the colorectal epithelial neoplasms and resected specimens was 26.7 ± 12.8 mm and 36.1 ± 13.3 mm, respectively. The mean operating time was 89.4 ± 68.9 minutes. The rate of en-bloc resection was 99.1% (218/220), and en-bloc resection with tumor-free lateral/basal margins (R0 resection) was 86.8% (191/220), respectively. The R0 resection rates according to histologic type, tumor size and location were 90.6% (87/96) in adenocarcinoma, 83.9% (104/124) in adenoma; 89.7% (70/78) in 0-20 mm, 86.4% (102/118) in 21-40 mm, 79.2% (19/24) in 41- mm ; 85.5% (53/62) in the rectum, 89.4% (42/47) in the sigmoid colon, 93.3% (14/15) in the descending colon, 90.5% (19/21) in the transverse colon, 78.3% (36/46) in the ascending colon and 93.1% (27/29) in the cecum. The mean operating time according to histologic type, tumor size and location were 85.3 ± 68.6 minutes in adenocarcinoma, 92.5 ± 69.4 minutes in adenoma; 64.9 ± 44.8 minutes in 0-20 mm, 90.3 ± 62.8 minutes in 21-40 mm, 164.1 ± 103.3 minutes in 41- mm ; 76.1 ± 67.7 minutes in the rectum, 80.5 ± 69.4 minutes in the sigmoid colon, 102.8 ± 74.5 minutes in the descending colon, 105.8 ± 71.8 minutes in the transverse colon, 94.8 ± 63.8 minutes in the ascending colon and 104.6 ± 72.1 minutes in the cecum. Perforation occurred in four cases (1.8%), which were managed with conservative treatment including endoscopic closure of the perforation. Post ESD bleeding occurred in 5 cases (2.3%), which were successfully treated by endoscopic hemostatic treatment.
Conclusion: ESD using CC is a safe and technically efficient method for resecting colorectal epithelial neoplasms.

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Disclosure of Interest: K. Akahoshi Conflict with: Patent, Y. Motomura: None declared, M. Kubokawa: None declared, J. Gibo: None declared, N. Kinoshita: None declared, S. Osada: None declared, K. Tokumaru: None declared, T. Hosokawa: None declared, R. Utsunomiya: None declared, A. Miyagaki: None declared, T. Sato: None declared, K. Miyamoto: None declared

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30
MANAGEMENT OF NON-OBSTRUCTIVE DYSPHAGIA – ROOM 7.1

OP360 PERORAL ENDOSCOPIC MYOTOMY FOR ESOPHAGEAL ACHALASIA: OUTCOMES OF THE FIRST 37 PATIENTS IN TURKEY

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Introduction: Per oral endoscopic myotomy (POEM) is a minimally invasive endoscopic treatment option for achalasia patients that has been performed since 2009 and is spreading rapidly around the World. POEM is a less invasive endoscopic approach than Heller myotomy, and the short-term data demonstrate that it offers excellent outcomes that appear to rival those of the laparoscopic Heller myotomy. We present our results of POEM which are the first experiences of Turkey.

Aims & Methods: Between May 2014 and March 2015, 37 patients with achalasia whose complaints recurred after pneumatic balloon dilatation underwent POEM. The procedure was performed at the endoscopy unit in the gastroenterology clinic under general anesthesia by an endoscopist who was experienced at endoscopic submucosal dissection (ESD) and was educated for POEM. Demographic data was recorded before the procedure and results of the procedure were recorded prospectively.

Results: The median age of the patients was 42 (16-72) years. Preoperative and postoperative median Eckardt scores were 10 (6-12) and 0 (0-2) respectively. The median total length of the procedure was 74 (39-158) minutes, tunnel length 17 (13-26) cm and the myotomy length was 14 (10-16) cm. Postoperative oral intake started at median 1 (1-2) day and length of stay was 5 (3-7) days. Capnoperiteneum developed during the procedure in 9 patients and was treated with veress needle. Mucosal injury developed in 2 patients and was carried out endoscopic hemoclips successfully. Four patients had grade A esophagitis at control endoscopy in third month after procedure.

Table: Demographic features and results of POEM procedures

	N = 37
Sex (Male/Female), n	20/17
Age mean (SD) (median; range) year	41.43 ± 14.19 (42;16-71)
Prior achalasia treatment,n (yes/no)	13/24
Achalasia sub-type; Unknown I/ II/ III, n	3/5/27/2
Tunnel length, mean (SD) (median; range) cm	17.81 ± 2.66 (17;13-26)
Myotomy length, mean (SD) (median; range)cm	13.59 ± 2.30 (14;10-19)
Procedure Time, mean (SD) (median; range) min	77.86 ± 22.99 (74; 39-153)
Adverse events, n-Capnoperitoneum-Mucosal injury	92
Veress needle decompression, n(%)	9 (24.3)
Time of oral intake, (median; range) days	1;1-2
Length of hospitalization, (median; range) days	5;3-7
Dysphagia Score, (median; range)PreoperativePostoperative	3;3-40;0-2
Eckardt Score, (median; range)PreoperativePostoperative	10;6-120;0-2

Conclusion: POEM for esophageal achalasia is a novel, safe and effective endoscopic treatment modality in centers that are experienced in advanced endoscopic techniques such as ESD.

Disclosure of Interest: None declared

OP361 INTRAOPERATIVE MEASUREMENT OF ESOPHAGOGASTRIC JUNCTION CROSS-SECTIONAL AREA BY IMPEDANCE PLANIMETRY PREDICTS CLINICAL OUTCOMES OF PEROREAL ENDOSCOPIC MYOTOMY FOR ACHALASIA: A MULTICENTER STUDY

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Introduction: Peroral endoscopic myotomy (POEM) has been introduced as an endoscopic alternative to surgical myotomy. The endoluminal functional lumen imaging probe (endoFLIP) evaluates esophagogastric junction (EGJ) geometry and pressure in response to volume distension in real time via impedance planimetry. It can be used to monitor physiologic changes that occur at EGJ during POEM.

Aims & Methods: The aim of this study was to evaluate whether endoFLIP measurements during POEM can predict postoperative clinical outcomes in terms of symptom relief and development of post procedure reflux. We conducted a retrospective review of achalasia patients who underwent POEM and intraoperative endoFLIP at three tertiary centers. Patients were divided into 2 groups based on clinical response measured by Eckardt Score (ES): good response (ES < 3) or poor response (ES ≥ 3). Post procedure reflux was defined as the presence of esophagitis and/or abnormal pH study. EGJ diameter, cross-sectional area (CSA) and distensibility measured by endoFLIP were compared. The optimal cut-off level of FLIP measurements in predicting clinical response was calculated from receiver operator characteristic (ROC) analysis.

Results: A total of 63 patients (32 male, mean age 48yr) underwent POEM and intraoperative endoFLIP. Of these, 50 (79%) patients had ES < 3 (response group) and 13 patients (21%) had ES ≥ 3 (non-response group) after POEM. There was no significant difference in age, gender, race, BMI, history of previous treatment, preoperative LES relaxation pressure, baseline ES, achalasia subtype and baseline endoFLIP measurements between the two groups. Overall, ES decreased from 7.33 to 1.11 post POEM ($p < 0.001$). Mean LES relaxation pressure (mmHg) decreased from 30.78 to 13.46 ($p < 0.001$). The mean diameter and EGJ CSA significantly increased from 6.57 mm to 10.49 mm ($p < 0.001$) and 36.40 mm^2 to 88.5 mm^2 ($p < 0.001$), respectively. The EGJ distensibility was significantly improved from 1.53 mm^2 /mmHg before myotomy to 4.75 mm^2 / mmHg after myotomy ($p < 0.001$). Comparing the two groups, post operative LES relaxation pressure was significantly lower in the response group (11.79 vs 18.33 mmHg, p 0.03). Post-myotomy CSA was significantly higher in the response group vs non-response group (90.63 vs 70.91 mm^2, p = 0.001). Using ROC curve, the cutoff value of intraoperative EGJ CSA of 80.0 mm^2 yielded sensitivity of 83.3% and specificity of 71% in predicting postoperative response (ES of < 3) with an area under the curve of 0.74. The final EGJ CSA was also significantly higher in patients who had reflux esophagitis after POEM; 99.5 (91.2 – 103.7) mm2 vs 79.3 (57.1 - 94.2) mm^2 ($p = 0.02$).

Conclusion: Intraoperative endoFLIP during POEM for treatment of achalasia is useful in predicting clinical response and post procedure reflux. Impedance planimetry is a potentially important tool to guide the extent and adequacy of myotomy during POEM.

Disclosure of Interest: S. Ngamruengphong: None declared, B. H. A. von Rahden Conflict with: Travel grant, support equipment for POEM procedrure from Karl Storz GmbH Tuttlingen, J. Filser: None declared, A. Tyberg: None declared, A. Desai: None declared, R. Sharaiha: None declared, A. Lambroza: None declared, V. Kumbhari: None declared, M. El Zein: None declared, A. Abdelgelil: None declared, S. Besharati: None declared, J. Clarke: None declared, E. Stein: None declared, A. Kalloo Shareholder: Apollo Endosurgery, M. Kahaleh Financial support for research: Gore, MI Tech, and Pinnacle and Mauna Kea Technologies., Consultancy:, Consultancy: Boston Scientific and Xlumena, M. Khashab Consultancy: Boston Scientific, Xlumena, and Olympus

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30
UPDATE ON NON-ALCOHOLIC STEATOHEPATITIS (NASH) – ROOM E1

OP362 VISCERAL AND PANCREATIC FAT ARE ASSOCIATED WITH LIVER DAMAGE AND ADVERSE METABOLIC PROFILE IN SUBJECTS WITH NON ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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Introduction: Abdominal adiposity is involved in the hallmark of metabolic syndrome and might be implicated in the onset and development of non alcoholic fatty liver disease (NAFLD). Ectopic fat accumulation in liver, but also in other organs like pancreas, has been indicated as a major risk factor for adverse lipid profile, hyperglycemia and insulin resistance. The aim of this work was to evaluate the impact of visceral, hepatic and pancreatic fat on metabolic alterations, lipid and inflammatory profile and histological liver damage, in patients with proven NAFLD.

Aims & Methods: In 34 non diabetic subjects with biopsy proven NAFLD, and 8 controls, we measured visceral (VF), subcutaneous, pancreatic and hepatic fat by magnetic resonance imaging. Gas chromatography mass spectrometry was used to assess FFAs composition, de novo lipogenesis index (DNL = palmitic/linoleic acid) and unsaturated to saturated fat ratio (PUFA/SFA). By use of tracers we evaluated lipolysis and endogenous glucose production (EGP) and calculated adipose tissue insulin resistance (Adipo-IR = Lipolysis x Insulin) and hepatic insulin resistance (Hep-IR = EGP x Insulin). Histology was scored according to Kleiner.

Results: VF correlated with both hepatic and pancreatic fat ($r = 0.47$ and $r = 32$, $p < 0.05$). Hepatic and pancreatic fat also correlated with each other ($r = 0.41$ $p < 0.05$). in subjects with NAFLD and fibrosis we observed an increase in VF (F1-4 = 2.9 ± 0.2 kg; F0 = 2.0 ± 0.1 kg; CT = 0.7 ± 0.1 kg, $p < 0.03$), hepatic fat (F1-4 = 0.45 ± 0.05; F0 = vs 0.32 ± 0.08; CT = 0.1 ± 0.1) and pancreatic fat (F1-4 = 0.40 ± 0.07; F0 = 0.22 ± 0.07; CT = 0.19 ± 0.03; $p < 0.05$) compared to CT and patients with steatosis but no fibrosis. In general, patients with fibrosis had a worse metabolic profile, with increased Adipo-IR (F1-4 = 8.7 ± 1.0; F0 = 7.4 ± 1.9; CT = 3.6 ± 0.5), Hep-IR (F1-4 = 126 ± 14; F0 = 102 ± 14; CT = 52 ± 6), and HOMA index (F1-4 = 3.4 ± 0.4; F0 = 2.6 ± 0.4; CT = 1.3 ± 0.2, all $p < 0.05$).

Visceral, hepatic and pancreatic fat correlated with metabolic parameters, e.g. 1) hyperinsulinemia, 2) hepatic, adipose tissue and peripheral (i.e., HOMA) insulin resistance and 3) parameters of lipotoxicity, such as increased DNL index and decreased PUFA/SFA ratio. Moreover, patients with higher visceral and hepatic fat showed a pro-inflammatory profile as shown by positive correlation with MCP-1 ($r = 0.51$ and $r = 0.56$; $p < 0.01$) and negative correlation with adiponectin ($r = -0.49$ and $r = -0.53$; $p < 0.001$).

Conclusion: In patients with NAFLD, beside hepatic fat also visceral and pancreatic fat are major risk factors for metabolic derangement. In addition, they are associated with an adverse lipid and inflammatory profile that might contribute to progression of liver disease and increased liver damage.

Reference

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Disclosure of Interest: None declared

OP363 PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE HAVE HIGH EXPRESSION AND ALTERED DISTRIBUTION OF CAVEOLIN-1 IN HEPATOCYTES

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Introduction: Nonalcoholic fatty liver disease (NAFLD) as the most common chronic liver disease represents an emerging health problem characterized with unresolved pathogenesis. Experimental models implied a possible role of caveolin-1 (cav1) in lipolysis, lipogenesis and pathogenesis of NAFLD.

Aims & Methods: The aim of this prospective study was to determine expression and distribution of cav1 in hepatocytes of NAFLD patients, as well as their relations to pathohistological changes, presence of metabolic syndrome, levels of liver enzymes and ultrasound characteristics. We included 66 biopsy-proven NAFLD patients and 15 controls that underwent liver resection due to non-diffuse liver disease. Pathohistological analysis of collected liver specimens was performed as well as additional immunohistochemical analysis of cav1 expression and distribution in hepatocytes. Low expression of cav1 was addressed for immunoreactivity seen only on basal membrane and high expression if immunoreactivity was seen additionally in cytoplasm of hepatocytes. Cav1 distribution was determinated according to natural course of progression of liver steatosis; immunoreactivity only in zone 3 was marked as unaltered, while periportal or translobular as altered distribution.

Results: In NAFLD patients, cav1 expression was positive in 59 (89.4%) cases while all controls (15 patients) had negative expression of cav1 in cytoplasm of hepatocytes (X^2, $p < 0.001$). Patients with high cav1 expression were younger (Mann-Withney U test, $p = 0.010$) and more often male (X^2, $p = 0.024$) when compared to NAFLD patients with low cav1 expression. Almost 70% (46 patients) of NAFLD patients had altered cav1 distribution and only 6.7% (1 patient) in control group, what was statistically significant (X^2, $p < 0.001$). NASH and NAFL/borderline groups, determinated according to NAFLD Activity score, had similar expression ($p = 0.199$) and distribution ($p = 0.709$) of cav1 in hepatocytes. Patients that had low cav1 expression had more often MS ($p = 0.041$) and detected fasting hyperglycemia ($p = 0.038$). Ones with altered cav1 distribution had wider waist ($p < 0.001$) and thighs ($p = 0.016$) circumference and more often normal blood pressure (X^2, $p = 0.048$).

Conclusion: Expression of caveolin-1 is high and distribution is altered in hepatocytes of patients with NAFLD compared to control group. This study implies the possible role of caveolin-1 in pathogenesis of NAFLD in humans but larger prospective studies are needed to confirm these pivotal results.

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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30
SCIENCE INFLUENCING CLINICAL PRACTICE IN BARRETT'S – ROOM E4

OP364 SQUAMOUS CELLULAR CARCINOMA ANTIGEN SERUM DETERMINATION AS A BIOMARKER OF BARRETT'S ESOPHAGUS AND ESOPHAGEAL CANCER: A PHASE III STUDY

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Introduction: The cost/effectiveness of surveillance in patients with Barrett's esophagus (BE) is still debated and the use of biomarkers in screening and surveillance not recommended. No information is available regarding SCCA-IgM determination in BE.

Aims & Methods: The study aimed at evaluating the potential role of the determination of the immunocomplexed form of Squamous Cell Carcinoma Antigen (SCCA-IgM) in screening for BE and in surveillance for esophageal adenocarcinoma (EAC).

SCCA-IgM levels were determined (ELISA) in 231 patients prospectively recruited in our Department among whom 53 with BE, 53 with EAC and 71 controls, including 42 blood donors and 65 patients with gastroesophageal reflux but with no endoscopic/ histologic diagnosis of BE (GERD). The cut-off levels for the determination of SCCA-IgM for BE/EAC versus controls and for Barrett "at risk" (long and/or dysplastic BE) versus BE "at low risk" (short non-dysplastic BE) were calculated by ROC curves. Immuno-staining for SCCA-IgM was obtained in a subgroup of patients.

Results: Median SCCA-IgM values were significantly higher in BE and EAC patients than in GERD ($p < 0.0001$). Patients with SCCA-IgM levels higher than the cut-off calculated on the basis of a ROC curve (91.5% sensitivity, 75.4% specificity, a positive predictive value 85.8%, negative predictive value 84.4%, AUC of 0.799) had a 33 times higher Relative Risk (RR) of harboring BE or EAC ($p = 0.0001$). Patients "at risk" (long or dysplastic BE) had SCCA-IgM levels significantly higher than those with short non-dysplastic BE ($p = 0.035$) and patients with SCCA-IgM above the calculated cut-off (sensitivity 85%, specificity 54%, PPV = 68%, NPV = 76%, AUC = 0.67) had a 15 times higher RR of having Barrett "at risk". SCCA was expressed in BE mucosa but not in cardiac- type gastric metaplasia.

Conclusion: Serum SCCA-IgM determination allows the identification of patients at risk for Barrett's esophagus and esophageal adenocarcinoma and the stratification of Barrett patients in subgroups with different cancer risk. Large, prospective studies are required to confirm this evidence in stage IV biomarker studies.

Disclosure of Interest: None declared

OP365 LONGITUDINAL SINGLE CELL CLONAL ANALYSIS REVEALS EVOLUTIONARY STASIS AND PRE-DETERMINED MALIGNANT POTENTIAL IN NON-DYSPLASTIC BARRETT'S ESOPHAGUS

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Introduction: Carcinogenesis is fundamentally an evolutionary process whereby cells that have acquired advantageous somatic mutations clonally expand via a process of Darwinian natural selection. Surveillance of Barrett's oesophagus allows us to study the evolutionary dynamics of a human neoplasm over time.

Aims & Methods: We used multicolor fluorescence in situ hybridization (FISH) on endoscopic brush cytology specimens collected from 320 non-dysplastic Barrett's patients to study clonal evolution at single cell resolution. For 195 of these patients we also analyzed material from a follow-up endoscopy (median interval 37 months). Patients were followed for a median of 43 months during which 20 patients (6.3%) progressed; 8 patients developed high-grade dysplasia (HGD) and 12 developed oesophageal adenocarcinoma after a median duration of 34 months. All samples were scored for abnormalities by FISH at seven markers including CEP7, CEP17, *p53, p16, Her-2/neu*, *20q*, and *MYC*, organized into two probe sets to measure clonal composition and clonal diversity within the Barrett's segment (i.e. Shannon diversity, Simpson diversity, richness, and average pairwise distance).

Results: Higher levels of clonal diversity at baseline were associated with increased risk of progression to HGD or cancer, this result being largely robust to the choice of diversity statistics, and the FISH probes included in the measure; univariate Cox proportional-hazards analysis showed that out of the 9 statistically significant predictors of progression, 7 were diversity-based, the two others being aneusomy and age (respectively 7th and 8th most significant) and they were still significant after adjusting for age and Barrett's segment length. Baseline genetic diversity remained in a stable dynamic equilibrium over time. Clonal expansions were rare; after correction for multiple testing, binomial analysis revealed 27 statistically significant clonal expansions and 45 clonal contractions over 993.6 patient years of observation, an average of 1 detectable clonal expansion by these methods every 36.8 patient years and 1 clonal contraction every 22.1 patient years. However, clonal expansions were not associated with progression in our cohort.

Conclusion: Our data indicated that the level of clonal diversity measured at baseline in non-dysplastic BE was indicative of progression risk, and that this level of diversity did not change significantly over time. This suggests a lack of strong clonal selection in Barrett's and that the malignant potential of 'benign' Barrett's lesions is predetermined, with important implications for surveillance programs.

Disclosure of Interest: M. Timmer: None declared, P. Martinez: None declared, C. Lau: None declared, S. Meijer: None declared, F. ten Kate: None declared, R. Mallant-Hent: None declared, A. Naber: None declared, A. van Oijen: None declared, L. Baak: None declared, P. Scholten: None declared, C. Böhmer: None declared, P. Fockens: None declared, J. Bergman: None declared, C. Maley: None declared, T. Graham: None declared, K. Krishnadath Conflict with: Dr. Krishnadath has a patent 10999US01 issued.

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30

A TAILORED APPROACH TO ADVANCED RECTAL CANCER – ROOM E2

OP366 CLINICAL OUTCOMES OF RECTAL NEUROENDOCRINE TUMORS AFTER ENDOSCOPIC RESECTION : A KASID MULTI-CENTER STUDY

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Introduction: Recently, an incidental detection of rectal neuroendocrine tumors (NET) is increasing as the rise of diagnostic sigmoidoscopy and/or colonoscopy. However, the clinical outcomes of these tumors, especially after endoscopic treatment, remain elusive.
Aims & Methods: We are aimed to evaluate the long-term clinical outcomes of endoscopically treated rectal NETs through conducting a large, multicenter study.
This study retrospectively analyzed the medical records of patients, who were endoscopically resected rectal NETs and followed for more than 24 months, from January 2000 to November 2011 in 15 university hospitals. End outcomes were determined by assessing local or distant recurrence or metachronous NETs.
Results: Of a total of 405 patients with rectal NETs, the mean tumor size was 5.9 ± 3.2 mm (range 1.0–22.0 mm) and synchronous rectal NETs were noted in four patients. Resection margin status was positive in 82 patients (20.2%) and indeterminate in 72 patients (17.8%). Of them, 15 patients (9.7%) underwent salvage treatment and residual tumors were found in 5 patients. During the follow-up (56.6 ± 34.4 months), 4 patients had local recurrence and there was no recurrence at distal organs. In addition, rectal metachronous NETs were found in 4 patients. In the 8 cases (2.0%) with recurrence or metachronous NETs, a tumor size < 10 mm at initial resection was observed in 6 patients (75%). Tumor size and synchronous rectal NET at diagnosis was a significant predictor for recurrence and metachronous lesion, respectively.
Conclusion: In the rectal NETs after endoscopic resection, recurrence or metachronous NETs are observed in not negligible proportion of cases during the follow-up. Tumor size and synchronous rectal NET at diagnosis is significantly associated with the risk of recurrence and metachronous lesion, respectively.
Disclosure of Interest: None declared

OP367 VE1 (BRAF V600E) IMMUNOHISTOCHEMISTRY IN COLORECTAL CANCER: ASSESSMENT OF ANTIBODY PERFORMANCE, HISTOPATHOLOGY, PROGNOSIS AND HETEROGENEITY IN THREE COLORECTAL CANCER COHORTS

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Introduction: $BRAF^{V600E}$ mutation occurs in approx. 9-12% of colorectal cancers (CRC). In addition to its diagnostic role in Lynch syndrome, $BRAF^{V600E}$ is a prognostic factor in metastatic CRC (and possibly other disease stages) and a potential predictive biomarker for future combined therapies.
Aims & Methods: Here, we validate the VE1 antibody against $BRAF^{V600E}$, assess regional heterogeneity of VE1 in primary and matched metastatic sites and investigate clinicopathological associations and survival in CRC patients stratified by VE1. VE1 immunohistochemistry was performed on eight formalin-fixed and paraffin-embedded CRC cell lines, on whole tissue sections and on a next-generation tissue microarray (ngTMA) of 65 cases including 34 CRCs, 23 malignant melanoma and 8 thyroid cancers, all with known mutational status for BRAF. Inter-observer agreement was assessed by three observers. First, in order to investigate heterogeneity within/among primary cancers and within/among matched distant metastatic lesions, all tumor blocks from 14 CRC patients with synchronous metastases were interrogated for VE1 on an ngTMA (n = 100 areas; 0.6mm cores). Second, prognostic and histopathological questions were addressed using a multiple-punch ngTMA of colon cancers with six cores/tumor (n = 259 patients; 0.6mm cores). Thirdly, preoperative biopsies from 125 surgically treated CRC patients with full clinicopathological and survival/follow-up information were mounted onto an ngTMA (1mm core) and investigated for clinical and histopathological differences.
Results: Using cell lines and the test cohort of 65 cases, VE1 was found to be homogeneously expressed and was 100% concordant with mutational status. Inter-observer agreement was 100%; however all observers assigned incorrect VE1 positivity to a single BRAF wild-type CRC. This tumor showed mucinous histology and patchy, discontinuous staining. Therefore, sensitivity and specificity were 100% and 93%. Evaluating all CRC tumor blocks from each case, primary CRC showed no heterogeneity. Four cases had $BRAF^{V600E}$ in primary cancers that were found in the corresponding metastatic lesions. VE1-positivity correlated with older age ($p = 0.0455$), mucinous histology ($p = 0.0277$), right-sided location ($p = 0.001$), tumor grade ($p < 0.001$), MLH1-deficiency ($p < 0.0001$), and poor prognosis in pM1 patients ($p < 0.0001$).
Conclusion: VE1 is highly specific and sensitive for $BRAF^{V600E}$. Results from the application on human tumor samples suggest that $BRAF^{V600E}$ mutation is not acquired during the metastatic process. Positive VE1 correlates with expected clinicopathological features associated with $BRAF^{V600E}$. Because of homogeneous expression throughout the tumor samples, TMA studies using VE1 are reliable.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30

COLORECTAL CANCER: BIOMARKERS AND SCREENING – ROOM E3

OP368 SIGNIFICANT RISK OF POST-COLONOSCOPY COLORECTAL CANCER DUE TO INCOMPLETE ADENOMA RESECTION - RESULTS OF A NATION-WIDE POPULATION-BASED COHORT STUDY

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Introduction: Resection of adenomas detected during colonoscopy decreases the risk of subsequent colorectal cancer (CRC). It does however not preclude the occurrence of CRC within a few years after colonoscopy. Many of these post-colonoscopy CRCs (PC-CRCs) are preventable, as they are thought to be due to missed or incompletely resected adenomas.
Aims & Methods: The aims of this study were to assess the overall incidence rate of PC-CRC in patients with one or more adenomas, to determine the risk of PC-CRC due to incomplete adenoma resection, and to identify adenoma characteristics associated with a high risk of PC-CRC due to incomplete adenoma resection. We performed a population-based cohort study identifying all patients with a first colorectal adenoma between 2000 and 2010 in PALGA, the nationwide Dutch Pathology Registry. Outcomes were the incidence rate of PC-CRC overall and of PC-CRC due to incomplete adenoma resection, defined as the occurrence of CRC between 6 months and 5 years after adenoma removal in the same colon segment. We performed a multivariable cox proportional hazard regression analysis to identify adenoma-related factors associated with both outcomes.
Results: During the study period, 119,233 patients were diagnosed with a first adenoma. Mean age was 64.0 years (standard deviation 12.8) and 53.9% were male. We excluded 11,489 patients in whom prevalent CRC was found (CRC before or within 6 months after the first adenoma). Of the remaining 107,744 patients, 1031 (0.96%) developed PC-CRC anywhere in the colon within 5 years (incidence rate 1.9/1000 person years). PC-CRC due to incomplete adenoma resection occurred in 324 of 133,519 adenomas (0.24%). Mean follow up per adenoma was 4.4 years (SD 1.1). The incidence rate of CRC due to incomplete adenoma resection was 0.6 per 1000 years of follow up. High-grade dysplasia (hazard ratio (HR) 2.54, 95% confidence interval (CI) 1.99-3.25), villous (HR 2.63, 95% > CI 1.79-3.87) and tubulovillous histology (OR 1.80, 95% > CI 1.43-2.27) were risk factors for PC-CRC due to incomplete adenoma resection.
Conclusion: In this nationwide cohort, PC-CRC due to incomplete endoscopic resection occurred in one in four hundred adenomas and even more frequently in adenomas with high-grade dysplasia and villous or tubulovillous components. Our results suggest that enhanced surveillance is indicated after removal of adenomas with high-grade dysplasia or villous components.
Disclosure of Interest: None declared

OP370 CIRCADIAN CHANGES IN CELL-FREE DNA AMOUNT, METHYLATED SEPTIN 9 AND TUMOR MARKERS IN PATIENTS WITH COLORECTAL CANCER

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Introduction: Methylated Septin 9 (SEPT9) is a sensitive and specific blood-based biomarker for colorectal cancer (CRC). However, its circadian rhythm and the relationship to the circadian cycle of cell-free DNA (cfDNA) amount and blood-based tumor markers have not been described yet. Therefore the aim of this study was to compare the circadian rhythm of SEPT9 with the cycle of cfDNA amount and the nowadays used blood-based tumor markers, such as CEA, AFP, CA19-9, TPA and CA72-4.

Aims & Methods: Plasma samples were collected four times a day (06:00, 12:00, 18:00 and 0:00) from 9 patients with CRC (5 with Stage I-II and 4 with Stage III-IV), from one with adenoma and from one healthy control. CfDNA was isolated from 3.5 ml plasma and bisulfit-converted using Epi proColon Plasma Quick Kit and methylated SEPT9 was detected by Sensitive PCR kit (Epigenomics AG). Cell-free DNA was extracted additionally with High Pure Viral Nucleic Acid Large Volume Kit (Roche) and measured by Qubit dsDNA HS Assay (Life technologies). Tumor markers (CEA, AFP, CA19-9 and CA72-4) were measured from plasma samples, as well.

Results: The lowest cfDNA amounts (mean 16.5 ng/ml) were observed out of the 4 times measurements at 0:00 in 83.3% (5/6) of Stage I-III patients. In Stage IV samples this low level (mean 41.1 ng/ml) was observed in other times of the day (6:00, 12:00 and 18:00). Within each stage, the highest cfDNA levels (mean 32.6 ng/ml) were measured at 6:00 and 12:00 in CRC I-III Stages and at 0:00 in Stage IV samples (mean 138.9 ng/ml). Comparing the cfDNA changes, higher differences were found in higher CRC stages (48%) than Stage I (22%). In normal control plasma, although cfDNA showed the lowest level (mean 14.3 ng/ml) compared with others, it showed a circadian rhythm and SEPT9 negativity at the same time. At 0:00, all cancer (100%) and adenoma cases were positive for SEPT9 methylation. At other times (6:00, 12:00 and 18:00) only 77.7% of CRC samples showed SEPT9 positivity. Stage I cancer samples were SEPT9 positive only at 0:00. Interestingly, the highest SEPT9 methylation level was found at 0:00 in most CRC cases. In 7 of 6 advanced tumors (Stage II-IV) highest DNA level and SEPT9 methylation showed high correlation. The cycle threshold (CT) level was altered by 3.2 CT values in Stage II, 2.5 CT values in Stage III and 1.9 CT values in Stage IV during 24 hours. In Stage I, SEPT9 was methylated only at 0:00. The level of tumor markers correlates with the amount of cfDNA during the four times measurement. Changes of CEA differences between Stage I-IV were 9-21%. This difference was 17-22% in AFP, 13-23% in CA19-9, 23-44% in TPA and 6-12% in CA72-4 markers.

Conclusion: In cases with low amount of cfDNA, such as adenoma and early stage cancer (Stage I), the time of blood draw for SEPT9 detection as CRC screening is essential, since positive results were measured only in the early hours. Contrarily, in CRCs from Stage II, SEPT9 methylation can be determine confidently, however it still follows a circadian rhythm.

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Disclosure of Interest: None declared

OP371 INCREASED DETECTION OF COLORECTAL CANCER WITH A COMBINATION FAECAL AND BLOOD SCREENING TEST

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Introduction: Screening with a faecal occult blood test (FOBT) leads to early detection and decreased mortality from colorectal cancer (CRC). In practice, however, FOBT screening programs have uncovered a number of challenges including relatively low compliance rates in some studies. Different types of tests may increase screening participation. Surveys suggest that people would prefer to complete a combination screening test involving a FOBT and a blood test if it had higher accuracy than the standard tests (1).

Aims & Methods: The aim of this study was to determine the CRC detection rate with a screening test combining a FOBT with a blood test, compared to FOBT alone.

Patients who were scheduled for colonoscopy completed a immunochemical FOBT (faecal immunochemical test (FIT), one sample, OC Sensor, Eiken) within two weeks of the colonoscopy, followed by a CRC blood test (Colovantage Plasma, Clinical Genomics) immediately before colonoscopy. FITs were analysed for haemoglobin content, and samples with $\geq 10\mu g$ haemoglobin/g faeces were deemed positive. Plasma was assayed for methylated *BCAT1* and *IKZF1* DNA, with the detection of either methylated gene considered positive. Colonoscopy and pathology reports were assessed and clinical parameters associated with test positivity were evaluated.

Results: The primary colonoscopy diagnosis in the 1381 people who completed both tests included cancer (4.8% of cases), high-risk adenoma (defined as the presence of adenoma with villous or serrated morphology, $\geq$10mm, high-grade dysplasia, or more than two tubular adenomas; 13.7%), low-risk adenoma (18.8%) and no neoplasia found (62.8%). The FIT was positive in 309 patients, and detected 78.8% of the cancers (52/66) and 42.3% of the high-risk adenomas (80/189). The specificity of the FIT in the cases without significant neoplasia was 84%. In the FIT-negative patients, the blood test detected an additional 7 cancers and 8 high-risk adenomas. These additional cancers were more likely to have lymphovascular invasion than cancers positive for FIT alone (50% vs 11%, $p = 0.04$), with a slightly higher prevalence of these cancers in males (85.7% vs 55.6%). The combined test sensitivity (for either test positive) was 89.4% for CRC and the specificity was 77.8%. Cases with CRC that were positive for both tests (34/61) had a relative risk of 23.0 for cancer when compared to those cases without a double positive result.

Conclusion: Combining FIT and blood test increased sensitivity over either test alone using an "either or" rule. Cancer cases positive by the blood test alone appeared to be phenotypically different to FIT positive cancers, which might have implications for therapy.

Reference

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OP372 NEW VOLATILE MARKER TEST TO DETECT COLORECTAL LESIONS

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Introduction: An ideal colorectal cancer (CRC) screening test would identify not only cancer but also high-risk colonic adenomas. There is still a space to improve the performance of non-invasive tests for CRC screening. Volatile marker tests based on nanoarray sensor technologies are presenting an attractive approach for screening and wide population-based applications being non-invasive, easy-to-use and low-cost diagnostic tools.

Aims & Methods: The study was aiming to investigate the feasibility of CRC and adenoma detection by measuring volatile organic compounds (VOCs) in the exhaled breath.

Alveolar exhaled breath samples were collected from 71 CRC patients, 13 patients with non-advanced adenomas (NAA), 10 – with high-risk adenomas (HRA), and 131 control patients. VOCs in the exhaled breath were measured by two different **Methods:** 1) gas chromatography coupled to mass-spectrometry (GCMS) and 2) cross-reactive nanomaterial-based sensor technology by using gold nano-particles and single-wall carbon nanotube combined with a pattern recognition method. For the latter approach classification success was calculated by (i) building an algorithm for 70% of the samples as a training set and (ii) randomly blinding 30% of the samples as a validation set.

Results: GCMS analysis revealed 5 VOCs having significant differences between the groups; these were ethanol, acetone, ethyl acetate, 4-methyl octane, and styrene.

The nanoarray analysis made it possible to differentiate CRC from the control group (validation set) with 85% sensitivity, 90% specificity, and 88% overall accuracy. Similarly good performance was demonstrated to detect adenomas, and differentiate between high- and low-risk lesions, although the small group size has to be mentioned as the limitation (see Table for details).

The table below is demonstrating the performance characteristics of nanomaterial-based sensor technology to detect colorectal cancer and adenomas.

	Sensitivity	Specificity	Accuracy
CRC (63) vs. controls (131)	85%	90%	88%
CRC (16) vs. Adenomas (16)	94%	88%	91%
Controls (16) vs. Adenomas (16)	94%	94%	94%
NAA (8) vs. HRA (8)	100%	88%	94%

CRC – colorectal cancer; NAA – non-advanced adenomas; HRA – high-risk adenomas

Conclusion: There is a good potential of VOC detection in exhaled breath by nanoarray sensor technology in diagnosing CRC and colonic adenomas. This testing approach should be further validated in CRC screening settings.

Disclosure of Interest: None declared

OP373 METFORMIN EFFICACY AND SAFETY FOR COLORECTAL POLYPS: A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

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Introduction: Colorectal cancer is one of the major neoplasms and a leading cause of cancer death worldwide, and new preventive strategies are needed to lower the burden of this disease. Metformin, a biguanide, which is widely used for treating diabetes mellitus, has recently been suggestive to have a suppressive effect on tumorigenesis and cancer cell growth. In a previous study conducted in non-diabetic subjects, we showed that oral short-term low-dose metformin suppressed the development of colorectal aberrant crypt foci (ACF). ACF have been considered as a useful surrogate biomarker of CRC, although the biological significance of these lesions remains controversial. We conducted a prospective randomized controlled trial to evaluate the chemopreventive effect of metformin against metachronous colorectal polyps and the safety of this drug in non-diabetic post-polypectomy patients.

Aims & Methods: This study is a multi-center, double-blind, placebo-controlled, randomized controlled trial to be conducted in non-diabetic patients with a recent history of undergoing colorectal polypectomy. All adult patients visiting the Yokohama City University hospital or affiliated hospitals for polypectomy was recruited for the study. Eligible patients were allocated randomly into either one of two groups: the metformin group and the placebo group. Patients in the metformin group received oral metformin at 250 mg per day, and those in the placebo group received an oral placebo tablet. At the end of 1 year of administration of metformin/placebo, colonoscopy was performed to evaluate the polyp formation.

Results: A total of 150 subjects were enrolled the study and allocated randomly into two group. The number of polyps (hyperplastic polyp and adenoma) at 1 year after the treatment was significantly lower in the metformin group in comparison with that in the placebo group (27/70 (38.6%) vs. 36/64 (56.3%), $p = 0.041$). Metformin at a low dose of 250 mg/d did not produce any severe side effects, including lactic acidosis, hypoglycemia, in this 1-year study.

Conclusion: This is the first study to explore the effect of metformin against colorectal polyp formation. Metformin activates AMPK, which inhibits the mammalian target of rapamycin (mTOR) pathway. The mTOR pathway plays an important role in the cellular protein translational machinery and cell proliferation. Patients with type 2 diabetes taking under treatment with metformin have been reported to be at a lower risk of cancer development than those not taking under treatment with metformin. We showed in this study that metformin suppressed the formation of metachronous colorectal polyps. Metformin has potential the colorectal cancer chemoprevention. Further study is needed.

Disclosure of Interest: None declared

OP374 THE MANAGEMENT OF MALIGNANT POLYPS IN COLORECTAL CANCER SCREENING PROGRAMS: AN ITALIAN MULTICENTRE SURVEY

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Introduction: Recognition of colorectal malignant polyps is increasing, mainly due to the diffusion of screening programs.

Although more and more information are being gathered regarding their management, treatment plans lack the evidence of randomized trials and still rely on observational studies, with high variability in clinical behaviour.

In 2012, a European panel has issued new guidelines in colorectal cancer (CRC) screening and diagnosis, including an update in histologic reporting [1].

Aims & Methods: We carried out a survey on all malignant polyps detected during CRC screening programs at 5 centres of North-Eastern Italy.

In all participating centres the followed protocol implies a colonoscopy in subjects aged 50-69 years of both sexes, who tested positive at immunochemical faecal occult blood test.

Cases diagnosed before the introduction of new histologic guidelines were reviewed by specialized pathologists

Results: In the period 2008-2013 306 malignant polyps were observed in 306 patients at 5 institutions located in the Veneto/Trentino region (Trento, Rovereto, Bassano del Grappa, Padova – Sant'Antonio Hospital, Feltre).

63% of patients were males. Mean age was 62.6 years (range 50-69).

The site distribution of the lesions was the following: rectum 24.3%, left colon 56.1%, right colon 19.6%.

72 patients (23.6%) were sent to direct surgery. 234 received an endoscopic treatment. 56.8% of them were sent to post-polypectomy radicalization surgery, and 12.8% of those had evidence of residual disease. As regards method of endoscopic treatment, an en bloc resection has been performed in 75.5% of cases. Involved, unsafe (<1mm) or invaluable resection margins and sessile morphology represented the most frequent determinants in the decision of subsequent surgery.

The mean number of lymph-nodes harvested during direct surgery was 9.6, whereas in the post-polypectomy surgery the mean number was 7.1 ($p = 0.027$, Student T test).

During a mean follow-up of 44 months (range 24-54), no recurrence of disease was diagnosed in endoscopically-treated population; 3 recurrences (2 cases of distant metastases and one case of lymph-nodal involvement) were observed in the high-risk population sent to radicalization surgery.

A histologic second opinion was acquired in 125 cases (53% of endoscopic resected lesions) and led to a change in the patient risk class in 18 cases (14.4%). 9 patients shifted from low to high risk class, 9 from high to low.

Conclusion: Although our rate of surgical treatment following endoscopic resection complies with other series, the rate of residual disease at surgery lies below the majority of international experiences.

Therefore, bearing in mind the potential risk of overtreatment in these patients, and given the fact that the lack of margin evaluation (mainly related to specimen fragmentation) has proved to be a frequent cause of attribution to high risk class, resection/handling of the lesion should be a major concern for endoscopists.

Finally, we believe that adhering to new histological reporting system and respecting guidelines on lymph-node harvesting (which recommend the resection of at least 12) may help in positively influencing the patient's prognosis.

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Disclosure of Interest: None declared

OP375 VALIDATION OF A SCORING SYSTEM TO PREDICT PROXIMAL NEOPLASIA FOR COLORECTAL CANCER SCREENING: A PROSPECTIVE STUDY

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Introduction: Flexible sigmoidoscopy (FS) and colonoscopy are two commonly used screening modalities. The risk of proximal neoplasia (PN) could influence the choice between these two screening tests. FS is now more popularly perceived, especially in European countries – following the publication of findings from landmark randomized trials.

Aims & Methods: This study developed a clinical scoring system to predict the risks of proximal neoplasia (PN), irrespective of the presence of distal neoplasia. Neoplasia include adenoma and advanced neoplasia, but not hyperplastic polyps. "Proximal" refers to a location in the colon which is proximal to the splenic flexure; whilst "distal" refers to the rectum, sigmoid and descending colon. We prospectively recruited 5,789 Chinese asymptomatic screening participants who received colonoscopy in Hong Kong (2008-2014). From random sampling of 2,000 participants, the independent risk factors were evaluated for PN using binary regression analysis. The odds ratios for these factors were used to develop a scoring system. The score range is 0-3 with two categories: 'average risk' (AR): 0-1 and 'high risk' (HR): 2-3. The other 3,789 screening participants formed an independent validation cohort. Each subject was scored based on their risk factors, and we evaluated the performance of the scoring system devised.

Results: The proportion of PN in the derivation and validation cohorts was 17.4% and 17.5%, respectively. According to the adjusted odds ratios from the derivation cohort, the following predictors of PN were used to assign scores to each subject: age 50-55 years (0), 56-70 (1), male gender (1), female gender (0), BMI < 25 kg/m^2 (0), BMI ≥ 25 kg/m^2 (1). Based on age, gender, and body mass index, 54% and 46% in the derivation cohort were classified as AR and HR, respectively. Among all subjects, the prevalence of PN in the AR and HR groups was 12.8% and 22.9%, respectively. Participants in the HR group had 1.67-fold (95% CI = 1.45 to 1.92, $p < 0.001$) increased risk of PN compared to the AR group (Table 1). The Hosmer-Lemeshow goodness-of-fit statistic evaluating the reliability of the validation sets had p values of 0.381, indicating a close match between predicted risk and real risk.

Conclusion: The scoring system bears potential to predict the risk of PN. It is anticipated that its use in clinical practice could assist physicians to risk stratify subjects for colorectal cancer screening, and offer an informed choice between FS and colonoscopy based on individual risk of PN. Future research should evaluate

Abstract number: OP375 Table 1: Prevalence of proximal neoplasia by risk tier

Derivation cohort			Validation cohort		
Risk Tier(Risk Score)	**No. of Subjects (%)**	**ProximalNeoplasia* (%)(95% CI)**	**No. of Subjects(%)**	**ProximalNeoplasia(%)(95% CI)**	**RelativeRisk(95% C.I.)**
Average Risk(0-1)	1,051(54.0)	120 (11.4)(9.6-13.5)	2,149(56.6)	288 (13.4)(12.0-14.9)	1.00
High Risk(2-3)	895(46.0)	212 (23.7)(21.0-26.6)	1,651(43.4)	370 (22.4)(20.4-24.5)	**1.67(1.45-1.92)P < 0.001**
Total	1,946 (100)	332 (17.1)(15.4-18.8)	3,800(100)	658 (17.3)(16.1-18.6)	

the scoring system in other countries with different ethnicity. The projected cost-effectiveness, acceptability, and practicality to implement this prediction tool in screening practices should be further addressed.
Disclosure of Interest: None declared

OP376 THE FAS (FECAL HEMOGLOBIN CONCENTRATION, AGE AND SEX) MODEL: DEVELOPMENT AND EXTERNAL VALIDATION OF A SIMPLE PREDICTIVE MODEL FOR COLORECTAL CANCER DETECTION IN SYMPTOMATIC PATIENTS

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Introduction: Predictive models for colorectal cancer (CRC) detection in symptomatic patients are based on subjective clinical criteria with low diagnostic accuracy. Simple to calculate predictive models based on easy to obtain objective variables are required.
Aims & Methods: The COLONPREDICT study is a prospective blind diagnostic test study aimed at developing a CRC predictive model in symptomatic patients. Fecal hemoglobin concentration was measured in the1572 patients included (CRC prevalence: 13.7%). We stratified fecal hemoglobin concentration into four groups; 0, 1-19.9, 20-199 and ≥200 μg Hb/g feces to build this model. A simpler predictive model (FAS) for CRC detection based on Fecal hemoglobin concentration, Age and Sex was developed using binary logistic regression. The validation cohort consisted of 1035 patients included in two studies done in Scotland, a pilot study (FITS) involving 280 patients (6 CRC) presenting in primary care with symptoms, a larger follow-up study (FITS+) with 755 individuals (28 CRC) and a third study performed in Barcelona (Bellvitge) involving 1030 patients (30 CRC). Fecal hemoglobin concentration was determined in all studies with the OC-Sensor®. We compared the diagnostic accuracy between initial and validation cohorts with ROC curves and AUC. At pre-established sensitivity thresholds in the initial cohort (90% and 99%), we determined if there were differences in the sensitivity and specificity between initial and validation cohorts with the Chi-square test.
Results: The Odds Ratio of the variables included in the FAS model were: age (year) 1.03 (95% confidence interval, CI: 1.02-1.05); male sex 1.6 (95% CI: 1.1-2.3); fecal hemoglobin concentration 1-19.9 2.0 (95% CI: 0.7-5.5); 20-199 16.8 (95% CI: 6.6-42) and ≥ 200 μg Hb/g feces 65.0 (95% CI: 26-164). The AUC of FAS model was 0.87 (95% CI: 0.85 to 0.90) in the initial cohort and 0.92 (95% CI: 0.89 to 0.94) in the overall validation cohort ($p = 0.01$). The overall diagnostic accuracy was increased in FITS (0.95, 95% CI: 0.92-0.99; $p < 0.001$) and Bellvitge studies (0.94, 95% CI: 0.91-0.97; $p = 0.001$) cohorts. However, no differences were found with the FITS+cohort (0.89, 95% CI: 0.93-0.94; $p = 0.6$). At the pre-established FAS model cut-off yielding 90% sensitivity (B coefficient: 4.5), no differences in sensitivity were found between initial (89.8%) and validation cohorts, both globally (87.5%; $p = 0.6$) or separately (FITS 100%; $p = 1.0$, FITS+ 82.1%; $p = 0.2$, Bellvitge 90.0%; $p = 1.0$). However, specificity was superior in the validation cohort (initial 71.3%, validation 85.9%, FITS 86.8%, FITS+ 85.4%, Bellvitge 87.5%; $p < 0.001$). At the pre-established cut-off with a 99% sensitivity (B coefficient: 2.12), the sensitivity in all the cohorts was 100%. In contrast, the specificity in the initial cohort was inferior (initial 13.9%, validation 22.1%, FITS 25.2%, FITS+ 26.3%, Bellvitge 25.2%; $p < 0.001$).
Conclusion: FAS is a simple method to calculate CRC predictive model from easily obtainable variables. Although we found differences in specificity, its sensitivity is similar in different settings and transferable over geography.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30
UPPER GI CANCER: MANAGEMENT PERSPECTIVES – ROOM E5

OP377 THE EFFECT OF HELICOBACTER PYLORI ERADICATION ON METACHRONOUS GASTRIC CANCER AFTER ENDOSCOPIC SUBMUCOSAL RESECTION

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Introduction: There are many epidemiologic studies about prophylactic effect of *Helicobacter pylori* (*H. pylori*) eradication on metachronous gastric cancer after endoscopic resection in patient with early gastric cancer. However, their results are controversial. We performed the study to evaluate whether *H. pylori* eradication could reduce the occurrence of metachronous gastric cancer after endoscopic submucosal dissection (ESD) in patient with early gastric cancer.
Aims & Methods: Between November 2005 and August 2013, the patients who were treated by ESD for early gastric cancer were enrolled (n = 484), and the follow-up data was reviewed retrospectively.
Results: We divided patients into three groups: those without *H. pylori* infection(n = 336), those who successfully underwent *H. pylori* eradication (n = 88), those who failed or didn't take *H. pylori* eradication (n = 60).
Metachronous recurrence was diagnosed in 20 patients (4.1%) in all patients, including 15 (4.5%) in the *H. pylori*-negative group, 3 (3.4%) in the eradicated, and 2 (3.3%) in the non-eradicated groups. Median time to metachronous recurrence was 30.1 months (range, 2 – 71 months). The odds ratio in the non-eradicated group compared with the *H. pylori*-negative and eradicated groups were 1.355 (P value = 1, 95% CI = 0.302 – 6.083) and 1.024 (P value = 1, 95% CI = 0.166 – 6.317), respectively.
H. pylori eradication didn't reduce metachronous recurrence of early gastric cancer. The risk factor of subsequent gastric metachronous cancer was a degree of mucosal atrophy. Odds ratio was 4.273 between the mild to moderate mucosal atrophy group and severe mucosal atrophy group. (P value = 0.002)
Conclusion: *H. pylori* eradication doesn't have prophylactic effect about the occurrence of metachronous gastric cancer after endoscopic resection in patients with early gastric cancer. And the risk factor of metachronous gastric cancer is the degree of mucosal atrophy.
Disclosure of Interest: None declared

OP378 THE PREDICTIVE INDICATORS FOR METASTASIS IN NON-AMPULLARY DUODENAL NEUROENDOCRINE TUMORS MEASURING 20 MM OR LESS IN GREATEST DIMENSION: A RETROSPECTIVE MULTICENTER STUDY

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Introduction: The algorithm of treatment (i.e., endoscopic resection (ER) or surgical resection) of non-ampullary duodenal neuroendocrine tumors (NAD-NETs) usually depends upon the size of the lesions. ER is generally recommended for NAD-NETs < 10 mm in diameter, but the clinical algorithm of proceeding to the additional treatment following ER has not been established. In addition, the treatment strategy for NAD-NETs of 10–20 mm in diameter has not been determined either.
Aims & Methods: In this study, we aimed to evaluate the detailed clinicopathological characteristics of NAD-NETs measuring ≤20 mm in diameter to clarify the predictive indicators of subsequent metastasis. The patients with NAD-NETs ≤20 mm in diameter treated at 12 institutions between May 1992 and April 2013 were enrolled in this retrospective study. Those with follow-up periods of < 24 months, unless metastasis was clinically identified, were excluded. Clinical records were retrieved, and histopathological findings of all cases were centrally reviewed by two expert pathologists who were blinded to any clinical information. We then analyzed the predictive indicators of metastasis using univariate analysis. As for independent variables, age (≤60 and > 60 years), gender, the number of the tumor (single and multiple), the presence of functional or hormonal syndrome, multiple endocrine neoplasia type 1, tumor size (≤10 and 11–20 mm), depth of the tumor invasion (confined to submucosa, and muscularis propria or deeper), World Health Organization (WHO) grade (G1 and G2), lymphovascular invasion, and peptide hormone and amine products were evaluated as categorical variables in this study.
Results: We could study 49 patients with a mean follow-up period of 66.5 months. There were 7 lymph node metastases (14.3%) and 3 distant metastases (6.1%). Thirty-five patients were initially treated with ER, and 14 with surgery. Correlation coefficient for Ki67 index and mitotic index obtained by two pathologists were extremely high, 0.9967 and 1.0, respectively. A univariate analysis revealed that the predictive indicators for metastasis were lymphovascular invasion (odds ratio [95% confidence interval] = 12.5 [2.01-77.9]; $P = 0.007$), multiple tumors (9.75 [1.46-65.4]; $P = 0.019$), a tumor size of 11–20 mm (6.67 [1.21-36.6]; $P = 0.029$), and WHO grade G2 (7.13 [1.16-43.9]; $P = 0.034$). Five-year overall and disease-specific survival rates were 86.1% and 97.2%, respectively. NAD-NETs were demonstrated to have immunoreactivity for gastrin, somatostatin, and serotonin in 75.5%, 36.7%, and 40.8% of the cases, respectively, but only 4 cases had a functional syndrome (Zollinger-Ellison syndrome).
Conclusion: This is the first study to demonstrate that the predictive indicators of metastasis in NAD-NETs ≤20 mm in diameter were lymphovascular invasion, multiple tumors, a tumor size of 11–20 mm, and WHO grade G2. These findings could provide clinically important information for determining the appropriate therapeutic approach and the clinical strategy of treatment following ER.
Disclosure of Interest: None declared

OP379 RANDOMISED TRIAL OF POST-DISCHARGE ENTERAL FEEDING FOLLOWING SURGICAL RESECTION OF AN UPPER GASTROINTESTINAL MALIGNANCY

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Introduction: Patients undergoing upper gastrointestinal surgery often eat poorly post operatively, despite dietetic input. The benefit of nutritional supplementation following hospital discharge is unknown. We examined the benefit of 6 weeks nutritional supplementation, via the patients feeding jejunostomy, on fatigue, quality of life and independent living.

Abstract number: OP379

	Energy %*		MFI-20^		EQ5D^		QLQ-OES18+	
	Active	Control	Active	Control	Active	Control	Active	Control
Discharge	58 (54,74)	65 (55,80)	42 (34,58)	58 (42,65)	10 (9,12)	12 (10,13)	35 (28,39)	27 (25,30)
3 weeks	114 (96,127)	79 (67,96)	47 (39,62)	60 (37,72)	12 (10,13)	12 (12,14)	32 (27,38)	30 (25,34)
6 weeks	117 (99,127)	75 (63,84)	64 (51,71)	67 (57,79)	12 (12,13)	13 (12,14)	29 (25,36)	29 (24,30)
12 weeks	72 (58,93)	101 (82,114)	62 (48,77)	66 (53,78)	12 (11,14)	14 (13,14)	30 (26,36)	30 (26,32)
24 weeks	78 (70,99)	81 (68,97)	61.9 (58,73)	66.4 (66,73)	13 (12,15)	15 (14,14)	29 (24,30)	28 (27,28)

*Percentage of calculated energy requirements taken^High score good, +Low score good

Aims & Methods: Patients undergoing oesophagectomy/gastrectomy for cancer had a feeding jejunostomy placed routinely at surgery. Jejunal feeding was instituted postoperatively. If jejunal feeding was tolerated at discharge consenting patients were randomly allocated (stratified by gastric/oesophageal) to nutritional supplementation (600Kcal/day) via their feeding jejunostomies or no jejunal supplement. All patients received oral supplements and dietetic input. Patients were assessed at discharge and 3, 6, 12 and 24 weeks following discharge for fatigue (MFI-20), quality of life (EORTC QLQ-OES18), health economic analysis (independent living: EQ5D) as well as completing 2 day dietary diaries. Results were analysed non-parametrically (Mann-Whitney) and data presented as medians with interquartile ranges.
Results: 44 patients (M:F 29:15) were randomised, 23 received jejunal supplements. There was no difference between the groups in age, sex, neo-adjuvant chemotherapy, ASA grade, type of operation, operative time, blood loss, length of hospital stay, and inpatient complications.
Percentage of calculated energy requirement actually received was greater in the supplemented group at weeks 3 and 6 ($p < 0.0001$). Jejunal supplementation did not suppress oral energy intake. There was no difference between the two groups for oral energy intake at any time period. No complications were seen from jejunal feeding in the community.
After hospital discharge, scores for MFI-20, EQ5D and EORTC QLQ-OES18 were not different between groups at any time point. From hospital discharge fatigue improved and plateaued at 6 weeks ($p < 0.05$ for both groups), independence at 12 weeks ($p < 0.05$ for both groups) but no improvement was seen in quality of life until 24 week in the active group alone ($p < 0.02$) and not at all in the control group.
Conclusion: Dietary intake following hospital discharge after oesophageal or gastric surgery is poor. Addition of jejunal feeding over and above dietary advice and sip feeds is effective in providing patients with an adequate energy intake. Increased energy intake however, produced no obvious improvement in measures of fatigue, quality of life or health economics. Interestingly improvement in fatigue and independence plateaued by 12 weeks whilst there was little evidence of improvement in quality of life at 24 weeks.
Disclosure of Interest: None declared

OP380 LONG-TERM OUTCOME OF MINIMALLY INVASIVE TREATMENT OF EARLY GASTRIC CANCER BEYOND ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: The prognosis of early gastric cancer chiefly depends on the presence of lymph node metastasis, which has been reported at rates from 2% to 18%, with the rate increasing in proportion to the depth of invasion. For this reason, the presence of nodal metastasis cannot be totally excluded following ESD of early gastric cancer.
Aims & Methods: The aim of this study was to evaluate the long-term outcomes of combined endoscopic submucosal dissection (ESD) with laparoscopic lymph node dissection (LLND) and endoscopic full-thickness resection (EFTGR) with laparoscopic regional lymph node dissection (hybrid natural orifice transluminal endoscopic surgery, hybrid NOTES) for early gastric cancer (EGC).
A total of 23 patients with EGC underwent combined ESD with LLND and hybrid NOTES for early gastric cancer beyond endoscopic submucosal dissection between February 2007 and August 2009. Then the patients received periodic endoscopicfollow-up over 5 years.The main outcome measures were curability, recurrent rate, and survival rates.
Results: The curative resection rate of all cases was 95.7% (ESD with LLND 90.0% vs. hybrid NOTES 100%, respectively). Incomplete resection was shown in 1 (tumor-positive vertical margin). Histologically, 11 cases were mucosal cancers, and 12 were submucosal cancers. And there were 12 undifferentiated cancers. The median tumor size was 3.4 cm (range, 1.2–5.7cm) in long diameter. The lymphovascular invasion was found in 3 cases with 1 lymph node metastasis. 5 patients underwent additional gastrectomy because of tumor-positive margins or treatment-related complications. During over 5 year follow-up periods, none showed local recurrence or lymph node metastasis. The 5 year overall survival rates and disease-free survival of the patients was100% in both.
Conclusion: Combined ESD with LLND and hybrid NOTES showed favorable long term clinical outcomes. They could be utilized as a bridge between ESD and gastrectomy in selected patients with a risk of lymph node metastasis.

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Disclosure of Interest: None declared

OP381 ANALYSIS OF RISK FACTOR IN SALVAGE ENDOSCOPIC RESECTION FOR LOCAL RECURRENCE AFTER CHEMORADIOTHERAPY FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Local failure after definitive chemoradiotherapy (CRT) is the major problem for patients with esophageal squamous cell carcinoma (ESCC). If the local failure is a superficial lesion without any metastasis, it can be treated with salvage endoscopic resection (sER). However, there are few reports about the clinicopathological risk factors of recurrence after sER for local failure.
Aims & Methods: The aim of this study was to clarify the risk factors of recurrence after sER for local failure after CRT for ESCC. We enrolled consecutive patients treated with sER for local recurrence between 1998 and 2013 in our institution, and excluded patients whose resected specimen was not contain cancer cells. The indication criteria for sER as followed: (1) no lymph node or distant metastasis after CRT, (2) absence of ulceration in primary site after CRT, (3) depth of tumor invasion evaluated as limited within T1. The procedure of sER was endoscopic mucosal resection (EMR) with 2 channel method or endoscopic submucosal dissection (ESD) using dual knife. Recurrence after sER was defined and divided in two patterns as follows: (1) locoregional recurrence: local recurrence which could not control with repeated endoscopic treatment and/or locoregional lymph node metastasis; (2) distant metastasis; distant lymph node or organ metastasis. All patients provided written informed consent before procedure and the study protocol was approved by institutional review board in our institution.
Results: A total of 72 patients were included in this analysis, and patient's characteristics before CRT were as follows: median age of 66 years (range: 44—83); male/female ratio of 68/4; baseline clinical TNM Classification (6th edition) cT1/T2/T3/T4: 37/8/23/4; cN0/N1: 44/28; cStage IB/IIA/IIB/III: 31/20/15/6. Characteristics of local failure before sER: residue just after CRT/ local recurrent: 19/53; Median tumor size, mm (range): 9.5 (3-43); Method of sER: EMR in 67/ ESD in 5. Pathological results of sER were as follows; depth of resected tumor T1a(M)/T1b(SM): 45/27; horizontal margin +/−: 11/61; vertical margin +/−: 8/64; lymphatic vessel invasion +/− 4/68; venous invasion +/−: 10/62. At a median follow-up period of 36 months (range, 3-175 months) after sER; 45 patients (63%) did not detect any recurrence, whereas 13 (18%) and 14 (19%) patients were detected locoregional recurrence and distant metastasis, respectively. And the progression free and overall survival at 3 years were 48.9% and 61.2%. Multivariate analysis revealed that advanced cT-stage (OR, 2.34; 95% CI, 1.13—4.84) and residual tumor (OR, 4.95; 95% CI, 1.21—20.20) after CRT were associated with a significantly higher risk of recurrence after sER.
Conclusion: The ER is one of the curative salvage treatment options for local failure after definitive CRT. The results from this study indicates that the characteristics of before CRT or sER are more influential risk factors for recurrence after sER compared with the pathological findings of endoscopic resected specimens.
Disclosure of Interest: None declared

OP382 SURVIVAL IMPACT OF POSTOPERATIVE BODY MASS INDEX IN GASTRIC CANCER PATIENTS UNDERGOING GASTRECTOMY

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Introduction: The relationship between body mass index (BMI) and the survival of postoperative gastric cancer patients is not clear, even though weight loss is inevitable after gastrectomy.

Aims & Methods: This study was to evaluate the relationship between BMI and long-term survival in gastric cancer patients undergoing gastrectomy. Patients who underwent gastrectomy for gastric cancer between 2000 and 2008 were included in the study (n = 1,909). Patients were divided into three groups based on their BMIs: low (< 18.5 kg/m^2), normal (18.5–24.9 kg/m^2), and high BMI (≥25.0 kg/m^2). Patient survival was compared according to BMI at two time points: baseline and 1 year after surgery. Laboratory data were obtained from patients who had surgery after 2006.

Results: Regarding BMI 1 year after surgery, overall survival, disease-specific survival, and recurrence-free survival were longer in the high BMI group than the low and normal BMI groups. In a Cox proportional hazards model, adjusting for the patient's age, sex, tumor stage, histology, and curative resection, a high BMI 1 year after surgery was associated with lower overall mortality compared to normal BMI (Hazard Ratio 0.51; 95% confidence interval, 0.26-0.98). However, BMI at baseline was not an independent prognostic factor. Total protein and albumin levels were slightly higher in the high BMI group 1 year after surgery.

Conclusion: BMI 1 year after surgery significantly predicted the long-term survival of patients with gastric cancer compared with the preoperative BMI. Aggressive nutritional support should be considered in these patients to improve their outcomes.

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Disclosure of Interest: None declared

OP383 LOW-TRAUMA FRACTURE AFTER GASTRECTOMY FOR GASTRIC CANCER: LONG-TERM FOLLOW-UP OBSERVATION STUDY

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Introduction: Gastrectomy is a known risk factor for decreased bone mass and it is expected to increase fracture incidence.

Aims & Methods: The aim of the study is to evaluate the incidence of low-trauma fracture in gastric cancer patients with gastrectomy and to figure out what predictive factors are.

We retrospectively reviewed 1687 patients who underwent gastrectomy for gastric cancer at St. Mary's hospital between September 1991 and December 2008. Patients with stage IV gastric cancer, history of cancer recurrence or other medical conditions that cause osteoporosis such as chronic liver disease, kidney disease and other cancer, were excluded. Among the patients with fracture, we excluded the patients with high energy injury. Low trauma fracture was diagnosed with annual bone scan, plain x-rays, MRI and medical records. We analyzed the incidence of low-trauma fracture by Kaplan-Meier analysis method. We evaluated the effects of age, sex, body mass index (BMI), anemia, tumor staging and type of gastrectomy.

Results: With median follow-up period of 94 months, the incidence of low-trauma fracture was 29.4% (332/1131). The cumulative incidence of fracture was 34.9 cases per 1000 persons-years. The cumulative incidence of fracture was 9.1% at 24th month after surgery, 19.6% at 48th month after surgery and it increased upto 24.8% at 60th month. Univariate analysis revealed that older age [Hazard ratio (HR) = 1.03, 95% confidence interval (CI) 1.02-1.04, $p < 0.001$], male (HR = 1.61; 95% CI = 1.25-2.07, $p < 0.001$), postmenopausal state (HR = 2.07; 95% CI = 1.27-3.36, $p = 0.003$), smoking (HR = 1.44, 95% CI = 1.14-1.80, $p = 0.002$) and stage III (vs. stage I; HR = 1.54; 95% CI = 1.08-2.18, $p = 0.016$) were risk factors for low trauma fracture after gastrectomy. Multivariate analysis showed that older age and smoking are risk factors. Type of gastrectomy and BMI did not significantly increase risk of fracture.

Conclusion: The incidence of low-trauma fracture was high in gastric cancer patients with gastrectomy, regardless of gastrectomy type. The patients with risk factors, such as old patients with smoking habits, require regular surveillance and medical interventions to prevent fracture.

Disclosure of Interest: None declared

OP384 DO ALL ELDERLY PATIENTS NEED TO UNDERGO ADDITIONAL SURGERY AFTER NON-CURATIVE ESD FOR EARLY GASTRIC CANCER?

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Introduction: When endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) results in a non-curative resection, additional surgery is recommended according to the Japanese gastric cancer treatment guidelines. However, for elderly patients, the contribution of additional surgery to their life prognosis is still controversial.

Aims & Methods: The aim of this study was to assess the survival outcomes of radical surgery compared with observation only in elderly patients after non-curative ESD. We reviewed existing data of all elderly patients (older than 80 years) who had undergone ESD for EGC at a prefectural Cancer Center between September 2002 and December 2012. We compared the overall and relapse-free survival rates after non-curative ESD between with and without additional surgery. According to the pathological results of ESD, the patients were divided into two groups: high-risk and low-risk. "High-risk" was defined as positive lymphatic or/and venous invasion, or submucosal deep (SM2) invasion. Cox proportional-hazards model was performed to estimate hazard ratio (HR) and 95% confidence interval (CI). Multivariate analysis was also performed to examine the effects of independent variables adjusted for the effects of each of the others.

Results: Of the 100 non-curative ESD patients, 20 patients underwent additional surgery and 80 were followed without surgery. There was no significant difference between the groups in Performance Status, American Society of Anesthesiologist score, comorbidities, and previous cancer history. Patients who did not undergo surgery tended to be older. The rate of high-risk patient was 95% in additional surgery group, and 49% in no additional surgery group. The median follow-up period in additional surgery group and no additional surgery group was 49.5 and 36 months, respectively. In additional surgery group, 2 patients (10%) died as a result of gastric cancer and 7 patients (35%) died from other causes. In no additional surgery group, 4 patients (5%) died from gastric cancer and 19 patients (24%) died from other causes. Overall 5-year survival rates in additional surgery group and no additional surgery group were 59 and 60% (log-rank p = 0.802, HR: 0.70 (95% CI 0.30-

Abstract number: OP383 Table 1: Cox proportional hazard models for cumulative incidence of low-trauma fracture in patients after gastrectomy

		Univariate analysis			Multivariate analysis		
Variables		HR	95% CI	*P* value	HR	95% CI	*P* value
Age		1.03	1.02-1.04	<.001	1.03	1.01-1.04	<.001
Male	vs. Female	1.61	1.25-2.07	<.001	1.18	0.36-3.91	.787
Postmenopausal	vs. Premenopausal	2.07	1.27-3.36	.003	1.49	0.89-2.49	.133
BMI		1.01	0.97-1.04	.786	0.99	0.96-1.03	.794
Diabetes mellitus		1.30	0.87-1.96	.202	1.11	0.73-1.68	.614
Smoking		1.44	1.14-1.80	.002	1.33	1.02-2.08	.038
Stage III	vs. Stage I	1.54	1.08-2.18	.016	1.46	0.37-1.20	.174
Subtotal gastrectomy	vs. Total gastrectomy	1.08	0.84-1.39	.528	1.04	0.81-1.35	.753

HR, hazard ratio; CI, confidence interval

1.62)). There was no significant difference in overall and relapse-free survival (log-rank p = 0.695, HR: 0.86 (95% CI 0.42-1.95)) between the groups. In high-risk patients, overall 5-year survival rate tended to be higher in additional surgery group than no additional surgery group (63% vs 53%). According to multivariate analysis, additional surgery was not an independent factor indicating a longer survival (HR: 1.70 (95% CI 0.60-4.58)).
Conclusion: In our retrospective study, additional surgery following non-curative ESD could not improve overall survival compared with non-surgical observation only. For the patients with histological findings of lymphovascular involvement or massive submucosal penetration, additional surgery might contribute to the extension of life expectancy. Thus, additional surgery after non-curative ESD may not be considered for all elderly patients, but for high-risk patients.
Disclosure of Interest: None declared

OP385 ADH1B AND ALDH2 ARE ASSOCIATED WITH METACHRONOUS SQUAMOUS CELL CARCINOMA AFTER ENDOSCOPIC RESECTION OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: A previous genome-wide association study identified two novel esophageal squamous cell carcinoma (ESCC) susceptibility genes, *ADH1B* and *ALDH2*. We investigated the characteristics of ESCC, and the relationship between "metachronous esophageal and/or pharyngeal squamous cell carcinoma (SCC) " and "the *ADH1B* & *ALDH2* risk alleles".
Aims & Methods: One hundred and twelve ESCC patients who had been treated by endoscopic resection were followed up by endoscopy for 12 months or longer. First, we performed a replication study to confirm the relationship between ESCC and "the *ADH1B* & *ALDH2* risk alleles" using 112 ESCC cases and 1,125 healthy controls. Next, we investigated the incidence and genetic/environmental factors for metachronous SCC development after endoscopic resection. We also analyzed the potential risk factors for metachronous SCC development using Cox's proportional hazards model.
Results: Rs1229984 located on *ADH1B* and rs671 located on *ALDH2* were significantly associated with ESCC progression ($P = 2.96 \times 10^{-15}$ [AA vs AG + GG], and $P = 9.14 \times 10^{-10}$ [TC vs TT + CC]). Patients with rs1229984, those with rs671, smokers, and heavy alcohol drinkers (43.5 g/day ethanol) developed metachronous SCC more frequently ($P = 2.34 \times 10^{-3}$, 1.53×10^{-3}, 5.39×10^{-3}, and 0.018, respectively), and the hazard ratios were 2.91 (95% confidence interval [CI] 1.46-5.81), 4.19 (95% CI 1.47-11.96), 4.45 (95% CI 1.56-12.73), and 2.53 (95% CI 1.17-5.46), respectively. Multiple logistic regression analysis revealed that rs1229984, rs671, and smoking status were independently associated with the risk of metachronous SCCs.
Conclusion: Our findings elucidated the crucial role of multiple genetic variations in *ADH1B* & *ALDH2* as metachronous biomarkers for ESCC patients.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30
DIAGNOSIS AND TREATMENT OF PANCREATIC TUMORS – ROOM E6

OP386 DISCRIMINATING PANCREATIC CYST TYPE AND GRADE USING CLINICAL CRITERIA: THE RESULTS OF A LARGE RETROSPECTIVE COHORT

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Introduction: The current preoperative classification of pancreatic cystic neoplasms is based on a combination of imaging and clinical criteria. However, the diagnostic performance of such criteria is relatively inaccurate. The aim of this study was to design an improved combination of preoperative features to enhance the classification of pancreatic cysts.
Aims & Methods: We retrospectively analyzed 1026 patients with pancreatic cystic neoplasms who underwent surgical resection. To determine which preoperative clinical and radiological features that best predicted cyst type and grade of dysplasia, various combinations of features were analyzed using the Multivariate Organization of Combinatorial Alterations (MOCA) algorithm. Millions of feature combinations were tested and the most informative features were then used to design composite clinical markers for each cyst category. This model was then validated in an independent cohort consisting of 130 patients.
Results: The first cohort consisted of 584 patients with intraductal papillary mucinous neoplasms (IPMN), 332 with serous cystadenomas (SCA), 78 with mucinous cystic neoplasms (MCN), and 42 with solid-pseudopapillary neoplasms (SPN). Composite clinical markers were identified that classified SCAs with 95% sensitivity and 83% specificity; SPNs with 89% sensitivity and 86% specificity; MCNs with 91% sensitivity and 83% specificity, and IPMNs with 94% sensitivity and 90% specificity. None of the individual features were as accurate as the composite markers. A composite marker was also developed that correctly identified SPN, MCNs or IPMNs with high-grade dysplasia or associated carcinoma, with 84% sensitivity and 81% specificity. When applied to an independent cohort of 130-patients, the composite clinical markers had high sensitivity for SCAs, SPNs, and MCNs (100%, 89%, and 90%, respectively), and modest sensitivity for IPMNs. The specificities of the composite clinical markers ranged from 71% to 88% for SCAs, SPNS, MCNs and IPMNs.
Conclusion: The composite markers identified here integrate clinical and radiologic observations into a coherent framework. These composite markers have improved performance characteristics over individual clinical features and offer the potential for a more accurate classification of pancreatic cystic neoplasms.
Disclosure of Interest: D. Masica: None declared, M. Dal Molin: None declared, C. Wolfgang: None declared, T. Tomita: None declared, M. Ostovaneh: None declared, A. Blackford: None declared, R. Moran: None declared, J. Law: None declared, T. Barkley: None declared, M. Goggins Conflict with: inventor royalties, M. Canto: None declared, M. Pittman: None declared, J. Eshleman: None declared, S. Ali: None declared, E. Fishman: None declared, I. Kamel: None declared, S. Raman: None declared, A. Zaheer: None declared, N. Ahuja: None declared, M. Makary: None declared, M. Weiss: None declared, K. Hirose: None declared, J. Cameron: None declared, N. Rezaee: None declared, J. He: None declared, Y. J. Ahn: None declared, W. Wu: None declared, Y. Wang: None declared, S. Springer: None declared, L. Diaz, Jr. Conflict with: inventor royalties, N. Papadopoulos Conflict with: inventor royalties, R. Hruban Conflict with: inventor royalties, K. Kinzler Conflict with: inventor royalties, B. Vogelstein Conflict with: inventor royalties, R. Karchin: None declared, A. M. Lennon: None declared

OP387 PATTERN OF RECURRENCE IN RESECTED IPMN OF THE PANCREAS: PRELIMINARY RESULTS FROM A MULTI-INSTITUTIONAL INTERNATIONAL STUDY

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Introduction: The natural history of the pancreas remnant in patients who have had partial pancreatectomy for IPMN has been investigated in studies containing a relatively small number of patients and with short follow-up.
Aims & Methods: The aim of this study is to collect a large number of patients underwent partial pancreatectomy for IPMN and then followed for a long period of time to better understand the natural history of this disease. A trial was planned in the European Study Group for Cystic Tumors of the Pancreas in order to investigate the recurrence pattern and the prognostic factors influencing the recurrence of IPMN after partial pancreatectomy. A preliminary analysis on data coming from 1686 patients included in the study is presented in this report.
Results: The overall recurrence rate was 15.7%. In 12.5% of patients the recurrence was represented by progression of clinically significant IPMN in the pancreas remnant, 2.2% developed liver metastasis, 0.4% peritoneal carcinomatosis, 0.3% local recurrence and 0.2% new onset pancreas cancer. The overall risk of progression of the diseases at 1, 5 and 10 yrs was 7%, 14% and 21% respectively. Comparing the 1, 5 and 10 yrs risk of progression in different morphologic types, mixed-type IPMN showed a worse prognosis (5%, 24.3% and 37.6%) compared to main duct type (4.3%, 18.2% and 25.7%) and branch duct type (6%, 15% and 28.7%) (p = 0.01). Comparing histology, patients with pancreatico-biliary type showed a 1, 5 and 10 yrs risk of recurrence (7.2%, 50.2% and 62.2%) higher than gastric (2.4%, 17.1% and 18.7%), intestinal (2.6%, 11.4% and 18.6%) and oncocytic (5.8%, 15.3% and 15.3%) ($p < 0.0001$). Data on frozen section of the resection margin was available in 747 patients. A positive resection margin was associated with an increased risk of recurrence at 1, 5 and 10 yrs (7.6%, 27.4% and 35.5% vs 3%, 12.6% and 18.5% respectively; $p < 0.0001$).
Conclusion: Our data show that mixed type IPMN, pancreatico-biliary histology and a positive resection margin are negative prognostic factors for recurrence in patients with IPMN who have had partial pancreatectomy.
Disclosure of Interest: None declared

OP388 PANCREATIC JUICE CYTOLOGY WITH THE CELLBLOCK METHOD IN PATIENTS WITH BRANCH-DUCT TYPE INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS: USEFULNESS FOR PREOPERATIVE DIAGNOSIS OF MALIGNANCY AND PATHOLOGICAL SUBTYPING

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Introduction: In recent years, we have attempted to improve the preoperative diagnosis of malignant branch duct intraductal papillary mucinous neoplasms (BD-IPMN) by introducing the cellblock method for pancreatic juice cytology (CB-PJC).
Aims & Methods
Aim: To elucidate the efficacy and safety of CB-PJC for the determination of surgical indication in patients with BD-IPMN.

Subjects: One hundred and thirty-eight patients (the total number of ERCPs: 168) with BD-IPMN from whom pancreatic juice was collected under ERCP for CB-PJC at our medical center between December 2005 and August 2014 were recruited to this study.
Methods: In these 138 subjects, we retrospectively evaluated the following: (1) the diagnostic efficacy of CB-PJC for Papanicolaou's classification and for identification of histological subtypes in 28 subjects with resected IPMNs, (2) the percentage of IPMN lesions which developed into invasive cancer and the progression of IPMN lesions in 66 subjects who underwent follow-up for more than 1 year after CB-PJC, and (3) post-ERCP adverse events in 168 ERCPs. The definition of malignancy by CB-PJC was determined to be Class IIIb-V according to Papanicolaou's classification system, and that for resected specimens was determined to be high-grade dysplasia (HGD) and invasive carcinoma derived from IPMN (IC). Pathological subtypes were classified as follows: gastric (G), intestinal (I), pancreatobiliary (PB), and oncocytic (O). The antibodies used for the immunostaining of CB-PJC and resected specimens were as follows: Ki-67, p53, MUC1, MUC2, MUC5AC, MUC6, and CDX-2.
Results: (1) In the 28 resected specimens, the pathological grade was IC in 9 patients, HGD in 5, and low-intermediate grade dysplasia (L-IGD) in 14. The sensitivity, specificity, and accuracy of CB-PJC for preoperative diagnosis of malignancy were 50%, 100%, and 68%, respectively, with only HÿŸE stain and AB-PAS stain, while they were 79%, 100%, and 89%, respectively, by adding immunohistological staining. The agreement rate of the preoperative subtype by CB-PJC with the subtype of resected specimens was 93%. (2) Details of 66 subjects were as follows: median follow-up period was 3.4 years, the rate of the existence of mural nodules was 18%, the rate of BD-IPMN 30 mm or more in size was 41%, and the subtype of CB-PJC was G in 57 patients, I in 4, and PB + G in 5. All 4 patients who underwent surgery during follow-up were pathologically diagnosed as L-IGD. In the remaining 62 patients without resection of IPMN during follow-up, the imaging onset of IC was not detected at all, while the progression of IPMN was detected in 14 patients (21%). Multivariate analysis revealed the risk factor of progression to be non-gastric type. The cumulative 5-year progression rate in this group was 89%. (3) The percentage of post-ERCP pancreatitis was 7.7% (13/168: mild, 12; moderate, 1).
Conclusion: The diagnostic efficacy of preoperative CB-PJC for malignant BD-IPMN was good. The results such as the excellent diagnostic yield of the pathological subtyping by CB-PJC and the impact of pathological subtype on the progression of follow-up IPMN may suggest the feasibility of applying preoperative subtyping by CB-PJC to decisions as to whether surgery is indicated.
Disclosure of Interest: None declared

OP389 COMPARATIVE ANALYSIS BETWEEN SENDAI GUIDELINES AND THE EUROPEAN EXPERTS CONSENSUS STATEMENT ON BD-IPMN OF THE PANCREAS

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Introduction: Management decisions on Branch-duct Intraductal Papillary Mucinous Neoplasms (BD-IPMN) of the pancreas are mainly based on imaging features. However, several consensus guidelines proposed different features predicting malignancy and no clarity exists about which lesions will progress to malignancy ultimately.
Aims & Methods: The aim was to perform a comparative analysis between Sendai guidelines and the European experts consensus statement on BD-IPMN. This retrospective study included 120 consecutive patients (65 males, mean age: 57.75 years) with a BD-IPMN histologically proven between 2006 and 2014. Neoplasms were classified as malignant if high-grade dysplasia or invasive carcinoma were detected. Symptoms, mural nodule and wirsung > 6mm were considered as indications for surgery according to the European consensus. Patients with one or more worrisome features or high-risk stigmata were considered as Sendai-positive. Finally, agreement between both guidelines and predictive values for malignancy were analyzed.
Results: The global malignancy rate was 30% (n = 36). Among the 93 European-positive patients, 31(33.3%) harbored a malignant tumor (sensitivity: 86.1%, specificity: 26.2%, accuracy: 45.8%), with 5 false-negative cases (4.2%). By contrast, within 89 Sendai-positive patients, 34 malignant BD-IPMN (38.2%) were found and only 2 false-negative cases (1.7%)(sensitivity: 94.4%, specificity: 34.5%, accuracy: 52.5%). There were 46 cases (38.3%) in disagreement, being 7 of them malignant forms. The features predicting malignancy within the 21 Sendai-positive European-negative patients were cyst size ≥ 30mm (n = 7), wirsung ≥ 5mm (n = 6), abrupt change in caliber of the Wirsung (n = 5) and thickened/enhancing walls (n = 12). The 25 Sendai-negative European-positive cases underwent surgery for relief of symptoms.
Conclusion: Sendai guidelines have a higher accuracy. Both consensus increased surgical indications.
Disclosure of Interest: None declared

OP390 COMPARING PROCORE NEEDLE WITH FINE NEEDLE IN ENDOSCOPIC ULTRASOUND-GUIDED TISSUE SAMPLING FOR SUSPECTED PANCREATIC CANCER

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Introduction: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is widely used for diagnosis of pancreatic mass lesions. In order to overcome some limitations of FNA, Endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) with ProCore needle was developed. A recent randomized trial showed that diagnostic sufficiency, technical performance, and safety profiles of FNA and ProCore needles were comparable for solid pancreatic mass.[1] However, there wasn't reported study to compare the diagnostic accuracy of both FNA and ProCore needle in the same patient yet.
Aims & Methods: This study aimed to compare the diagnostic accuracy of both FNA and ProCore needles in patients with suspected pancreatic cancer. We conducted crossover randomized control study at Samsung Medical Center between July 2013 and February 2015. A total of 60 consecutive patients who was suspected to have an unresectable pancreatic cancer were enrolled. We performed four needle passages on each patient with twice by 22G FNA (EZ Shot2; Olympus) and twice by 22G ProCore (EchoTip ProCore; Cook Medical) needle. The order which needle should be used first was randomized. The primary outcome was diagnostic accuracy and the secondary outcomes included specimen quality, and rate of complication.
Results: The mean age of 60 patients was 61.6 ± 10.0 years, and 58.3% of them were male. The mean size of 60 lesions was 3.13 ± 0.85 cm. The locations of them were respectively 26.7%, 11.7%, 41.7% and 20% in the head, uncinated process, body, and tail. The overall diagnostic accuracy did not differ between ProCore and fine needle (94.9% vs. 93.3%, p = 1.000). Furthermore, the adequacy, cellularity and blood contamination of specimen was comparable between two needles. None of the complications including bleeding, infection and pancreatitis were reported after procedure.

Table 1: Total diagnostic accuracy

	FNA		FNB		
	N	%	N	%	*P*
Cytologic diagnosis					0.743
No	6	10.0	4	6.8	
Yes	54	90.0	55	93.2	
Histologic diagnosis					0.670
No	16	26.7	13	22.0	
Yes	44	73.3	46	78.0	
Diagnosis					1.000
No	4	6.7	3	5.1	
Yes	56	93.3	56	94.9	

Conclusion: The diagnostic accuracy, specimen quality, and safety profiles are comparable between ProCore and fine needle in suspicious unresectable pancreatic cancer. (Clinical trial registration number: NCT01876069)

Reference

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Disclosure of Interest: None declared

OP391 INTERACTION BETWEEN SURGICAL AND ONCOLOGICAL PALLIATIVE THERAPIES IN PANCREATIC CANCER UNRESECTABLE AT SURGERY

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Introduction: Pancreatic cancer (PC) is frequently diagnosed at highly recalcitrant stages. In patients with locoregional disease, curative-intent resection may significantly prolong survival and improve quality of life; however, up to 30% are found to be unresectable at exploratory laparotomy (EXL) due to unexpected locally advanced or metastasized (LA/M) disease. A prophylactic double bypass (PDB, hepaticojejunostomy and gastroenterostomy) to prevent malignant bile and duodenal obstruction, represents the standard of care; however, minimal-invasive on-demand strategies are under debate. The aim was to compare PDB with EXL alone regarding postoperative outcome, subsequent initiation of palliative chemotherapy (PCT) and disease-specific survival (DSS) in unexpected LA/MPC.

Aims & Methods: An observational cohort study was conducted between 2004 and 2013 on patients found to have locally advanced or metastasized PC at EXL. The diagnosis was confirmed histologically. Demographics, operative and post-operative data were recorded together with outcomes of postoperative PCT and observation/supportive care (OSC). DSS was determined using the Kaplan-Meier method, pairwise comparison was performed using the log-rank test, prognostic interactions between PDB, EXL, PCT and OSC were investigated using Cox's regression model.
Results: Of 503 patients with pancreatic cancer who preoperatively had been considered resectable, 104 were found to be unresectable at laparotomy (38 locally advanced PC, 36 liver metastasis, 30 carcinomatosis, unresectability rate 20.7%). Patients with non-disseminated LAPC had a longer survival (9.9 months; 95%CI 8.2, 11.5) than patients with systemically disseminated PC (liver metastasis 3.6 months; 95%CI 2.4, 4.8; $p = 0.002$, peritoneal carcinomatosis 3.7 months; 95%CI 2.4, 5.0; $p = 0.264$). Seventy-four patients underwent PDB (30 EXL +/- GE). PDB was associated with longer operation time, higher blood loss, higher rate of major complications and prolonged length of stay; however, EXL/PDB groups showed no differences regarding 30/90-days mortality, PCT initiation rate or median DSS (EXL 6.7, PDB 8 months, $p = 0.174$). Compared to OSC, PCT was associated with significantly prolonged median DSS for locally advanced (16 vs 6 months, $p = 0.046$) and metastasized PC (10 vs 2 months, $p < 0.001$). PCT receivers with prior EXL had a significantly better median survival than PCT receivers with prior PDB (18.5 vs 11.6 months, $p = 0.023$).
Conclusion: The data of the present study indicate that patients with pancreatic cancer found to be unresectable at laparotomy may not have long-term benefits from prophylactic double bypass procedures. In the light of new, more effective chemotherapy regimens and less invasive alternatives to surgical bypass, this vulnerable patient group deserves additional prospective studies to define optimum palliation strategies.

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Disclosure of Interest: None declared

OP392 PROGRESSION OF PANCREATIC CANCER WITH LUNG METASTASIS IS RELATIVELY SLOW

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Introduction: Lung metastasis from pancreatic cancer is rare and the prognosis after lung metastasis is unknown.
Aims & Methods: We investigated the prognostic factors in patients with pancreatic cancer with lung metastasis. Medical records from prospectively registered database for unresectable or recurrent pancreatic cancer receiving chemotherapy between September 2007 and December 2014 were reviewed and those who met the following criteria were analyzed. 1. Certain distant metastasis was found on CT scans, 2. The diagnosis of adenocarcinoma was confirmed from primary or metastatic lesions, and 3. Performance status (PS) was 0 or 1.Background characteristics (sex, age, PS, metastatic site (lung alone or others), the values of CEA, CA19-9, WBC, Hb, ALP, CRP, Alb) were analyzed for overall survival (OS) by univariate and multivariate analyses and prognostic factors were determined. Survival from the final chemotherapy (BSC survival) was also analyzed in these factors.
Results: A total of 335 patients were included in the analyses. Median OS and median BSC survival was 200 days and 64 days, respectively. Lung metastasis, PS, CEA, CA19-9, WBC, and ALP were significant prognostic factors for OS in univariate analysis and lung metastasis (hazard ratio (HR) = 1.68, 95% CI, 1.033-2.727; $p = 0.036$), PS, CA19-9 and WBC were independent prognostic factors in multivariate analysis. Lung metastasis, PS, CEA, CA19-9 and WBC were significant prognostic factors for BSC survival in univariate analysis and lung metastasis (HR = 1.73, 95% CI 1.076-2.795, $p = 0.024$), PS, CA19-9 and WBC were independent prognostic factors in multivariate analysis.OS and BSC survival in patients with lung metastasis were 311 days and 121 days, respectively.
Conclusion: Lung metastasis alone from pancreatic cancer indicates slow progression compared to other metastasis.
Disclosure of Interest: None declared

OP394 CATHETER DRAINAGE VERSUS RELAPAROTOMY FOR SEVERE PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY: A MULTI-CENTRE PROPENSITY-MATCHED ANALYSIS

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Introduction: Postoperative pancreatic fistula (POPF) after pancreatoduodenectomy is a potentially life-threatening complication. Treatment consists of catheter drainage or relaparotomy. We compared these treatment strategies in a multicentre study.
Aims & Methods: In a retrospective observational cohort study all patients with severe POPF (ISGPF grade B/C) following pancreatoduodenectomy between January 2005 and September 2013 in 9 centres of the Dutch Pancreatic Cancer Group were analysed. Patients were divided in two groups based on the initial intervention for POPF: catheter drainage or relaparotomy. We performed propensity score matching to correct for selection bias. Primary endpoint was mortality. Secondary endpoints included new onset organ failure.
Results: Out of 2196 of pancreatoduodenectomies, 309 patients underwent an intervention primarly for a severe POPF: 227 patients (73%) underwent primary catheter drainage while 82 (27%) underwent primary relaparotomy. Of all patients treated with primary catheter drainage, 83% was treated with catheter drainage only. A total of 75 patients undergoing primary relaparotomy were successfully matched to 75 patients undergoing primary catheter drainage (i.e. had well balanced baseline characteristics). Mortality was significantly lower after primary catheter drainage than after primary relaparotomy (17% vs. 36%; risk ratio [RR] 0.48, 95% confidence interval [CI] 0.28-0.80, $P = 0.007$), as was multiple-organ failure (20% vs. 39%, RR 0.51, 95% CI 0.29- 0.30, $P = 0.02$).
Conclusion: Primary catheter drainage is associated with better clinical outcomes, including lower mortality, compared to primary relaparotomy in patients with severe pancreatic fistula after pancreatoduodenectomy.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30
INTERVENTIONAL BILIARY ACCESS AND DRAINAGE – ROOM B3

OP395 EVALUATION OF UTILITY OF DIAGNOSTIC AND THERAPEUTIC ERC USING A SHORT DOUBLE-BALLOON ENDOSCOPE IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY: A JAPAN MULTICENTER PROSPECTIVE DB-ERC STUDY

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Introduction: Endoscopic approaches for pancreatobiliary diseases in patients with surgically altered gastrointestinal anatomy had been difficult. However, newly developed double-balloon endoscope (DBE) facilitated a variety of endoscopic interventions in such patients. The aim of this study was to make a prospective assessment on the efficacy and safety of ERC using a short DBE (DB-ERC) in postoperative patients with various types of gastrointestinal reconstruction.
Aims & Methods: This study was conducted as a multicenter, single arm, prospective trial at 5 tertiary care academic centers and 3 community based hospitals in Japan (UMIN-CTR number, 000010375). Biliary disease patients with altered gastrointestinal anatomy were enrolled. The primary endpoint was the success rate of reaching a targeted site (major papilla or choledochojejunostomy anastomosis). The secondary endpoints were assessment of safety, success rate of cannulation and contrast injection of the targeted bile duct, and success rate of treatments relevant to ERC.
Results: From June 2013 to May 2014, 316 patients were invited to the study and 2 patients declined. A total of 314 patients were enrolled, though 3 patients were cancelled prior to procedures. The reasons for cancellation were; 1 patient died from the primary disease, another suffered from bradycardia caused by sedative, and the other spontaneously passed biliary stones. The final figure of participants was 311. The success rate of reaching the targeted site defined as the primary endpoint was 97.7% (304/311). The respective success rates of ERC-related

interventions defined as the secondary endpoints were; diagnosis 96.4% (293/304) and therapy 97.9% (283/289). Regarding adverse events, the occurrence rate was 10.6% (33/311). Additionally, the success rates of reaching the targeted site by type of surgical reconstruction methods were; Roux-en-Y (R-Y): 97.0% (197/203), Billroth II (B-II): 96.2% (25/26), pancreaticoduodenectomy (PD): 100% (44/44), pylorus-preserving pancreaticoduodenectomy (PpPD): 100% (31/31), and others: 100% (7/7). The diagnostic success rates by type of surgical reconstruction methods were; R-Y: 97.0% (191/197), B-II: 100% (25/25), PD: 98.0% (43/44), PpPD: 90.0% (28/31), and others: 85.7% (6/7). The therapeutic success rates by type of surgical reconstruction methods were; R-Y: 97.9% (185/189), B-II: 100% (24/24), PD: 100% (43/43), PpPD: 96.3% (26/27), and others: 83.3% (5/6). The occurrence rates of adverse events by type of surgical reconstruction methods were; R-Y: 10.3% (21/203), B-II: 23.1% (9/26), PD: 2.3% (1/44), PpPD: 6.5% (2/31), and others: 0% (0/7).

Conclusion: DB-ERC for biliary diseases in patients with altered gastrointestinal anatomy is extremely effective and safe for reaching the targeted site and for completing the ERC-related interventions. DBE provides high and stable performance in assisting ERC in such patients, and especially the use of a short type DBE should be recommended.

Disclosure of Interest: None declared

OP396 INTERNATIONAL MULTICENTER COMPARATIVE TRIAL OF EUS-GUIDED BILIARY DRAINAGE VS. ENTEROSCOPY-ASSISTED ERCP IN PATIENTS WITH SURGICAL ANATOMY AND BILIARY OBSTRUCTION

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Introduction: ERCP is challenging in patients with surgically altered UGI anatomy with reported cannulation rates of enteroscopy-assisted ERCP (e-ERCP) between 48 and 70%. EUS-BD techniques potentially offer multiple advantages in these patients. It is currently unknown how e-ERCP and EUS-BD compare in such patients.

Aims & Methods

Aims: 1) to compare efficacy and 2) safety of both techniques and 3) study predictors of these outcomes.

Methods: This was an international multicenter comparative cohort study at 10 tertiary centers (3 US, 3 European, 3 Asian and 1 South American; 2 centers with published expertise on e-ERCP and 8 centers on EUS-BD) between 2008 and 2014. All patient with altered UGI anatomy who presented with benign or malignant biliary obstruction and subsequently underwent e-ERCP (2 centers) or EUS-BD (8 remaining centers) were included. Outcomes data included technical success (biliary access with cholangiography and stent placement (when indicated)), clinical success (resolution of biliary obstruction) and adverse events (graded according to the ASGE lexicon).

Results: A total of 98 patients (mean age 58yr, female 67%, malignant biliary obstruction 36%) underwent EUS-BD [n = 49; Hepatogastrostomy (HG) 33 (67.4%), antegrade stenting (AG) 10 (20.5%), rendezvous 2 (4%), Hepatojejunostomy 3 (6.1%), Hepatoduodenostomy 1 (2%)] or e-ERCP [n = 49; single balloon enteroscopy (SBE)-ERCP 5 (10.2%), double balloon enteroscopy (DBE)-ERCP 42 (85.7%), or colonoscope-ERCP 2 (4.1%)]. There was higher frequency of malignant obstruction in the EUS-BD group ($p < 0.0001$), but higher frequency of Roux-en-Y (RY) anatomy ($p < 0.0001$) and native ampulla ($p < 0.0001$) in the e-ERCP group. Technical success was achieved in 48 (98%) patients in the EUS-BD group as compared to 32 (65.3%) patients in the e-ERCP group (OR 12.48, $p = 0.001$). Clinical success (intention-to-treat) was attained in 88% of patients in EUS-BD group as compared to 60.4% in the e-ERCP group (OR 2.83, 95% CI 1.10-7.31, $p = 0.03$). Procedural time was significantly shorter in the EUS-BD group (55min vs 95min, $p < 0.0001$). Adverse events occurred more commonly in EUS-BD group (20% vs. 4%, $p = 0.01$). However, majority (90%) of complications were mild/moderate. Length of stay was significantly longer in the EUS-BD group (6.6d vs. 2.4d, $p = < 0.0001$). On multivariate analysis, EUS-BD was independently associated with increased rate of clinical success (OR 4.31, $p = 0.02$) and adverse events (OR 8.74, $p = 0.01$).

Conclusion: EUS-BD offers multiple advantages over e-ERCP in patients with surgical UGI anatomy, including higher technical success, higher clinical success, and reduced procedural times. However, EUS-BD is also associated with increased rate of adverse events, although severe events are uncommon.

Disclosure of Interest: M. Khashab Consultancy: Boston Scientific, Olympus America, Xlumena, M. El Zein: None declared, K. Sharzehi: None declared, F. Marson: None declared, O. Haluszka: None declared, A. Small: None declared, Y. Nakai: None declared, D. H. Park: None declared, R. Kunda: None declared, A. Teoh: None declared, I. Peñas: None declared, M. Perez-Miranda Consultancy: Boston Scientific, Xlumena, V. Kumbhari: None declared, S. Ngamruengphong: None declared, A. Messallam: None declared, S. Van der Merwe Consultancy: Boston Scientific, Cook endoscopy, E. Artifon: None declared, A. Ross: None declared

OP397 OUTCOMES OF PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY FOR THE RELIEF OF MALIGNANT JAUNDICE IN ENGLAND BETWEEN 2001 AND 2014

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Introduction: Percutaneous transcutaneous cholangiography (PTC) is widely utilised to relieve malignant obstructive jaundice, especially when endoscopic retrograde cholangiopancreatography (ERCP) has failed or surgical resection is not indicated. Recent local audit data suggests PTC carries a high peri-procedural mortality and complication rate and there is a lack of national outcome data.

Aims & Methods: Using Hospital Episode Statistics (HES), subjects with cancer of the pancreas, biliary tree, gallbladder, small intestine and liver that underwent PTC were identified. Mortality, major complication rates, readmission and variation in outcomes between healthcare providers were examined. Associations between age, sex, comorbidity, cancer type and mortality were examined using multivariate regression analysis.

Results: Between April 2001 and March 2014, 15,390 subjects were identified (49.8% male). 2,175 underwent surgical resection after PTC and 13, 216 had no surgical intervention. The crude 30-day mortality was 9.7% for subjects undergoing surgery after PTC and 27.7% for palliative subjects and three-month mortality 25.8% and 55% respectively. The 30-day readmission rate for palliative subjects was 19.7%. The major complication rate was 25.9% in the surgical resection group and 24% in the palliative group. The most common complications were cholangitis (28.1%), acute kidney injury (21.4%), displacement or blockage of the stent (15.4%) and other sepsis (22.2%). In subjects undergoing PTC for palliation, increasing age was strongly associated with 30-day mortality (65-74 years OR 1.88(95% CI 1.31-2.71), p 0.001, 75-84 years 2.51(1.74-3.61), $p < 0.001$ and > 85 years 3.53(2.43-5.12), $p < 0.001$). 30-day mortality was also associated with a higher Charlson medical co-morbidity score of 10-14 (1.16(1.05-1.28), p 0.002) and > 20 (1.23(1.09-1.39), p 0.001). Female subjects had a better outlook at 30 days (0.83(0.76-0.89), $p < 0.001$). The type of cancer causing biliary obstruction was not associated with 30-day mortality. There was a large variation in 30-day mortality between healthcare providers for palliative subjects. Excluding providers that performed less than 5 PTCs per year, 30-day mortality varied between 6.3 and 50%. In the five healthcare providers that performed more than 250 PTCs per year, 30-day mortality was less than 30%.

Conclusion: In subjects undergoing PTC for the palliative relief of malignant jaundice, 30-day mortality is 27.7%, major complications occur in 24% and readmission occurs in 19.7%. There is a large variation in outcomes between healthcare providers. Mortality is highest in older males with increasing co-morbidity and careful multidisciplinary selection of patients who will benefit from PTC for relief of significant symptoms from jaundice or as a bridge to chemotherapy is clearly merited.

Disclosure of Interest: None declared

OP398 MULTICENTER RANDOMIZED PHASE II STUDY: PERCUTANEOUS BILIARY DRAINAGE VS EUS GUIDED BILIARY DRAINAGE : RESULTS OF THE INTERMEDIATE ANALYSIS

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Introduction: Since 10 years, EUS guided biliary drainage is an option as EUS guided choledoco-duodenostomy or Hepatico-gastrostomy. Two small randomized studies showed no difference between EUS guided BD vs Percutaneous drainage. The aim of this work was to evaluate in a multicenter randomized study the percutaneous biliary drainage (PBD) vs EUS guided biliary drainage (EBD) in patients with an obstructive jaundice when ERCP failed or impossible due do duodenal involvement or previous Surgery as gastrectomy or Wipple resection.

Aims & Methods: Inclusion criteria were: Benign or malignant obstructive jaundice with failure of ERCP.

Exclusion criteria were : ascites, Blood coagulation disorders, stenosis of the right bile duct.

Randomization ratio was 1 : 1, with a stratification by indication (benign vs malignant) and by centers (4 centers were included). The route of the biliary drainage was randomized as PTB (arm A) and EGD (arm B). But the choice of the EGD technique was free for the operator as (Anterograde transpapillary stenting, choledoco-duodenostomy, hepatico-gastrostomy). The main goal was to evaluate the specific morbidity and mortality during the 30 days following the biliary drainage in each arm. To prove a decrease of 50% of the morbidity rate in the EGD arm (A = 30%, B = 15%), 55 patients should be included in the EGD arm (B) as a Simon plan in 2 steps with an intermediate analysis to exclude severe adverse events in the EGD arm.

Results: Forty seven patients from 4 centres were included between 2011 to 2013. Six patients were excluded. Forty one patients were randomized(Arm A ; n = 21/ Arm B ; n = 20). The 2 groups were similar except the sex ratio (Female : Arm A, n = 11 ; Arm B, n = 2 ; p = 0.0036). The biliary stenosis was

malignant in 37 cases (Arm A, n = 19 ; Arm B, n = 18). Biliary access was successful in 100% in the Arm A and in 95% in the Arm B. Technical success was respectively 17/21 (85%) in the Arm A and 19/20 (95%) in the Arm B. No difference was showed regarding the decrease of the bilirubin level after the drainage in the two arms. Hospitalization time was significatively shorter in the Arm B (6 days range 3-30 days) than the Arm A (12 days range 2-52 days) p = 0.02. Nine patients died 30 days following the biliary drainage, 6 deaths were directly due to the procedure (Arm A = 3, Arm B = 3). A specific complication occurred in Twelve patients (60%) in the Arm A vs 7 (35%) in the Arm B : Bleeding (A = 4[19%], B = 1 [5%]), Cholangitis (A = 3 [15%], B = 1 [5%]), Sepsis not related to cholangitis (A = 7 [35%], B = 5 [25%]), Bile leakage (A = 1[5%], B = 1 [5%]).

Conclusion: Complication rate was higher in the Arm A (60%) vs Arm B (35%), we have decided to stop the Arm A and to continue to include patients only in the EGD Arm up to reach the total number of 55 patients.

Disclosure of Interest: None declared

OP399 EUS-GUIDED BILIODIGESTIVE ANASTOMOSIS FOR DRAINAGE OF MALIGNANT DISTAL BILIARY OBSTRUCTION USING A NOVEL CAUTERY-TIPPED LUMEN-APPOSING STENT DELIVERY SYSTEM: A LARGE RETROSPECTIVE MULTICENTER EUROPEAN STUDY

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Introduction: EUS-guided biliary drainage (EUS-BD) is a minimal invasive alternative for palliative treatment of unresectable malignant distal biliary obstruction in patients who failed ERCP. A novel lumen-apposing, self-expanding fully covered metal stent incorporated in an electrocautery enhanced delivery system has been developed to facilitate creation of bilio-digestive anastomosis and decrease the risk of complications. The aim of our study was to evaluate the safety, feasibility and clinical effectiveness of this new device for EUS-BD in these patients.

Aims & Methods: Retrospective analysis of all consecutive patients with unresectable malignant distal biliary obstruction who failed ERCP and who between August 2013 and April 2015 underwent EUS-BD using the study device (Hot-Axios™, Xlumena Inc., Mountain View, California, USA) in 5 European tertiary referral centers. Technical success was defined by adequate placement of stent with established drainage. Clinical success was defined by ≥90% decrease of obstructive parameters. Procedural complications as well as need for re-interventions were evaluated.

Results: 49 patients (Mean age 73 ± x yrs.; M/F: 23/26) were included. Cause of biliary obstruction was pancreatic cancer (28), bile duct cancer (11) and others in 10 cases. Indication for EUS-BD was duodenal obstruction in 27and failed cannulation in 22. CBD access was used 38 patients and gallbladder (GB) access in 11. The procedure was performed transduodenally in 41 and transgastrically in 8. Mean CBD diameter was 16.6mm (10-30). In 22 patients access of the target was achieved using a 19G needle with guidewire placement, which was followed by insertion of the Hot-Axios, while in 27 direct access with Hot-Axios was performed. Stent diameters were 6x8mm (16), 8x8mm (12) and 10x10mm (22). Technical success was achieved in all but one patient (97.9%). All procedures were performed under primary EUS guidance with help of endoscopic and/or fluoroscopic guidance at the discretion of the endoscopist. Clinical success was achieved in 46 of the 48 patients (95.8%) with successful stent placement. Failures were due to bile peritonitis in one case requiring surgery and unsuccessful drainage due to involvement of cystic duct by the malignant process in another one drained through the GB. During follow up, 2 patients (4.2%) suffered from cholangitis that was successfully treated with placement of a plastic stent through the Hot-Axios. Two additional patients required reinterventions for lithotripsy of bile duct stones via Axios stent. In all 40 (100%) patients with follow up ≥ 2 weeks the stent was patent at the end of follow up (mean 128d; range 18-595). 23 patients in the group have follow ≥3month (mean: 196d, range 93 -595), 20 (86.9%) of them showed stent patency without any reintervention.

Conclusion: EUS-BD by creating a biliodigestive anastomosis with the CBD or the GB using the Hot-Axios delivery system for palliative treatment of obstructive malignant jaundice after failed ERCP is feasible, safe and highly clinically effective. Long-term patency of the stent is encouraging and future multicenter prospective studies are warranted to further explore this issue.

Disclosure of Interest: None declared

OP400 EUS-GUIDED BILIARY DRAINAGE FOR MALIGNANT BILIARY TRACT OBSTRUCTION COMPARED TO ERCP WITH TRANSPAPILLARY BILIARY DRAINAGE: RANDOMIZED CONTROLLED TRIAL IN SINGLE INSTITUTION

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Introduction: Obstructive jaundice is a major adverse effect of pancreatic or biliary carcinoma. This adverse event requires treatment, especially in patients who cannot be treated surgically due to concurrent chemotherapy. ERCP with biliary stenting is a gold standard method of treatment for obstructive jaundice. However, this method is associated with several problems, such as post-endoscopic ERCP pancreatitis. In addition, ERCP with biliary stent insertion cannot be performed in patients with selective cannulation failure of the major papilla or an inaccessible papilla due to duodenal invasion or altered anatomy due to previous surgeries. The alternative method under these conditions is PTBD. However, PTBD can lead to several adverse events, such as cholangitis, bile leakage and pneumothorax. Moreover, the frequency of major complications, such as prolonged hospital stay and permanent adverse sequelae, is 4.6% > 25%, and that of procedure-related deaths is 0% > 5.6%. Cosmetic issues due to external drainage also compromise the patient's quality of life. Endoscopic ultrasound-guided biliary drainage (EUSBD) has been developed and performed by experienced endoscopists

Aims & Methods: The aims of this study was to compare success rate in both technical and functional as well as procedure-related complications between ERCP with biliary stent insertion and EUBD. The prospective randomized controlled study was conducted and 30 patients were enrolled; 15 for each EUSBD and ERCP with biliary stent insertion arm. (http://clinicaltrials.gov/show/NCT01421836)

Results: There was the total of 30 patients with extrahepatic malignant biliary tract obstruction (19 male, 11 female). There were 27 patients with unresectable PDACs, 1 patient with distal CBD cancer and 2 patients with metastatic LN compressing distal biliary tract: lung cancer, colorectal cancer. The median OS of the study patients were 8.8 months (0.8 ~36 mo) and there was no significant difference between the two groups: EUSBD 9.1 mos vs. ERCP 8.4 mons (p = 0.5). There were no significant difference between stent patency and both technical and functional success rate. There was one patient with post-ERCP pancreatitis in ERCP biliary biliary stent group and chemotherapy schedule was delayed around 5-7 days. However, it was not statistically significant in terms of complications.

Conclusion: This study showed that EUSBD was not only safe but also as efficient as compared to conventional ERCP with biliary stent insertion in patients with malignant biliary obstruction. In addition, EUSBD technique has a great advantage over the patients not feasible to ERCP with bilary stent and can avoid PTBD for their quality of life.

Disclosure of Interest: None declared

OP401 EUS-GUIDED GALLBLADDER DRAINAGE FOR ACUTE CHOLECYSTITIS IN HIGH SURGICAL RISK PATIENTS USING A NOVEL CAUTERY-TIPPED LUMEN-APPOSING STENT DELIVERY SYSTEM: A LARGE RETROSPECTIVE MULTICENTER EUROPEAN STUDY

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Introduction: Percutaneous gallbladder drainage (PTGBD) is the treatment of choice in high-risk surgical patients with acute cholecystitis (AC). Continuous drainage, however, is associated with patient discomfort and risk of inadvertent drain removal, which may lead to bile leakage and need for re-intervention. Recently EUS-guided transmural gallbladder drainage (EUS-GBD) has become a minimal invasive alternative to PTGBD. We evaluated the safety, the feasibility and clinical effectiveness of a novel lumen-apposing, self-expanding fully covered metal stent incorporated in an electrocautery enhanced delivery system, which facilitates direct puncture of the target, insertion and stent release in a one-step-fashion.

Aims & Methods: Retrospective analysis of all consecutive patients with AC who, between October 2013 and April 2015, underwent EUS-GBD using the study device (Hot-Axios™, Boston Scientific Corp., Natick, MA, USA) in 6 European tertiary referral centers. Technical success was defined by adequate placement of the stent with established drainage. Clinical success was defined by resolution of AC. Procedural complications as well as need for re-interventions were evaluated.

Results: 28 patients (Mean age 72yrs; 41-96); M/F: 13/15) with AC (16 calcolous, 12 acalcolous) not eligible for surgery because of severe comorbidity or advanced malignancy underwent EUS-GBD. The procedure was performed transduodenally in 16 cases and transgastrically in 12. In 16 patients access to the GB was achieved using a 19G needle with guidewire placement, which was followed by insertion of the Hot-Axios, while in 12 direct access with Hot-Axios was done. Stent was placed under EUS/Endoscopic control in 11 cases, while in 17 cases occasional use of fluoroscopy was utilized. Stent diameters were 10x10mm (26) and 15x10 (2). Technical success was achieved in all but one patient (96.4%), in whom gastric wall perforation occurred that required cholecystectomy and suturing of the perforation. Clinical success was achieved in all patients with successful stent placement (100%). Long-term complications occurred in 2 patients (7.4%). One had recurrent cholecystitis that was successfully treated by insertion of a pigtail through the Axios stent. The other patient developed Bouveret's syndrome necessitating lithotripsy. One patient needed reintervention for lithotripsy of cholecystolithiasis for maintaining of stent patency and healing of preexisting cholecystocutanous fistula. In all 22 (100%) patients with technical success and

follow up ≥14 days the stent was patent at the end of follow up (mean 143d; range 14-407).
Conclusion: EUS-guided gallbladder drainage in patients with high surgical risk using the Hot-Axios delivery system is feasible, safe and highly clinically effective. Randomized controlled studies comparing EUS-GBD performed with the study device with PTGBD are needed before this procedure can become the standard of care.
Disclosure of Interest: None declared

OP402 ENDOSONOGRAPHY-GUIDED GALLBLADDER DRAINAGE VERSUS PERCUTANEOUS CHOLECYSTOSTOMY AS A DEFINITIVE MANAGEMENT FOR ACUTE CHOLECYSTITIS IN PATIENTS THAT ARE UNFIT FOR SURGERY

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Introduction: Percutaneous cholecystotomy (PC) is the standard treatment for acute cholecystitis in patients that are unfit for surgery. Recently, endosonography-guided gallbladder drainage (EGBD) has emerged as a potential alternative treatment in these high-risk patients. However, there is no data on how the procedure compares to percutaneous cholecystostomy as a definitive management for acute cholecystitis in patients that are unfit for surgery.
Aims & Methods: This was a retrospective review of all patients who suffered from acute cholecystitis and received EGBD between October 2011 and August 2014 in the Prince of Wales Hospital and the University Hospital Rio Hortega. The patients that received EGBD were matched with those that received PC based on sex, age and American society of anesthesiology grading. All patients included were deemed unfit for surgery by surgeons or anesthesiologist. EGBD was performed using a linear echoendoscope (GF-UCT180 Olympus, Japan) and a lumen apposing stent (AXIOS, Xlumena, CA, USA), draining the gallbladder to the stomach or duodenum. The primary outcome was the overall adverse event rate. Secondary outcomes included technical and clinical success rates, hospital stay, the number of unplanned admissions and mortality.
Results: A total of 116 patients were included (EGBD vs PC = 58:58). There were no significant differences in background demographics. All procedures were technically successful (100% vs 100%) and the clinical success rates were comparable (93.1% and 100%, P = 0.119). When comparing EGBS with PC, significantly more patients in PC group suffered from overall morbidities (25.9% vs 70.7%, $P < 0.001$) and required more frequent unplanned admissions (6.9% vs 70.7%, $P < 0.001$). The most common causes of readmission in the PC group were due to tube dislodgement and blockade. Whilst in the EGBD group, procedural adverse events were significantly higher (17.2% vs 0%, P = 0.001) and the most common procedural adverse event was stent malposition. The rates of recurrent acute cholecystitis were low in both groups (0% vs 3.4%, P = 0.717) and no difference in overall mortality was observed (P = 0.115).
Conclusion: EGBD and PC were both effective means of obtaining gallbladder drainage. In the absence of percutaneous tubing, EGBD reduced the overall morbidities and number of unplanned admissions. While, the higher rate of procedural adverse events may be related to the learning curve associated EGBD. Thus, EGBD may potentially replace PC as the treatment of choice in patients that are unfit for surgery.

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Disclosure of Interest: None declared

OP403 PROSPECTIVE INTERNATIONAL MULTICENTER STUDY ON EUS-GUIDED BILIARY DRAINAGE FOR PATIENTS WITH MALIGNANT DISTAL BILIARY OBSTRUCTION AFTER FAILED ERCP

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Introduction: EUS-guided biliary drainage (EUS-BD) has emerged as an alternative to traditional radiologic and surgical drainage procedures. However, prospective multicenter data are lacking.
Aims & Methods: The primary outcome of this prospective study (NCT01889953) was to assess the clinical success of EUS-BD. Secondary outcomes included technical success, rate and severity of adverse events, and long-term outcomes. **Methods:** All consecutive patients at 12 tertiary centers (5 US, 5 European, 1 Asian, 1 South American) with malignant distal (≥ 2cm from the hilum) biliary obstruction and failed ERCP underwent EUS-BD using either rendezvous (REN), direct transluminal (TL) [Choledochoduodenostomy (CDS), Hepatogastrostomy (HGS), Hepatoduodenostomy (HDS)], or antegrade (AG) stenting techniques. Technical success was defined as successful stent placement in the desired position. Clinical success was defined as drop in bilirubin by 50% at 2 weeks or to below 3 at 4 weeks. Adverse events were prospectively tracked and graded according to the ASGE lexicon's severity grading system. Overall survival and duration of stent patency were calculated using Kaplan-Meier estimate.
Results: A total of 95 patients (mean age 66yr, female 44%, pancreatic cancer 55%) underwent EUS-BD [REN 11, AG 12, TL 72 (CDS 53, HGS 15, HDS 4)]. Reason for EUS-BD was obscured ampulla by invasive cancer or enteral stent (n = 49), altered anatomy (n = 9), failed deep biliary cannulation (n = 20), gastric outlet obstruction (n = 17). Electrocautery was used during 66.67% of procedures (coaxial 38.67%, non-coaxial 28%). EUS-guided cholangiography was successful in 94 (99%) patients. Technical success was achieved in 91 (95.7%) patients (metallic stent 83, plastic stent 8). Mean procedure time was 41 minutes (range 8-207). Clinical success was achieved in 85 patients (95%, intention to treat; 89.4%, per protocol analysis). There was significant decrease in bilirubin at 4 weeks (13.9 vs. 1.86, $p < 0.0001$). A total of 10 (10.5%) adverse events occurred: pneumoperitoneum (n = 2), sheared wire (n = 1), bleeding (n = 1), bile leak (n = 3), cholangitis (n = 2), and perforation (n = 1): 4 graded as mild, 4 moderate, 1 severe, and 1 fatal (due to perforation). There were no predictive factors of clinical success or occurrence of adverse events (all $p > 0.05$). A total of 24 (25%) patients died of disease progression during the study period. The median patient survival was 491 days. The mean stent patency was 536 days (95% CI 383-689) and the one-year stent patency was 61%.
Conclusion: This is the first prospective international multicenter study on EUS-BD and demonstrates the excellent efficacy and safety of EUS-BD when performed by experts. Based on these results, a study comparing EUS-BD to percutaneous drainage is being planned.
Disclosure of Interest: M. Khashab Consultancy: Boston Scientific, Olympus America, Xlumena, S. Van der Merwe Consultancy: Boston Scientific, Cook endoscopy, R. Kunda: None declared, M. El Zein: None declared, A. Teoh: None declared, F. Marson: None declared, C. Fabbri: None declared, I. Tarantino: None declared, S. Varadarajulu: None declared, R. Modayil: None declared, S. N. Stavropoulos: None declared, I. Peñas1: None declared, S. Ngamruengphong: None declared, V. Kumbhari: None declared, J. Romagnuolo: None declared, R. Shah : None declared, A. Kalloo: None declared, M. Perez-Miranda Consultancy: Boston Scientific, Xlumena, E. Artifon: None declared

WEDNESDAY, OCTOBER 28, 2015 08:30–10:30
ABSTRACTS ON FIRE: GUT MICROBIOTA IN LOWER GI DISEASES – HOTSPOT

OP404 IDENTIFICATION OF A GUT MICROBIAL SIGNATURE LINKED TO SEVERITY OF IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder affecting around 10-15% of the western population. Alteration in gut microbiota composition has been reported in IBS patients or IBS subgroups in some studies (Rajilić-Stojanović *et al*., 2011; Jeffery *et al*., 2012) with different microbial ecology outcomes. Larger sample size studies are needed to take into account the heterogeneity of IBS pathophysiology.
Aims & Methods: In our study, 130 subjects including 95 IBS (ROME III, all subtypes, n = 78 severe IBS, IBS-SSS > 300) and 35 healthy controls were thoroughly characterized for symptom severity (IBS-SSS, GSRS), psychological comorbidities (HAD, FIS, PHQ-15, VSI) and quality of life (IBSQoL). A combined nutrient and lactulose challenge test (Le Nevé *et al.,* 2013) with symptom assessment and measurement of exhaled H_2 and CH_4 was performed in all subjects. Unprepared sigmoid colon biopsies and stool samples were obtained. Paired fecal and mucosal microbiota were then analyzed by 16S rRNA targeted pyrosequencing with LOTUS v1.32 using USEARCH v7 to identify Operational Taxonomical Units (OTUs, 97% identity, molecular species similarity levels), and GreenGenes database (release version 13.8 August 2013). Microbial enterotype stratification was identified using previously described methods with the Dirichlet multinomial bayesian statistics (Holmes

et al., 2012). Machine learning procedure to identify microbial IBS signature was carried out using L1 regularized logistic regression using the LIBLINEAR library (Fan *et al*., 2008) validated through a ten-fold independent cross-validation. In addition, quantitative PCR was used to detect archaea methanogens in stool samples.
Results: 16S rRNA microbiota OTU-based data complexity was reduced using a machine learning procedure into a "species-specific IBS severe signature", consisting of ~100 bacterial OTUs (extracted out of 2,900 total OTUs detected in the dataset) linked to IBS severity as assessed by IBS-SSS. This IBS severity microbial signature has been further confirmed in sigmoid mucosal microbiota (n = 57, AUC = 0.80) and an external validation stool set (n = 46, AUC = 0.68), allowing to discriminate severe IBS from mild/moderate IBS patients and healthy controls. Using this OTUs based signature, IBS symptom severity score was, as a gradient, significantly and negatively associated to 1) exhaled CH_4, 2) presence of Archaea methanogens 3) microbial species richness and 4) enterotypes enriched either with *Clostridiales* or *Prevotella* species. This IBS severity signature was independent from age, gender, BMI and exhaled H_2.
Conclusion: Overall, our study indicates that IBS symptom severity is associated with a distinct signature at the fecal microbiota level. Exhaled CH_4, enterotypes stratification and mucosal microbiota are linked with this signature. Whether this indicates a causal role of gut microbiota alteration in the genesis of IBS symptoms remains to be investigated.

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OP405 SEROLOGIC PREDICTOR OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN IRRITABLE BOWEL SYNDROME

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Introduction: Small intestinal bacterial overgrowth (SIBO) is common in the irritable bowel syndrome (IBS). Up to now, little is known about study regarding serologic markers of small intestinal bacterial overgrowth. The purpose of the present study was to determine possible serologic markers of small intestinal bacterial overgrowth in irritable bowel syndrome.
Aims & Methods: We reviewed the charts for patients who showed irritable bowel syndrome symptoms with documented results for lactulose breath test. Univariate and multivariate models were used to identify which markers were useful in predicting small intestinal bacterial overgrowth, and receiving operating characteristics curves were used to find the specificity, sensitivity, and the negative and positive predictive values.
Results: Of the 740 patients, 243 (32.8%) were found to have SIBO. Subjects with SIBO had significantly higher total bilirubin than those without SIBO. On multivariate analysis, SIBO was independently associated with serum total bilirubin. The best cut-off of serum bilirubin was ≥4.5 mg/ dL [AUROC 0.67 (95% CI 0.63–0.72)] predicting SIBO with sensitivity 63%, specificity 63%, positive predictive value 62% and negative predictive value 75%.
Conclusion: Increased total bilirubin is serologic predictor for the presence of small intestinal bacterial overgrowth in irritable bowel syndrome patients.
Disclosure of Interest: None declared

OP406 EPIDEMIOLOGY OF POST INFECTIOUS IRRITABLE BOWEL SYNDROME FOLLOWING CLOSTRIDIUM DIFFICILE INFECTION

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Introduction: Infectious gastroenteritis (IGE) is the most commonly identified risk factor for development of irritable bowel syndrome (IBS). Long-term gastrointestinal sequelae have been reported after IGE caused by bacterial, viral and parasitic pathogens. However, there is very limited epidemiological information for post infectious (PI)-IBS development following *Clostridium difficile* infection (CDI).
Aims & Methods: Our aim was to determine the incidence and risk-factors for PI-IBS development among culture-confirmed cases of CDI. We sent postal surveys to 683 cases of CDI reported to the Mayo Clinic microbiology laboratory during Sep 2012-Nov 2013. Phone calls were made to reach non responders. Participants were asked to complete the Rome III IBS questionnaire for current and pre-CDI GI symptoms and details on the CDI episode. Electronic medical records were reviewed. Predictive modelling was done using logistic regression to evaluate demographic, CDI and psychological characteristics as risk-factors for PI-IBS development.
Results: The overall survey response rate was 46.1% (315/683). 205 of the 315 *C. difficile* cases that responded were known to be at-risk for PI-IBS development (excluding cases with pre-existing IBS prior to the *C. difficile* episode, cases with missing data and cases with an alternative diagnosis such as inflammatory bowel disease or microscopic colitis). Those with repeated infections after the index episode were excluded prior to defining them as PI-IBS. 25.4% of those at risk (52/205) met the Rome III criteria for IBS. The IBS phenotype was mixed in 27 (52%), diarrhea-predominant in 21 (40.4%), constipation-predominant in 2 (3.9%), and undifferentiated in 2 (3.9%). The mean (±SEM) IBS symptom severity score was 238.3 (13.8). The Table lists comparsion of demographic, enteritis-related and psychological variables among PI-IBS cases and controls.

Variable	PI IBS (52)	Controls (153)	p- value
Mean age (±SEM)	55.7 (± 2.4)	58.3 (±1.5)	0.39
Gender, Females	61.5%	54.9%	0.40
Bloody diarrhea during CDI	22.4%	32.9%	0.18
Fever during CDI	26%	38.5%	0.12
Duration of CDI symptoms > 7 days	78.8%	60.4%	0.02
Hospitalized during CDI	59.6%	57.9%	0.83
Mean (± SEM) HADS anxiety score	9.8 (±0.4)	8.1 (±0.2)	<.0001
Mean (± SEM) HADS depression score	8.5 (±0.2)	8.5 (±0.1)	0.78

From a multivariable model, CDI symptoms > 7 days (p=0.03) and current anxiety score on Hospital Anxiety and Depression Scale ($p < 0.001$) were associated with development of PI-IBS following *C. difficile* infection.

Conclusion: Like other bacterial infections, CDI is associated with the risk of development of IBS. Longer duration of CDI symptoms and current anxiety are associated with the diagnosis of *C. difficile* PI-IBS. This chronic sequela of PI-IBS should be considered during active management and follow up of patients with CDI.
Disclosure of Interest: None declared

OP407 FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT C. DIFFICILE INFECTION: A 2-YEAR EXPERIENCE FROM A EUROPEAN REFERRAL CENTRE

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Introduction: Fecal microbiota transplantation (FMT) from healthy donors is considered an effective treatment against recurrent *Clostridium difficile* infection (rCDI). To date, however, FMT is available only in few Centers worldwide. FMT was implemented in our Centre since June 2013
Aims & Methods: To report outcomes of a large series of patients treated with FMT for rCDI in a European academic tertiary care Centre after 2 years of experience. All patients treated with FMT for rCDI in our Centre were prospectively identified. Follow-up data, including diarrhea, *C. difficile* toxin status and adverse events were collected and analyzed.
Results: 35 subjects (M/F: 17/18; mean age 69, range 31-91) received FMT from healthy donors because of rCDI (mean n° of recurrences: 3, range 2-6). Mean Charlson Comorbidity Index score was 3. Inpatient/outpatient ratio was 2.2. Eight patients received multiple infusions, for a total of 47 procedures. All procedures were performed by colonoscopy. In 9 patients, endoscopic appearance of pseudomembranous colitis (PMC) was observed. The mean follow-up was 9 months (range 1-22 months). Resolution of rCDI occurred in 33 of the 35 treated patients (94%). No patients experienced further recurrences after FMT. Fecal material was provided by unrelated donors in 45% of cases. Both fresh and frozen feces were used. *K. Pneumoniae*-related sepsis occurred in one patient (3%) 24 h after the transplant, and resolved after antibiotic treatment. In 2 patients (6%), all suffering from concomitant urinary infections, a transient, self-limiting bacteriemia was observed 1 to 6 days after FMT. Two subjects died because of overwhelming CDI from 1 to 10 days after FMT failure. Eight patients died 6 to 12 months after FMT, because of their own comorbidities (mainly cardiovascular disease) not relatable to the procedure.
Conclusion: FMT by colonoscopy achieved a 94% resolution rate of rCDI in our series. Our results confirm the efficacy of FMT in the treatment of rCDI in a large series of European patients, with a mean follow-up of 9 months. Dissemination of FMT is warranted to provide a better management of patients with rCDI.
Disclosure of Interest: None declared

OP408 ABOLISHED NEED FOR SURGERY IN C. DIFFICILE INFECTION AFTER THE IMPLEMENTATION OF FECAL MICROBIOTA TRANSPLANTATION IN AN ACADEMIC TERTIARY CARE CENTRE

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Introduction: *C. difficile* infection (CDI) is increasing in both incidence, severity and mortality. Total abdominal colectomy is recommended to manage complicated severe infection. Nevertheless, surgery is associated with poor long-term survival and significant morbidity. CDI recurrences greatly increase the risk of severe complications and the need for surgery. Fecal microbiota transplantation (FMT) is considered an effective treatment against recurrent CDI (rCDI). FMT is available at our Centre since June 2013.
Aims & Methods: To assess the evolution of the need for surgery in CDI after the implementation of FMT programme in an academic tertiary care centre. Medical charts of all patients referring our hospital from January 2010 to April 2015 because of CDI were reviewed retrospectively. Total number of subjects with CDI/year, as well as raw numbers and annual rates of CDI-related surgery and FMT procedures were respectively assessed.
Results: Throughout the study period, 901 patients with CDI were identified. Overall, 18 patients underwent surgery because of severe rCDI. No patients at first infection who required surgery were identified. Thirty-five patients underwent FMT, and 37% of them had severe disease.
Number of patients diagnosed with CDI increased gradually over years, being, respectively, 54 in 2010, 116 in 2011, 200 in 2012, 212 in 2013, 268 in 2014, and 71 in 2015 (until April 2015).
Surgery rates (n° of surgical procedures/patients with CDI), despite an initial increase (from 2010 to 2012), rapidly decreased over years, until their complete abatement, concomitantly with the implementation of FMT, being, respectively, 1.9% in 2010, 2.6% in 2011, 5% in 2012, 1.9% in 2013, 0% in 2014, and 0% in 2015. FMT rates (n° of FMT procedures/patients with CDI), instead, progressively increased over years since 2013 (3.3% in 2013, 6% in 2014, 22.5% in January-April 2015).
The raw numbers of surgical and FMT procedures were, respectively: 1 and 0 in 2010, 3 and 0 in 2011, 10 and 0 in 2012, 4 and 7 in 2013, 0 and 16 in 2014, 0 and 12 in 2015 (April 2015).
Conclusion: In our retrospective series, the implementation of FMT was associated with the abatement of surgical procedures for CDI, despite the increasing epidemic of the infection. This may be explained both by the prevention of further recurrences and complications of CDI provided by FMT and by the increased attention to CDI by physicians. Should our findings be confirmed by further studies, FMT may assume an even greater importance in the management of rCDI.
Disclosure of Interest: None declared

OP409 A SUBSET OF PATIENTS WITH NON-INFECTIOUS DIARRHEA HAVE ALTERED GUT MICROBIOTA SIMILAR TO C. DIFFICILE INFECTION

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Introduction: Non-infections diarrhea is commonly associated with chronic gastrointestinal disorders such as functional diarrhea, irritable bowel syndrome, inflammatory bowel disease, and microscopic colitis. The pathophysiology of diarrhea remains poorly understood, but recent data suggests a role for alterations in the gut microbiota.
Aims & Methods: The aim of this study was to assess gut microbial alterations in patients with non-*Clostridium difficile* diarrhea in comparison to patients with *C. difficile* infection (CDI) and healthy volunteers.
Stool samples from patients with *C. difficile*-negative diarrhea, active CDI, and healthy volunteers were collected and stored at -80°C. MoBio DNA isolation kits were used for stool DNA extraction. Sequencing was performed on the 16S rRNA V4 region using an Illumina MiSeq platform. Data analyses were conducted in QIIME and R-3.1.2.
Results: We profiled gut microbial communities from 115 patients with *C. difficile*-negative diarrhea (76 females, age 46.5 ± 1.6 years) and compared them to 92 patients with CDI and 110 healthy volunteers. Among the patients with *C. difficile*-negative diarrhea, 16 (14%) had Crohn's disease, 13 (11%) had ulcerative colitis, 7 (6%) had viral gastroenteritis, 21 (18%) had IBS, and 56 (49%) had other causes of diarrhea. Gut microbial communities from patients with CDI were significantly different (PERMANOVA $p < 0.05$) from healthy volunteers as assessed by the unweighted UniFrac distance metric (β diversity). A subset of patients with *C. difficile*-negative diarrhea (n = 54 of 115) had markedly altered gut microbial communities characterized by lower relative abundances of *Bacteroidetes* and higher relative abundances of *Proteobacteria*. These alterations resembled gut microbial changes in patients with CDI. Additionally, these alterations were associated with clinical risk factors commonly linked to the development of CDI: recent antibiotics (odds ratio; 95% confidence interval; 0.24; 0.08-0.67; p = 0.003), immunosuppression (0.32; 0.13-0.77; p = 0.006), current hospitalization (0.21; 0.06-0.68; p = 0.004), recent hospitalization (0.26; 0.07-0.83; p = 0.01), and prior CDI (0.06; 0.001-0.43, $p < 0.001$). The remaining *C. difficile*-negative patients (n = 61 of 115) had gut microbial communities that resembled those of healthy volunteers.
Conclusion: A subset of patients with *C. difficile*-negative diarrhea but clinical risk factors associated with CDI - including hospitalization, prior CDI, recent antibiotics, and immunosuppression - exhibit gut microbial alterations similar to those seen in patients with CDI. These clinical risk factors may instigate changes in the gut microbial community resulting in diarrhea and increased susceptibility to CDI.

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Disclosure of Interest: None declared

OP410 SELECTIVE DECONTAMINATION OF THE DIGESTIVE TRACT AT THE INTENSIVE CARE UNIT PROMOTES SPREAD OF CLOSTRIDIUM DIFFICILE INFECTION

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Introduction: An outbreak of a single clone of *Clostridium difficile* ribotype 027 occurred at the VU University Medical Center, involving 19 medical departments. Several risk factors for CDI are known, but factors specifically associated with hospital-wide outbreaks are less well defined.
Aims & Methods: Primary aim is to determine risk factors associated with hospital-wide spread of clonal *Clostridium difficile*-infection (CDI) due to ribotype 027.
We performed a case control-study during an outbreak of CDI due to a single clone of *C. difficile* ribotype 027 in a 750-bed tertiary care medical centre.
Microbiological ***Methods:*** *C. difficile* isolates were characterised by ribotyping, Amplified Fragment Length Polymorphism, and Multi Locus Sequence Typing. A selection of strains (n = 10) was also characterised by Whole Genome Sequence analysis.
Participants: cases (n = 79) were diagnosed with CDI due to *C. difficile* ribotype 027 during hospitalization between May 2013 and March 2014. Each case was matched to 4 controls for age and medical specialty (n = 316); controls stayed on the same ward as the index patient within 48 hours of diagnosis and had no known history of CDI.
Variables: medical charts were reviewed for demographic, clinical and healthcare associated characteristics.
Statistical Methods: Odds Ratios (OR) and their 95% Confidence Intervals (95% CI) were calculated by univariate and multivariate conditional logistic regression (SPSS version 20).
Results: Nearly all patients with CDI (75/79) had used antibiotics prior to CDI, compared to 176/316 of controls (OR 7.37; 95% CI 2.44 to 22.30). Cases were more likely than matched controls to have stayed on a high care ward like ICU or MCU (OR 5.64; 95% CI 2.03 to 15.65), had a longer length of stay (11-25 days: OR 3.50; 95% CI 1.19 to 10.30; > 25 days: OR 4.38; 95% CI 1.31 to 14.68), and had been recently (< 90 days) admitted before this admission (OR 2.19; 95% CI 1.06 to 4.55). Cases were less likely to have been admitted to a ward with a known CDI patient that was nursed in isolation (OR 0.24; 95% CI 0.09 to 0.63). There was no significant association with the number of ward transfers or the use of proton pump inhibitors (PPI). The overall 30-day mortality was 18% for cases and 8% for controls (HR 2.25; 95% CI 1.06 to 4.76). For participants that stayed on a high-care ward during their hospital admission (cases n = 45; controls n = 81), the use of selective decontamination of the digestive tract (SDD) was strongly associated with acquiring CDI, also when adjusted for sex, Apache IV score, Charlson comorbidity index and length of stay (OR 9.95; 95% CI 3.29 to 30.08).
Conclusion: In this large outbreak, caused by a single clone of *C. difficile* ribotype 027, antibiotic use appeared as a prerequisite for acquisition of this outbreak strain. We identified stay on a high-care unit but especially the use of SDD as a major risk factor for acquisition of CDI. Restriction of SDD use during an outbreak of CDI might be a possible measure to prevent furher spread that merits further investigation.
Disclosure of Interest: None declared

OP411 GENETIC INFLUENCE ON COMPOSITION OF THE INTESTINAL BACTERIA IN HEALTHY FIRST DEGREE RELATIVES (FDR) OF CROHN'S DISEASE (CD) SUBJECTS

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Introduction: Genome-wide association studies (GWAS) have identified numerous genetic associations with inflammatory bowel disease (IBD) most of which

encode proteins involved in immunity, host defense against microbes, and gut homeostasis. IBD patients have a dysbiosis. However as inflammation influences the composition of the microbiota, it is unknown whether these differences are a cause or result of intestinal inflammation.

Aims & Methods: In order to determine if the composition and diversity of gut microbiota are associated with host genetic makeup we assessed the stool microbiome in a cohort of 1,273 healthy Caucasian FDR of CD patients. 16S rDNA were sequenced from the stool and MiSeq sequences were processed using the QIIME pipeline. After rarefaction at 30,000 reads per sample, bacterial alpha diversity was estimated. Genotyping and imputation was performed using the HumanCoreEXOME chip and IMPUTE2. Polygenic heritability (H2R) of the gut microbiota was calculated using SOLAR software. Analysis of 50 demographic and environmental factors identified age as the most important factor associated with microbial makeup and it was included as covariate in subsequent analysis. Genome-scans at every microbial taxonomic level were carried out on imputed SNPs with a minor allele frequency $>5\%$. We used a generalized estimating equation assessing the association between the taxa and potential genetic effects controlling for age, sex, and the first three genetic principal components in European origin subjects. We performed a sensitivity analysis using two models: a log-normal model on the non-zero outcomes and a two-part log-normal model fitting both a logistic model on the absence/presence of the taxa and the log-normal model described before.

Results: Overall, the dominant phyla in these samples were Firmicutes (relative abundance of $64.2\% \pm 14.1$, (mean $\pm$ SD)), Bacteroidetes ($26.9\% \pm 15.0$), and Actinobacteria ($5.0\% \pm 5.2$). A total of 91 out of 253 taxa showed significant heritability ($25\% < H2R < 67\%$, $3.2 \times 10^{-6} <$ p-value < 0.05). No significant associations were observed between genotype and bacterial alpha diversity and no associations were observed among 123 SNPs known to be associated with IBD. However among 3,727,707 high-quality SNPs, as many as 65 SNPs reach genome-wide significance (p-value $< 5 \times 10^{-8}$) for association with the relative abundance of 34 microbial taxa.

Conclusion: These results suggest that host genetic variants are associated with differences in intestinal microbiota composition in healthy FDR. This study differs from prior analysis of microbiota in patients with CD where the composition of the microbiota was influenced by the effects of treatment and the inflammatory process itself. It remains to be determined if the genetic associations with microbiome differences identified are related to the risk of developing Crohn's disease.

Disclosure of Interest: None declared

OP412 THE DYSBIOSIS INDEX DOES NOT DISTINGUISH CHILDREN WITH CROHN'S DISEASE FROM HEALTHY SIBLINGS

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Introduction: Patients with Irritable Bowel Syndrome (IBS) are often used as controls in studies of the Crohn's disease (CD) microbiome. However, digestive symptoms among the IBS-controls could be associated with microbial dysbiosis. An alternative design is to use healthy siblings of CD patients as controls. As healthy siblings should be free from such symptoms, comparisons with CD patients should be more straightforward. Further, familial controls offer the possibility to tease out hereditary or dietary factors.

Aims & Methods: Our aims were to compare the microbial community composition of stool samples from healthy siblings and pediatric CD patients, to characterize their microbiomes at the functional level and to investigate the familial effect on measurements of community diversity and the potential relationship between dysbiosis and the CD phenotypes, using the Dysbiosis Index (DI), a recent measure of microbial dysbiosis, which was originally derived from a dataset dominated by biopsy samples taken from CD patients, and was shown to be associated with clinical disease severity.

Metagenomic sequences from stool samples of 5 pediatric CD patients and their siblings were obtained using MiSeq on both whole-metagenome sequencing and16S ribosomal RNA fragments. Microbial composition profiles based on 16S ribosomal RNA genes were derived from the green genes database. To obtain functional assignment, sequences were searched against 28 representative KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways, with putative functions ultimately assigned by using HUMAnN. Microbial composition profiles were analyzed using QIIME and STAMP, and functional profiles were inferred using STAMP and BiomeNet. Microbial dysbiosis was determined for each sample as implemented in QIIME.

Results: Examination of phylotypes that contribute to the dysbiosis index revealed that considerable among-sample variability was shared between siblings. For example, some pairs of healthy and CD siblings exhibited highly similar frequencies of phylotypes that contribute to the dysbiosis index. Clearly, in these cases it is inappropriate to attribute the CD phenotype to the presence of those lineages. Furthermore, none of the samples scored as dysbiotic according to the ensemble index, and there was no consistent relationship between sibling pairs in terms of the magnitude of their scores. Similar results were obtained at the functional level. Bayesian modeling of metabolic structures via BiomeNet also revealed a close association between many healthy and CD siblings.

Conclusion: The DI of stool samples is not able to distinguish healthy siblings from pediatric patients with Crohn's disease. We hypothesize that this is because the DI is based on too few microbial lineages. We suggest that the dysbiosis index might be improved by inclusion of more indicator lineages and functional information. Comparison to sibling controls indicates that there is a strong familial effect on both microbiome composition and function that can vary considerably among sibling pairs. This effect must be accommodated if microbiome-derived information is going to make a practical contribution to clinical care in the future.

Reference

1. Gevers et al. *Cell Host Microbe*. 2014;15(3):382-92.

Disclosure of Interest: K. Dunn: None declared, J. Connors: None declared, B. MacIntyre: None declared, A. Stadnyk: None declared, J. Bielawski: None declared, N. Thomas: None declared, A. Otley: None declared, J. Van Limbergen Financial support for research: Abbvie, Lecture fee(s): Abbvie, Janssen, Nestle, Consultancy: Nestle

OP413 EXCLUSIVE ENTERAL NUTRITION TREATMENT RESTORES THE MUCOSA-ASSOCIATED INTESTINAL MICROBIOME IN CHILDREN WITH CROHN'S DISEASE

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Introduction: Aberrant host immune responses to the intestinal microbiome are likely to contribute to Crohn's disease (CD) pathogenesis. Intestinal microbiome dysbiosis is reported in both adult and pediatric CD. Exclusive enteral nutrition treatment (EEN), by sterile liquid formula as the only intake of nutrients for 6-8 weeks as monotherapy, is recommended as remission induction treatment in pediatric CD. However, the mechanisms by which EEN induces remission in pediatric CD is still obscure. We hypothesize that EEN exerts its action by restoring the intestinal microbiome.

Aims & Methods: The aim was to compare the mucosa-associated intestinal microbiome before and after eight weeks of EEN in treatment-naive children with CD. Mucosal biopsies from ileum and left colon were collected from eight children with newly diagnosed CD before and at the end of eight weeks of EEN. Biopsies were frozen in liquid nitrogen and stored in -70 C. To determine the microbiome the16S™ Metagenomics Solution (Thermo Fisher Scientific) was used. After DNA extraction, seven hypervariable regions (V2, V3, V4, V6, V7, V8, and V9) of bacterial 16S rRNA were amplified using Ion 16S™ Metagenomics Kit (Thermo Fisher Scientific). The amplified fragments were sequenced on the Ion PGM™System (Thermo Fisher Scientific). The Ion Reporter™ Software was used for initial data processing and analysis.

Results: All children were in clinical remission at the end of EEN, and a repeat colonoscopy revealed macroscopic and histologic improvement but not full mucosal remission. In all children the mucosa-associated intestinal microbiome in both ileum and left colon changed radically with an increased overall bacterial diversity. Also, a shift in microbiome composition followed EEN, with decreased abundance in bacterial orders bacteroidales and enterobacteriales.

Conclusion: The positive clinical and histological response to EEN in children with CD correlated to an increased diversity in the mucosa-associated intestinal microbiome. These findings support the hypothesis that EEN exerts its effects in pediatric CD by restoring the mucosa-associated intestinal microbiome.

Disclosure of Interest: None declared

OP414 THE GUT MICROBIOME DIFFERENTIATES CLINICAL PHENOTYPES IN MODERATE TO SEVERE CROHN'S DISEASE: RESULTS FROM THE CERTIFI STUDY

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Introduction: The aim of this study was to investigate the relationship between the fecal microbiome and clinical phenotypes in subjects with moderately to severely active Crohn's disease (CD). Specifically, the potential of the microbiome to differentiate among Crohn's patient sub-groups as defined by specific clinical traits was examined.

Aims & Methods: CERTIFI was a Phase 2b multicenter, randomized, double-blind, placebo controlled clinical trial to evaluate the efficacy and safety of ustekinumab therapy in subjects with moderately to severely active CD who had previously not responded to anti-TNFα therapy. Fecal samples from 100 subjects, collected at screening, week 4, week 6, and week 22 study visits, and stored at -80°C, were selected for microbiome analysis. Bacterial DNA was extracted from the fecal samples using the MoBio PowerSoil DNA Isolation kit and subjected to 16S rRNA sequencing and shotgun metagenomic sequencing. 16S rRNA sequencing was performed on the GS-FLX 454 Titanium platform and the sequences were assigned genus-level annotations. Metagenomic sequencing was performed on the Illumina HiSeq 2000 using 100 base pair paired-end processing. Filtered sequences were mapped against the MetaCyc database of metabolic pathways and enzymes. Spearman correlation, LEfSe, logistic regression, and Adonis were applied to identify bacterial taxa or metabolic pathways that were associated with clinical variables of interest.

Results: The gut microbiome of individuals with CD was characterized by pronounced inter-personal variation in the presence and relative abundance of specific bacterial taxa. Despite this heterogeneity, bacterial abundances and metabolic pathways correlated with patient sub-groups defined by specific baseline clinical traits. The baseline CDAI score significantly associated with the relative abundance of several bacteria, including Parabacteroides (rho = -0.42, P < 1e-4). The metagenomic data supported this result, demonstrating correlation between specific metabolic pathways and CDAI score. Baseline CRP, fecal calprotectin (FCALP), and lactoferrin (FLACT) concentrations also correlated with baseline bacterial abundances of specific taxa, including Dialister (rho = 0.36, P = 3e-4, Spearman correlation with FCALP), and with metagenomic data. Previous response to anti-TNFα therapy did not significantly correlate with the abundance of any specific bacteria or with metagenomic data.
Conclusion: The fecal microbiome demonstrated the ability to discriminate clinical phenotypes in moderately to severely active CD patients who had previously not responded to anti-TNFα therapy. The strongest associations between metadata and the microbiome, supported by 16S and metagenomic data, were observed for CDAI score, FCALP, and FLACT. The results suggest the potential application of the fecal microbiome as a molecular marker of disease severity in CD.
Disclosure of Interest: T. Ding Financial support for research: Janssen R & D, LLC, S. Telesco Conflict with: Employee Janssen R & D, LLC, C. Monast Conflict with: Employee Janssen R & D, LLC, C. Brodmerkel Conflict with: Employee Janssen R & D, LLC, T. Yatsunenko Financial support for research: Janssen R & D, LLC, A. Das Conflict with: Employee Janssen R & D, LLC, P. Schloss Financial support for research: Janssen R & D, LLC

OP415 THE IMPORTANCE OF THE MUCOSAL ANTIMICROBIAL PEPTIDE EXPRESSION AND GUT MICROBIOTA IN ANTI-TNF THERAPY RESPONSE IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Anti-TNF therapy is a common treatment for patients with ulcerative colitis (UC). However, about 30-50% of the patients do not respond to the treatment and it is not understood why some patients respond while others do not. Antimicrobial peptides (AMPs), a part of the innate defense against intestinal microorganisms, and the gut microbiota are essential for gut homeostasis and may be of importance for treatment effects of anti-TNF therapy.
Aims & Methods: The aim of this study was to determine AMP and microbiota profiles in patients with UC before start of anti-TNF therapy and correlate these data to therapy outcome.
Blood, biopsy and fecal samples were obtained before anti-TNF treatment from anti-TNF therapy-naïve UC patients. Therapy response was assessed by Mayo score 12-14 weeks after treatment initiation, and response was defined as a decrease in Mayo score of $\geq$3 points. Biopsies were cultured for 24h and used for quantitative proteomic analysis by mass spectrometry or directly frozen for rtPCR analysis. AMP levels in serum were measured by ELISA. Microbiota analysis of fecal samples was performed using the GA-map^{TM} Dysbiosis Test (Genetic Analysis AS, Oslo, Norway) where dysbiosis indexes of 1-2 are considered normal while 3-5 denotes increasing dysbiosis. Multivariate factor analysis (SIMCA-P+ software; Umetrics, Umeå, Sweden) was used to examine relationship between AMP levels and bacterial content to therapy outcome.
Results: Among the 31 included patients, 17 patients responded to the therapy. According to the proteomic analysis of cultured biopsies (from 3 responders and 3 non-responders) Defensin 5 (Def5), eosinophil cationic protein (ECP) and bactericidal/permeability-increasing protein (BPI) were recorded in responders but not in non-responders. Gene expression of 11 AMPs or genes associated with AMP expression were analyzed in biopsies: Def5, ECP, BPI, Cathelicidin (CAT), Lysozyme, hβ-defensin 2, HMGB1, HMGN2, HistoneH1.5, 40S ribosomal protein S19 and HDAC1. Multivariate data analysis showed that responders and non-responders clustered differently when studying mRNA levels of the 11 genes. The most important nominators for therapy response were increased expression of Def5 (median (IQR), resp vs. non-resp; 0.598 (0.079-2.694) vs. 0.034 (0.005-0.211), p = 0.006) and ECP (0.00025 (0.00013-0.00053) vs. 0.00012 (0.00009-0.00014), p = 0.03) and decreased expression of CAT (0.0040 (0.0016-0.0133) vs. 0.0133 (0.0057-0.0498), p < 0.05). Responders also had higher serum levels of ECP compared with non-responders (33.7 ng/ml (18.7-98.9) *vs.* 7.5ng/ml (3.4-41.3) p = 0.03). Microbiota analysis of fecal samples (4 responders and 3 non-responders) revealed that non-responders tended to have higher dysbiosis indexes compared to responders (4.7 (4-5) vs. 3.3 (2-5), p = 0.097). Also, non-responders had low levels of Faecalibacterium prausnitzii while responders showed normal levels.
Conclusion: Anti-TNF therapy responders and non-responders display different patterns of mucosal AMP expression and gut microbiota before start of therapy. This indicates that infliximab therapy benefits from a defined anti-microbial defense pattern and that the intestinal microbial composition may be different in the two patient cohorts.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 11:00-12:30
VIDEO CASE SESSION - ROOM F1

OP416 RAPID AND SAFE ENDOSCOPIC TREATMENT OF ZENKER'S DIVERTICULUM WITH A NEW SCISSOR LIKE ESD DEVICE

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Introduction: Zenker's diverticulum (ZD) represents a diverticulum of the mucosa of the pharynx above the cricopharyngeal muscle. Traditionally, ZD has been treated by neck surgery or rigid endoscopy. Endoscopic therapy is based on cutting the septum between the ZD and the esophageal lumen. Therefore, a variety of endoscopic methods have been used, including laser, stapler, harmonic scalpel, argon plasma coagulation, or needle knives. Here, we present the potential of a novel device originally developed for endoscopic submucosal dissection (ESD) for rapid and safe therapy of Zenker's diverticulum.
Methods: For the purpose of this study, the Clutch Cutter (Fujifilm, Tokyo, Japan) was used. The device was introduced late October 2014 to the European market and is a forceps-type resection device for ESD. The device has a 0.4mm wide and 3.5mm long serrated cutting edge. The device is rotatable and the outer side of the forceps is insulated to avoid burning of surrounding tissue. With a diameter of 2.7mm the device is compatible with most conventional endoscopes. For electrocautery, the Vio 200 D-system (Erbe, Tübingen, Germany) with the following settings was used: Forced coagulation 30W, Endo Cut Q with effect 1, duration 3, interval 1.
Results: With the patient under conscious sedation a single channel endoscope (Olympus, Tokyo, Japan) is carefully advanced in the esophagus. Directly below the upper esophageal sphincter one can clearly identify the Zenker's diverticulum which is also highlighted by the barium swallow examination. After inspection of the duodenum and the stomach the endoscope is withdrawn and a conventional feeding tube is placed through the nose of the patient. Afterwards, a clear distal cap is attached to the endoscope. The feeding tube is placed under endoscopic visualization in the gastric antrum. Afterwards, the endoscope is placed in front of the septum between the ZD and the esophageal lumen and the Clutch Cutter is advanced through the working channel of the endoscope. Subsequently, the forceps of the Clutch Cutter is opened and pushed against the septum to grasp the tissue. Electrocautery is applied and the procedure is repeated until the septum is completely cut. Of note, the Clutch Cutter device allows to selectively catch and dissect the muscle fibers. Neither bleeding nor any post procedural complications occurred. Total procedure time was 6 minutes. The patient resumed a normal diet for 48 hours. Follow-up endoscopy after 2 days revealed a significant improvement.
Conclusion: The newly introduced ESD device Clutch Cutter is a promising device for rapid and safe endoscopic treatment of Zenker's diverticulum.
Disclosure of Interest: None declared

OP417 AN EFFECTIVE ENDOSCOPIC CLOSURE TECHNIQUE OF LARGE MUCOSAL DEFECTS AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION USING ENDOLOOP AND ENDOCLIPS FOR PATIENTS ON ANTITHROMBOTIC DRUGS

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Introduction: Delayed bleeding after gastric endoscopic submucosal dissection (ESD) is more common in patients on antithrombotic drugs, occurring in 11.6% [1]. Little is known about the prevention of post-ESD bleeding in those patients. There are case reports of complete endoscopic closure using endoloop and endoclips after endoscopic resection [2]. We aimed to investigate the technical feasibility of this endoscopic closure technique after gastric ESD in patients at high risk of bleeding who were on antithrombotic drugs.
Methods: This pilot study included 15 patients on antiththrombotic drugs who underwent a total of 16 gastric ESDs followed by endoscopic closure using endoloop and endoclips between May 2013 and April 2015. An endoloop was opened through the first accessory channel of double channel endoscope and endoclip was also prepared through the other channel after gastric ESD. We hooked endoclip on the endoloop and then anchored the endoloop along the edge of the mucosal defect using the hooked endoclips. Then the mucosal defect was closed by tightening the fixed endoloop. Plural endoloops were used as necessary for large mucosal defects. Complete closure was defined as achieving visible endoscopic closure for the whole mucosal defect and successful closure was defined as that over three fourth endoscopically. We evaluated complete closure rate, successful closure rate, procedure time for closure and post-ESD bleeding.
Results: Patients characteristics were as follows; male/female = 13/2, median age = 78 year old (67-93), aspirin/cilostazol/ticlopidine/warfarin/novel oral anticoagulant/others = 6/5/2/3/2/3 (with overlapping). ESD locations were upper/middle/lower = 3/8/5 and median resected specimen size was 33.5mm (19-65). Median procedure time for closure was 13.5 min (7-43) and mean number of endoloops was 1.4 (1-3). Complete closure rate and successful closure rate were 75% and 88%, respectively. Delayed bleeding occurred in one ESD (6.3%), which failed in closure due to trouble in releasing endoloop.
Conclusion: Endoscopic closure of mucosal defect after gastric ESD using endoloop and endoclips was technically feasible. Further prospective study is warranted to investigate the prevention of post-ESD bleeding in patients on antithrombotic drugs.

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2. Matsuda T, et al. Complete closure of a large defect after EMR of a lateral spreading colorectal tumor when using a two-channel colonoscope. *Gastrointest Endosc*. 2004.

Disclosure of Interest: None declared

OP418 EUS-GUIDED GASTROJEJUNOSTOMY FOR MANAGEMENT OF GASTRIC OUTLET OBSTRUCTION OF BENIGN ETIOLOGY

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Introduction: Techniques to create an EUS-guided gastrojejunostomy (EUS-GJ) include direct EUS-GJ and balloon-assisted EUS-GJ. The balloon-assisted technique provides a target (fluid-filled balloon) for transgastric puncture. However, after transgastric needle puncture into the jejunum, there is a concern that the jejunal loop will fall away and the wire will be lost during tract dilation. To circumvent this, we attach a polypectomy snare to the balloon catheter and grasp the wire within the small bowel. Therefore, tension can be put on the wire without a concern of losing access. A 48-year-old male was referred for management of gastric outlet obstruction (GOO) secondary to a chronic calcific pancreatitis associated duodenal stricture. He had failed to respond to multiple through-the-scope balloon dilations and was not suitable for an enteral stent. After a multidiscliplinary meeting, the decision was made to proceed with EUS-GJ and lumen opposing stent insertion.

Methods: The duodenal stricture was dilated to 15mm allowing for passage of the paediatric colonoscope into the jejunum. Then a stiff 0.035-inch guidewire was passed through the working channel of the endoscope into the small bowel. Dilute contrast was injected into the small bowel and an enterogram was obtained. The endoscope was then exchanged out for the balloon/snare catheter which was passed over the wire and inflated in the jejunum. The fluid-filled balloon was localized transgastrically by EUS and was punctured with a 19-gauge needle. A stiff 0.035-inch wire is then advanced through the needle, through the open snare into the small bowel. The snare was then closed to secure the wire. The needle was exchanged out and the tract was subsequently dilated using modified needle-knife (bent tip) and a 4mm dilating balloon (stent delivery system is 10.8F in diameter). The lumen opposing stent was then advanced over the wire, deployed and subsequently the lumen was dilated to 15mm.

Results: Total procedure time was 43 minutes. The patient was kept nil per oral overnight and upper gastrointestinal series the following day demonstrated a patent stent. The patient was dicharged home with a 5-day course of prophylactic oral antibiotics and full-fluid diet for 10 days. The patient was subsequently commenced on a normal diet.

Conclusion: EUS-GJ is a minimally-invasive, effective and safe method of managing GOO. The duration of stent placement necessary to establish a permanent and patent fistula after stent removal needs to be ascertained.

Reference

1. Khashab MA, Baron TH, Binmoeller KF and Itoi T. EUS-guided gastroenterostomy: a new promising technique in evolution. *Gastrointest Endosc* 2015; May; 81(5): 1234–6.

Disclosure of Interest: V. Kumbhari: None declared, S. Ngamruengphong: None declared, M. El Zein: None declared, A. Tieu: None declared, G. Aguila: None declared, M. Khashab Financial support for research: Cook Medical, Consultancy: Boston Scientific, Olympus America, Xlumena

OP419 CREATION OF GASTRO-GASTROSTOMY AND DUODENO-JEJUNOSTOMY USING LUMEN APPOSING STENTS FOR ACCESS TO CHOLEDOCHOJEJUNOSTOMY

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Introduction: Treatment of biliary diseases is challenging in altered anatomy. EUS-guided access using fully covered lumen apposing metal stents (FCLAMS) allows for safe creation of a fistula between lumens and stabilization of lumen walls for more direct access.

Methods: 28-year-old woman who had Roux-en-Y gastric bypass, had a cholecystectomy that was complicated by common bile duct injury and subsequent recurrent cholangitis requiring multiple surgeries, including choledochojejunostomy, resection of segments 5 and 6 with revision of Roux limb. Recurrent episodes of cholangitis required multiple percutaneous interventions. She was referred for endoscopic management of recurrent cholangitis with internalization of biliary drainage.

Entersocopy-assisted ERCP was unsuccessful in reaching the biliary anastomosis. Contrast injection through the PTC drain showed abutment of the Roux limb with the duodenum. Re-establishment of the native anatomy in order to access to the bile duct was planned. In the first step, a gastro-gastric fistula was created under EUS-guidance, and a FCLAMS was placed between the two gastric segments. Three weeks later the second step was performed in which an EUS scope was advanced through the stent to the native duodenum where the Roux limb was identified and a duodeno-jejunal fistula was created under EUS guidance. A FCLAMS was then advanced across the new duodenojejunal fistula and deployed. The EUS was removed and a pediatric colonoscope was inserted through both FCLAMS and the choledochojejunostomy was visualized. The bile duct was cannulated and a biliary stent placed. Afterwards the patient was able to have her PTC drains removed, had resolution of pain and no recurrence of cholangitis.

Results: We have successfully used multiple FCLAMS to achieve biliary access in a patient with gastric bypass and choledochojejunostomy. There were no complications. This access can be used for repeat long-term interventions.

Conclusion: This case demonstrates successful use of multiple FCLASs to establish access in a patient with altered anatomy in order to treat recurrent cholangitis.

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Disclosure of Interest: None declared

OP420 TRANSHEPATIC PERCUTANEOUS ENDOSCOPIC JEJUNOSTOMY TO THE AFFERENT LOOP USING LUMEN-APPOSING METAL STENT FOR TRANSPROSTHETIC ENDOTHERAPY

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Introduction: Percutaneous transenteric approaches allow ERCP when enteroscopy fails. Percutaneous-Assisted Transprosthetic Endotherapy (PATENT) uses large calliber metal stents to allow percutaneous duodenoscope passage into the GI tract. We present a triple modification of currently reported PATENT techniques: a) Transhepatic antegrade cholangioscopy and abdominal ultrasound to guide direct PEJ placement; b) Lumen-Apposing Metal Stent instead of tubular SEMS; and c) Direct cholangioscopy via PATENT. A patient with 9 prior laparotomies, including Billroth-2 gastro-jejunostomy and Roux-en-Y hepatico-jejunostomy had severe relapsing biliary sepsis and hepatholithiasis on MRI. Further percutaneous or surgical intervention was ruled out.

Methods: A three-staged intervention was carried out. 1st: EUS-guided Hepatico-Jejunostomy (EHJ) with two overlapping covered SEMS from the B2 afferent jejunal limb into the left hepatic duct. 2nd: Transhepatic antegrade cholangioscopy through the EHJ and the surgical hepaticojejunostomy into the Roux-en-Y afferent limb to guide D-PEJ. Transilumination was not obtained despite close proximity on fluoroscopy. Transabdominal ultrasound was used to monitor percutaneous puncture of the Roux-en-Y afferent limb. A 15 mm diameter Lumen-Apposing Metal Stent was placed as conduit for PATENT. 3rd: Retrograde percutaneous cholangioscopy via PATENT to dilate a dominant right hepatic duct stricture and to rule out residual hepatolithiasis.

Results: The patient recovered uneventfully and remains well at 7-month follow-up.

Conclusion: This case illustrates custom-made approaches combining emerging EUS & percutaneous transenteric procedures with novel stent technology to relieve biliary obstruction where standard approaches fail.

Disclosure of Interest: V. Busto Bea: None declared, F. Santos Santamarta: None declared, G. Gonzalez Redondo: None declared, R. Sanchez Ocaña: None declared, C. Herrero Quiros: None declared, C. De La Serna: None declared, M. Perez Miranda Consultancy: Boston Scientific and Xlumena

OP421 WHAT ARE YOU DOING IN THERE? A CASE OF AN UNUSUAL PANCREATIC LESION

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Introduction: Schwannomas are benign spindle cell tumors derived from the Schwann cells that line the nerve sheaths. Extracranial neuromas typically occur in the peripheral extremities. Visceral location of these tumors is rare. Pancreatic schwannomas are uncommon and often difficult to diagnose given their similarity with more common pancreatic cystic lesions.

Methods: A 62-year-old female with a past medical history of type II Neurofibromatosis presents with a two-year history of abdominal pain and 15

pound unintentional weight loss. Patient had a recent normal upper endoscopy and colonoscopy. No change in her symptoms with proton pump inhibitors or anti-spasmodic therapy. MRI of the abdomen and pelvis revealed a multilobulated circumscribed mass between the uncinate process of pancreas and C-loop of duodenum measuring 2.7 x 2.0 cm. Mass showed increased signal on T2 as well as prominent surrounding lymph nodes. Endoscopic ultrasound showed a complex of hypoechoic masses in the uncinate process, the largest of which measured 2.3 cm. In some views, there were cystic components to these lesions. FNA revealed a spindle cell neoplasm which stained positive for S-100, consistent with schwannoma.

Results: Pancreatic schwannomas arise from the nerve sheath of the branches of the vagus nerve which courses through the pancreas. These tumors are slow growing and rarely malignant. They are typically located in the head and body of the pancreas. 60% of these lesions are cystic, and as such can mimic more common cystic pancreatic lesions such as cystadenoma, intraductal papillary mucinous neoplasm, and pseudocysts. These tumors are typically asymptomatic on presentation, but can present with abdominal pain and weight loss. On cytology, schwannomas are composed of spindle cells with indistinct cytoplasmic borders with wavy nuclei embedded in a collagenous matrix. Schwannomas stain strongly positive for S-100 protein. Given their slow growth and low rate of malignant transformation, treatment is typically enucleation or watchful waiting if asymptomatic.

Conclusion: Although pancreatic schwannoma is a rare and benign disease, it should be considered in the differential diagnosis of pancreatic lesions with cystic changes. The diagnosis of pancreatic schwannoma is difficult given its common appearance and low yield of specimen collection with fine needle aspiration.

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Disclosure of Interest: None declared

OP422 ENDOSCOPIC BAND LIGATION: AN EFFECTIVE THERAPY FOR ACTIVE DIVERTICULAR BLEEDING

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Introduction: Colonic diverticular bleeding is the most common cause of lower gastrointestinal bleeding in adults. Recently, new endoscopic techniques have been developped to identify the responsible diverticulum and achieve immediate mechanical hemostasis. Band ligation has been proposed as a safe and effective endoscopic approach and recent studies defend this technique is superior to hemoclips and should therefore be attempted as the initial therapy for active diverticular bleeding.

Methods: The authors present a video case of diverticular bleeding successfully diagnosed and treated by endoscopy using band ligation technique. The gastroscope *GIF-Q165, Olympus®*, and the band-ligator device *SpeedbandSuperview Super, Boston Scientific®*, were used in this procedure.

Results: A 84-year-old female patient with past medical history of hypertension, cerebral vascular disease and end-stage kidney disease under dialysis, not on anticoagulation or antiplatelet therapy, was admitted with sudden, painless severe hematochezia, hypovolemic shock and acute severe anemia (hemoglobin 6.9 g/dL). After bowel preparation, a full colonoscopy with ileoscopy was performed, showing bright red blood in the transverse and left colon and multiple sigmoid diverticula. Vigorous water lavage was performed, allowing identification of a diverticulum with active bleeding in the sigmoid colon. A marking clip was placed near to the responsible diverticulum. After switching to a conventional gastroscope with the band-ligator attached to the tip, aspiration and eversion of the bleeding diverticulum was performed and an elastic band was placed around its base, producing immediate hemostasis. Then, the opposite colonic wall was tattooed. Within a 3-months follow-up, no complications and no rebleeding were documented.

Conclusion: Band ligation proved to be a safe and effective endoscopic treatment for active diverticular bleeding.

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Disclosure of Interest: None declared

OP423 EMR DISSECTION OF A 100MM 90% CIRCUMFERENTIAL LATERALLY SPREADING TUMOUR OF THE RECTUM

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Introduction: We present the case of a 80-year-old man presenting with PR bleeding. At colonoscopy he was found to have a 100mm Paris 0-IIa/Is Kudo IV laterally spreading tumour of the rectum, from 7 to 17 cm from the anal verge. He was referred to Westmead Hopsital, Sydney for endoscopic resection.

Methods: The resection of this lesion was performed piecemeal by endoscopic mucosal resection (EMR). The specific techniques involved are demonstrated including snare placement, multiple snare types and resection of a wide margin of normal tissue to prevent recurrence [1]. Snare tip soft coagulation is demonstrated as an effective method to control intraprocedural bleeding [2]. Use of multiple angles, multiple resections and retroflexion over a fold is shown to be required in the complete resection of the lesion.

Results: A new technique described at Westmead is also demonstrated in the video. EMR dissection describes the technique required to perform EMR of large lesions with Paris Is components and extending over folds. Numerous resections are often required to delineate the plane of the resection and isolate the Is component with that component resected last if possible and en bloc. Submucosal invasion is more likely in lesions with Is components and is most likely beneath the Is area [3]; en bloc resection allows ease and accuracy of histopathological assessment once this area has been dissected from the surrounding tissue.

Conclusion: We have demonstrated the possibilities of a novel resection technique termed EMR dissection, alongside multiple standard techniques. This type of lesion is presenting more frequently to endoscopists as the boundaries of possibility with endoscopic resection are extended. We hope this video is informative to our European colleagues who encounter such lesions in their centres.

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Disclosure of Interest: None declared

OP424 POCKET CREATION-TUNNELING METHOD FOR TREATMENT OF RECTAL GIANT (18 CM) LATERAL SPREADING TUMOR WITH ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection(ESD) is an effective and safe method, enabling en-bloc complete resection of lesions. Pocket-creation method is an ESD technique which helps safe dissection of the submucosal area and en-bloc resection of the lesion(1). We report a case of laterally spreading tumor (LST) in rectum 18cm in size which was successfully resected by ESD using two different techniques.

Methods: Procedure was performed after the patient was sedated with spinal anesthesia technique at endoscopy unit. Submucosal invasion was evaluated by chromoendoscopy and by endoscopic ultrasonography before ESD. To achieve en-bloc resection and benefit from gravity, ESD was planned as follows: open a tunnel at anal site of the lesion to proximal site when the patient is on left lateral position and then connect the tunnel to the right site of the lesion. Afterwards for the benefit of gravidity and clear sight re-position the patient to right lateral, join the tunnel to the left site of the lesion. A mixture of sodium hyaluronate, indigo carmine was injected for submucosal elevation. After 2-3 cm of dissection the mixture of saline, epinephrine and indigo carmine was used for quicker injection. ESD was performed using Dual Knife.

Results: The patient was a 61-years-old male with giant LST at rectum starting at 3 cm from the anal canal and extending proximally measured 13 cm endoscopically. The resected tumor was taken out as en-bloc and measured 179*108 mm. The procedure time was 224 minutes. Pathologic examination showed intramucosal carcinoma, lateral and vertical margins were clear. No complication occurred during or after the procedures. Two months later no residual tissue was seen on colonoscopic examinations.

Conclusion: Two different techniques; Pocket creation tunnelling method (PCM-t) and gravidity effect of standard ESD, were used together for an effective and controlled dissection of giant lesion which was successfully removed en-bloc. As the lumen of colon is narrow, with standard ESD technique the dissected lesion can completely block the lumen, decrease maneuver capacity of the endoscope. When PCM-t is performed, dissection can be done with control because dissected lesion does not fall directly into the lumen. Colorectal ESD is an effective and safe method for large lesions in experienced hands and using both techniques together may provide en bloc resection.

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Disclosure of Interest: None declared

OP425 A CASE OF PERFORATION DURING COLORECTAL ESD WITH NO SERIOUS ADVERSE EVENTS AFTER APPLICATION OF POLYGLYCOLIC ACID SHEETS AND FIBRIN GLUE

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Introduction: Endoscopic submucosal dissection (ESD) for large colorectal tumors is an effective method of treatment with a high curative resection rate, but is also accompanied with a relatively high rate of perforation. In cases where perforation cannot be endoscopically closed, emergency surgical treatment is frequently required. The use of polyglycolic acid (PGA) sheets, a surgical suture material, adhered with fibrin glue, has been reported to prevent leakage after surgical resection. However, there have been no reports on the efficacy of PGA sheets with fibrin glue after perforation during colorectal ESD.
Methods: An asymptomatic 72-year-old male patient underwent colonoscopy due to positive fecal occult blood tests, resulting in the discovery of a laterally spreading tumor in the descending colon. The patient was referred to our institute, and preoperative magnifying endoscopy examination revealed characteristics that were suggestive of adenoma. However, there were irregular areas within the lesion, and early stage adenocarcinoma could not be ruled out. ESD was advised for en bloc resection.
Results: ESD was performed at our endoscopy unit under conscious sedation. Treatment began smoothly, but as ESD progressed, the target submucosal layer regressed into a fibrotic layer. During dissection of the fibrotic layer perforation occurred, which further widened as dissection of the fibrotic layer continued, and eventually led to an enormous perforation with the underlaying omentum clearly visible. Endoscopic clip closure of the perforation was attempted, but complete closure was technically unfeasible. Clip closure of the perforations was discontinued, and as an emergency measure the perforation was covered with multiple strips of polyglycolic acid sheet, and adhered with fibrin glue. After this procedure, there was no visible perforation remaining and no apparent signs of continuous gas leakage, achieving clinical complete closure of the perforations. The patient displayed a slight fever the day after ESD, but was otherwise asymptomatic, with no significant changes in laboratory findings. Postoperative CT findings revealed free air in the abdominal cavity, but with no signs of peritonitis. Oral diet was begun on day 7 after ESD, and the patient was discharged with no adverse events.
Conclusion: This is a case report of colorectal perforation where the application of polyglycolic acid sheets and fibrin glue was effective in closure of perforation. In cases where complete clip closure of colorectal perforation is not technically feasible, this novel method may be useful for minimizing adverse events. Further evaluation is required for confirmation.
Disclosure of Interest: Y. Sakaguchi: None declared, Y. Tsuji Lecture fee(s): Olympus Medical Systems, HOYA Pentax, Eisai, GUNZE, CSL Behring, M. Fujishiro Financial support for research: Astellas Pharmaceutical, Takeda Pharmaceutical, Zeria Pharmaceutical, Otsuka Pharmaceutical, Astrazeneca Pharmaceutical, Dainihon-Sumitomo Pharmaceutical, Taiho Pharmaceutical, Ajinomoto Pharmaceutical, and, Eisai for his department outside the submitted work, Lecture fee(s): Olympus Medical Systems, HOYA Pentax, Eisai, MSD, Daiichi-Sankyo Pharmaceutical, Astrazeneca Pharmaceutical, Aska Pharmaceutical, Taisho-Toyama Pharmaceutical, Otsuka Pharmaceutical, Zeria Pharmaceutical, Takeda Pharmaceutical, Astellas Pharmaceutical, Seikagaku Corp., Johnson & Johnson, Ajinomoto Pharmaceutical, Amco, Novartis Pharmaceutical, Boston Scientific, and, Boehringer-Ingelheim, outside the submitted work, Conflict with: non-financial support from HOYA Pentax, Olympus Medical Systems, and, Fujifilm for his department outside the submitted work, K. Koike: None declared

WEDNESDAY, OCTOBER 28, 2015 11:00–12:30
RECENT ADVANCES IN DIVERTICULAR DISEASE AND MICROSCOPIC COLITIS – ROOM E3

OP426 PREDICTIVE VALUE OF THE "DICA" ENDOSCOPIC CLASSIFICATION ON THE OUTCOME OF THE DIVERTICULAR DISEASE OF THE COLON: AN INTERNATIONAL STUDY

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Introduction: The endoscopic classification DICA (Diverticular Inflammation and Complication Assessment) has been recently developed for patients suffering from diverticulosis and diverticular disease.
Aims & Methods: The aim of this study was to assess its predictive value on the outcome of the disease. We reassessed retrospectively patients in whom endoscopic videos and/or photos and/or clinical follow-up were available. For each patient, we recorded: age at the time of disease occurrence; severity of DICA (grade 1, 2 or 3) at the time of diagnosis; months of follow-up; therapy taken during the follow-up; occurrence/recurrence (in months) of diverticulitis.
Results: The study enrolled 1651 patients (793 M, 858 F, mean age 66.6 ± 11.1 years): 939 (56.9%) patients were classified as DICA 1, 501 (30.3%) as DICA 2 and 211 (12.8%) as DICA 3. The mean follow-up was 29.5 ± 28.7 months. Acute diverticulitis (AD) occurred/recurred in 263 (15.95) patients ; surgery was necessary in 57 (21.7%) of those cases.
DICA was the only factor significantly associated to the occurrence of diverticulitis ($p < 0.0001$) and surgery ($p < 0.0001$) either at univariate or multivariate analysis. At each level of DICA classification a significant increase of diverticulitis occurrence was detected (HR (95% CI): DICA 1 vs DICA 3: 18.992 (12.267 to 29.406); $p < 0.0001$).
Therapy with various regimens was taken by 869 (52.6%) patients during the follow-up. With respect to prevention of occurrence/recurrence of diverticulitis, assumption of therapy was effective only in DICA 2 patients with HR (95% CI) of 1.796 ($p = 0.002$); therapeutic regimens including mesalazine were the only effective therapies to reduce diverticulitis occurrence/recurrence compared to no therapy (HR (95% CI) mesalazine-based therapies vs no therapy: 0.2103 (0.122 to 0.364), $p < 0.0001$).
Conclusion: DICA classification is a valid parameter to predict the risk of diverticulitis occurrence/recurrence in patients suffering from diverticular disease of the colon.
Disclosure of Interest: None declared

OP427 EFFICACY OF RIFAXIMIN AND DIETARY FIBER ON SYMPTOMS OF UNCOMPLICATED DIVERTICULAR DISEASE OF THE COLON

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Introduction: Dysbiosis is common in patients with diverticular disease of the colon. Available data show the efficacy of poorly absorbed antibiotics and dietary fiber in achieving symptomatic relief in patients with uncomplicated diverticular disease. However, their value in the prevention of inflammatory complications of the disease needs to be further explored.
Aims & Methods: The aim of the study was to comparatively evaluate the long-term efficacy of Rifaximin and dietary fibers in reducing symptoms and to prevent both recurrent attacks and complications such as diverticulitis. 282 patients (161 males, 121 females, age 65.4 ± 7.4 years) from two gastroenterological units were enrolled in the study in two treatment schedules in a randomized fashion: Group 1 (172 pts) rifaximin 400 mg BID; Group 2 (110 pts) dietary fiber supplementation (Colon Help 20 gr/day). Treatments were administered 10 days every month for 9 months. Inclusion criteria were: endoscopic and/or radiologic evidence of diverticular disease of the left colon and the presence of symptoms attributable to diverticular disease without signs of diverticulitis.
Results: Clinical evaluations (Global Symptomatic Score – GSS), endoscopic and imagistic evaluations were performed at admission and at 3 month intervals. Analysis of standardized deviates showed that both treatments were effective in reducing tenesmus, bloating, diarrhea, well-being and bleeding ($p < 0.0001$; $p = 0.01$; $p = 0.01$; $p = 0.01$; $p = 0.04$ and $p = 0.03$, respectively after 9 months). GSS declined in both groups, but a greater reduction was evident in the rifaximin group (intention-to-treat analysis 3.31 ± 2.68 vs 5.86 ± 4.55, $p < 0.001$; per-protocol analysis: 3.50 ± 2.56 vs 6.32 ± 4.21, $p < 0.001$). The patients treated with rifaximin showed a more marked reduction in symptom frequency. Complications occurred in 5 patients of group I (3 cases of rectal bleeding and 2 of diverticulitis) and in 9 patients of the fiber group (3 cases of intestinal infections, 2 of rectal bleeding and 4 of diverticulitis) – $p = 0.031$. Side effects occurred in 7 patients of the rifaximin group and 5 patients of the fiber group ($p = NS$).
Conclusion: Cyclic administration of rifaximin and dietary fiber is effective for the symptomatic relief of uncomplicated diverticular disease of the colon. Some symptoms and complications showed greater improvement with rifaximin, which is safe and well-tolerated by patients.
Disclosure of Interest: None declared

OP428 DISTRIBUTION OF HISTOLOGICAL LESIONS OF MICROSCOPIC COLITIS (MC): OVER 9 MC OUT OF 10 CAN BE DIAGNOSED BY A LEFT COLONOSCOPY: RESULTS OF THE FRENCH NATIONAL COHORT ANGH

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Introduction: The aims of this study were to evaluate the characteristics and topography of histological diagnosis lesions of MC, lymphocyte (LC) and collagen (CC), from the national cohort COLMI (1) conducted between September 2010 and June 2012 in 26 French general hospitals.

Aims & Methods: The patients of the cohort with MC were included. The diagnosis of CC or LC was made by colonoscopy with multiple biopsies of the rectum and colon. Collagenous colitis was defined by a sub epithelial collagen layer reaching or exceeding 10 mm thickness, and LC by an increased intra-epithelial lymphocytes count reaching or exceeding 20 lymphocytes per 100 epithelial cells. Diagnoses of CC and LC were made according to these predefined criteria by the pathologists working in each center. It has been established that the diagnosis of MC is highly reproducible (2).

Results: 129 had MC (LC 87 and 42 CC): 99 patients (72 LC and 27 CC) had colonic biopsies in each segment and were retained for analysis. The median thickening of the collagen membrane significantly increased of the rectum to the right colon, respectively 14.5+/-15.8 microns, 15.2+/-20, 20+/-11.8, 22.5+/-16.2. The median rate LIE was significantly lower in the rectum (22.5%+/-21.5) and identical at the level of the left, transverse and right colon, respectively 30%+/-22.2, 23.4+/-30%, 30%+/-22.3. The diagnostic sensitivity of the biopsies was maximal in the right colon, respectively 93% and 97% for CC and CL, and minimum in the rectum, 77% and 74% for CC and CL. The achievement of rectal and left colic biopsies allowed the diagnosis of CC and CL in 93% and 94% of cases. Performing additional biopsies beyond the splenic flexure allowed to diagnose all of MC. In case of CC, a lesser collagen thickening of the basement membrane was significantly associated with the presence of an autoimmune disease ($p = 0.02$). No significant correlation was observed between the intensity of the histological lesions and clinical and biological severity. In case of CL, a rate higher of intra-epithelial lymphocytes count was significantly associated with the absence of abdominal pain ($p = 0.01$) and a shorter duration of diarrhea ($p = 0.001$).

Conclusion: The diagnostic sensitivity of colonic biopsies is maximal in the right colon and minimum in the rectum. The achievement of rectal biopsies and colic left in a short colonoscopy to diagnose more than 9 microscopic colitis out of 10.

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Disclosure of Interest: None declared

OP429 RISK OF COLORECTAL POLYPS AND CANCER IN MICROSCOPIC COLITIS

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Introduction: Microscopic colitis (MC) is a disease characterized by chronic watery diarrhea, normal radiological and endoscopic appearance but microscopic inflammation. MC includes two distinct entities: lymphocytic (LC) and collagenous colitis (CC). Following the biology of MC, prolonged and increased colonic inflammation could increase the risk of colorectal polyps, adenomas and cancer.

Aims & Methods: The aim of this study was to assess the risk of colorectal polyps, adenomas and colorectal cancer (CRC) in patients with MC.

We conducted a cohort study using a nationwide population-based pathology database (PALGA) from the Netherlands (1991-2014). All incident (newly diagnosed), histologically confirmed cases of MC (lymphocytic, collagenous or unspecified) among adults (≥18 years) were identified and followed until first occurrence of colorectal polyp, adenoma or cancer, death (life expectancy of Dutch standard population was assumed) or end of study period. As a measure of the relative risk, the observed number of CRC events in the MC cohort was compared to the number of expected events in the general Dutch population (based on Dutch cancer registry), yielding the standardized incidence ratio (SIR) with 95% Confidence Intervals (CI). The one-year and five-year risk of CRC after MC diagnosis was calculated by Kaplan Meier analysis.

Results: Out of 10,826 potential MC cases, 7,897 were classified as incident MC cases (n = 4.397 collagenous; n = 2.671 lymphocytic; n = 954 unspecified type) of whom 56% were female. Median age at MC diagnosis was 60 years (IQR 49-71) with 2.5% having celiac disease at time of MC diagnosis. During follow-up (median 7.2 years IQR 3.7-11.5), a total of 702 patients were diagnosed with colorectal adenomas, yielding an incidence rate (IR) of 1155.0 (95% CI: 1071.9-1242.8) per 100,000 person-years (PYs); 321 with polyps (other than adenomas) resulting in an IR of 511.6 (95%CI: 457.9-569.9) per 100,000 PYs; and 91 with CRC yielding an IR of 142.4 (95%CI: 115.3-173.9) per 100,000 PYs. IRs were particularly high in the first year following MC diagnosis, and lowered over time. The SIR for CRC was 1.8 (95% CI: 1.4-2.2) over all time periods. When divided in time after MC diagnosis SIR was 5.6 (95%CI: 4.0-7.7) in the first year after MC diagnosis, 1.6 (95%CI: 0.7-3.3) in the second year after MC diagnosis and 1.8 (95%CI: 1.3-2.3) thereafter. The risk of CRC in the first year after MC diagnosis was 0.46% (0.32-0.62) and five years was 0.84% (0.66-1.09).

Conclusion: The risk of colorectal cancer was higher among incident microscopic colitis patients in this large Dutch nationwide cohort as compared to the general population. The increased incidence may be due to prolonged and continued colonic inflammation. Particularly in the first year following MC diagnosis high incidences of colorectal polyps, adenomas and cancer were observed, potentially because of more medical attention, which decreased over time. Whether surveillance for colorectal cancer should be considered in patients with MC needs further investigation.

Disclosure of Interest: None declared

OP430 RIFAXIMIN TREATMENT INCREASES LACTOBACILLUS ABUNDANCE IN PATIENTS WITH DIFFERENT GASTROINTESTINAL AND LIVER DISEASES

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Introduction: Rifaximin is a non-absorbable antibiotic with beneficial effects in several gastrointestinal diseases (ulcerative colitis UC, Crohn's disease CD, irritable bowel syndrome I, diverticular disease DD) and in hepatic encephalopathy. Rifaximin has non-traditional effects on gut microbiota about which a little is known.

Aims & Methods: Aim of our study was to evaluate the effect of rifaximin administration (1200 mg/daily, 10 days) on gut microbiota composition in Caucasian patients with different gastrointestinal diseases (ulcerative colitis, Crohn's disease, irritable bowel syndrome, diverticular disease) and hepatic encephalopathy. Inclusion criteria were no exposure to antibiotics, pre-/probiotics and bowel colonoscopy preparation for at least one month, and omnivore normocaloric diet for at least one year. Fecal samples were collected at baseline (time a), at the end of treatment (time b) and 1 month after the end of treatment (time c). Microbiota composition was assessed by a metagenomic gene-targeted approach (16S rRNA) using the Roche 454 GS Junior, following DNA isolation from stool samples stored at –80°C. Data were analyzed in Qiime. Biostatistic analysis was performed using R-statistics packages.

Results: Nineteen patients were enrolled in the study and all of them completed the follow-up (overall number of faecal samples: 57). No rifaximin-related sides effects were reported. Principal coordinates analysis according to weighted Unifrac distance measure did not show any significant clustering of samples according to rifaximin treatment timepoint ($p = 0.854$; permutational multivariate analysis of variance).Differential abundance analysis computed by allowing for disease effects revealed an increased abundance of Lactobacillaceae at family level (time c vs time a adj.p = <0.0001; time c vs time b adj.p = 0.001) and of Lactobacillus (time c vs time a adj.p = <0.0001; time c vs time b adj.p = 0.001).Notably, rifaximin treatment did not change significantly intra-individual bacterial diversity (alpha-diversity measures: median Chao1 time a/b/c 21/20/22 $p = 0.401$, Shannon time a/b/c 1.45/1.13/1.6 $p = 0.102$).

Conclusion: Rifaximin treatment is able to increase the abundance of the beneficial bacteria Lactobacillus in patients with different gastrointestinal and liver diseases without affecting the overall microbiota composition and intra-individual bacterial diversity.

Disclosure of Interest: None declared

OP431 UTILITY OF ENDOSCOPIC EXAMINATION IN DIAGNOSING ACUTE GRAFT-VERSUS-HOST DISEASE OF THE GASTROINTESTINAL TRACT

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Introduction: Acute graft-versus-host disease (GVHD) occurring within 100 days post-transplant is a critical factor influencing prognosis in transplant recipients. However, because the disease is rare, only a few studies have investigated the endoscopic features of GVHD.
Aims & Methods: In this study, we retrospectively investigated the diagnostic accuracy for acute GVHD in the GI tract and revealed the characteristic endoscopic findings. Between January 2005 and June 2012, 868 patients underwent allogeneic hematopoietic stem cell transplantation at our hospital. Of 377 patients who developed GI symptoms such as diarrhea, nausea, and vomiting, 278 patients were diagnosed based on histopathological assessment of the biopsy specimen taken during upper (GS) or lower (CS) GI endoscopy within 100 days of transplantation. After excluding patients infected with cytomegalovirus, 234 cases (100 GS, 134 CS) were examined to investigate the characteristic endoscopic findings of GVHD and their positive predictive value (PPV).
Results: Biopsy revealed GVHD in 197 (84.2%) patients who had undergone GI endoscopy. The rate of positive biopsy by GI region was 79.2% (76/96) for the stomach, 84.0% (42/50) for the duodenum, 86.5% (83/96) for the terminal ileum, and 88.9% (119/134) for the colon. Frequent endoscopic findings were mucosal change (53.8%) and luster (52.6%) in the stomach; villous atrophy (46.3%) in the terminal ileum; and low vascular permeability (75.6%), edema (68.1%), and tortoiseshell pattern of the mucosa (61.4%) in the colon. No abnormal findings were observed in 65.8% of patients with GVHD in the duodenum. The PPV was 100% for the following findings: mucosal exfoliation in the stomach; villous atrophy, ulcer, and mucosal exfoliation in the terminal ileum; and ulcer and mucosal exfoliation in the colon. It was ≥90% for redness, edema, and erosion in the terminal ileum; and redness, edema, erosion, tortoiseshell pattern, and reduced vascular permeability in the colon. The PPV was ≥80% for mucosal change, luster, redness, and ulcer in the stomach; and edema and erosion in the duodenum. Furthermore, 94.4% (17/18) of patients with mucosal exfoliation throughout the GI tract had Grade 3 or 4 GVHD.
Conclusion: Despite the post-transplantation conditions, the diagnostic accuracy of GI endoscopy for GVHD was 84.2%. Useful endoscopic findings for the diagnosis of GVHD were mucosal change and luster in the stomach; villous atrophy in the terminal ileum; and tortoiseshell pattern, edema, and low vascular permeability in the colon.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 11:00-12:30
COLORECTAL CANCER: CARCINOGENESIS - DETECTION - PREVENTION – ROOM E5

OP432 COLORECTAL CANCER RISK IN PATIENTS WITH BOTH LYNCH SYNDROME AND INFLAMMATORY BOWEL DISEASE

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Introduction: Lynch Syndrome (LS) and inflammatory bowel disease (IBD) are associated with an increased colorectal cancer (CRC) risk due to genetic (LS) and inflammatory (IBD) factors. Reported lifetime risks of CRC development for patients with LS range from 22 to 74%. IBD patients bear a 1.5 to 2 times greater CRC risk compared to the general population. The increased CRC risk has resulted in recommendations for surveillance and treatment in both patient groups. Although relevant for surveillance and treatment strategies, it is unknown whether CRC risk is further increased in patients that suffer from both LS and IBD. We therefore aimed to establish CRC risk in patients with both LS and IBD.
Aims & Methods: We established a cohort of LS patients assembled from two LS referral centers in The Netherlands (Radboud University Medical Center, Nijmegen; Academic Medical Center, Amsterdam). Patients with confirmed mutations in the mismatch repair genes associated with LS, including MLH1, MSH2 (and EPCAM deletion-mediated MSH2 methylation), MSH6 or PMS2 mutations, were eligible for inclusion. We linked the established LS cohort to PALGA (Dutch Pathology Registry with nationwide coverage) to identify patients with both IBD and LS. Subsequently, we compared patients with both LS and IBD (cases) and LS patients without IBD (controls) by adopting a retrospective cohort study approach in order to establish CRC risk.
Results: 15/1046 (1.4%) LS patients also carried a diagnosis of IBD, including 8 (53.3%) patients with ulcerative colitis (UC), 6 (40.0%) with Crohn's disease (CD) and 1 (6.7%) with indeterminate colitis. Disease extent in UC involved the total colon in 62.5% (5/8) and the left-sided colon in 37.5% (3/8). CD patients had either ileal involvement (50%, 3/6) or ileocolonic involvement (50%, 3/6). Despite a younger age at study inclusion in the case group (median 38.0 y versus 52.0 y, p = 0.001), the rate of CRC development was not significantly different between cases (4/15, 26.7%) and controls (313/1045, 30.4%; Table 1). The 4 cases developed CRC at a younger age compared to controls (median 36.0 y versus 46.0 y, p = 0.042). However, cumulative CRC incidence was similar between both groups (p = 0.124). All CRC patients in the case group concerned UC patients resulting in a higher cumulative CRC incidence for the UC subgroup (4/8, 46.4% at age of 38) compared to controls (313/1031, 7.0% at age of 38, $p < 0.001$).

Variable	Cases(n = 15)	Controls(n = 1031)	p-value
Male sex, n (%)	7 (46.7)	474 (45.3)	0.916
Age at study inclusion, median (range)	38.0 (26-69)	52.0 (18-100)	0.001
Lynch type			0.414
MLH1, n (%)	5 (33.3)	256 (24.8)	
MSH2, n (%)	2 (13.3)	310 (30.1)	
PMS2, n (%)	1 (16.7)	128 (12.4)	
MSH6, n (%)	7 (46.7)	337 (32.7)	
Colorectal cancer, n (%)	4 (26.7)	313 (30.4)	1.000
Age at diagnosis CRC, median (range)	36.0 (34-42)	46.0 (16-86)	0.042

Conclusion: Patients with both IBD and LS developed CRC at a younger age compared to LS patients without IBD, although cumulative CRC incidence was similar. In our unique cohort, CRC only developed in patients with UC and LS. Patients with UC showed a higher cumulative CRC incidence compared to LS patients without IBD.
Disclosure of Interest: None declared

OP433 LIQUID BIOPSY-BASED DETECTION OF COLORECTAL ADENOMA AND CANCER CASES USING FOUR TISSUE-SPECIFIC DNA METHYLATION MARKERS

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Introduction: Investigation of aberrant DNA methylation pattern of several genes may serve as a diagnostic marker for colorectal cancer (CRC) in tissue samples. Cell-free DNA (cfDNA) in the circulatory system can originate from tumor tissue; therefore the evaluation of tumor-related methylated DNA in plasma fraction – as a liquid biopsy - can be a simple and promising method for cancer screening.
Aims & Methods: Our purpose was to identify effective DNA methylation markers in tissue samples of colorectal neoplasia patients. Furthermore, our aims were to compare the cfDNA quantity of patient groups and to analyse the methylation pattern of 4 selected markers in plasma samples. Colon biopsies were collected from healthy (n = 15), adenoma (AD, n = 15) and CRC (n = 15) patients. Pyrosequencing was performed by PyroMark and GS Junior System to define the methylation levels of 19 genes showing decreased mRNA expression on the basis of whole genome gene expression profiling by HGU133 Plus 2.0 microarrays (Affymetrix) (Galamb et al. 2012). Furthermore, EpiTect Methyl qPCR Array (Qiagen) was used to characterize the methylation patterns of 96 genes in healthy (n = 10), low-grade dysplasia (LGD, n = 17), high-grade dysplasia (HGD, n = 6), and CRC (n = 17) samples. After plasma DNA isolation and concentration measurement [normal (n = 20), AD (n = 20) and CRC (n = 20)], bisulfite conversion treatment was performed. 4 potentially hypermethylated markers (SDC2, PRIMA1, SFRP1, SFRP2) were selected for DNA methylation analysis and multiplex preamplification method was developed. Methylation percent of the candidate genes was determined using quantitative methylation-specific PCR and the CT values were compared to a calibration curve based on methylated and non-methylated standard samples.
Results: 6 genes were found to be hypermethylated ($p < 0.05$) in tissue samples of both adenoma and CRC groups (e.g. SDC2, SFRP1) by pyrosequencing. Using qPCR method, we identified 10 candidate genes that were hypermethylated in more than 85% of tumor samples (e.g. SFRP1, SFRP2, SLIT2). Interestingly, the highest mean DNA methylation was measured in HGD, followed by LGD and CRC specimens. In case of plasma samples, the average of total yield (ng) of N, AD and CRC samples was 34 ± 17ng, 63 ± 39ng and 86 ± 23ng, respectively. The methylation of SDC2, PRIMA1, SFRP1, SFRP2 was observed in 95%(19/20), 95%(19/20), 80%(16/20), 80%(16/20) of patients with CRC; 75%(15/20), 80%(16/20), 85%(17/20), 85%(17/20) of adenoma samples; and 20%(4/20), 20%(4/20), 25%(5/20), 30%(7/20) of the healthy controls. Using combined analysis, at least 3 markers were methylated in 95% of CRC, 80% of AD and only 10% of normal samples.
Conclusion: Hypermethylation of tumor-specific genes was detected in tissue samples and 4 selected markers were used as combined epigenetic markers from high-volume plasma samples for CRC screening successfully with high specificity. A two-step amplification procedure was developed to detect adenoma and CRC cases with high sensitivity, despite of the low concentration of cfDNA.

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Disclosure of Interest: None declared

OP434 WHOLE-EXOME SEQUENCING OF SIX AFFECTED INDIVIDUALS IN A FAMILY WITH AN AUTOSOMAL DOMINANT INHERITED SERRATED POLYPOSIS PHENOTYPE

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Introduction: In serrated polyposis syndrome (SPS), characterized by the development of multiple serrated polyps in the colorectum, an association with heritable germline aberrations is suspected. Identification of germline aberrations underlying this clinical phenotype is important for clinical management since SPS patients are at high risk to develop colorectal cancer. We describe a large family with an autosomal dominant inheritance pattern in which we searched for the causative germline mutation.

Aims & Methods: We applied whole-exome sequencing (WES) on germline DNA of six affected family members from two generations. We screened for pathogenic germline variants in genes previously associated with multiple serrated polyps (1). Additionally, we focused on all rare (minor allele frequency (MAF) <0.01) germline variants shared between the six affected family members. Co-segregation analysis was performed for all shared variants. For one remaining variant, RNA expression levels as well as possible allele specific expression bias were determined using EBV-transformed B-lymphocytes derived from affected and unaffected family members.

Results: We encountered truncating variants in two previously described genes (1); one nonsense variant (p.E49*) in *PIF1* and one deletion affecting the canonical splice site of *RBL1*. Both variants did not co-segregate with the development of serrated polyps in the family and the variant in *PIF1* was frequently encountered in our control dataset ($n=2.329$; MAF 0.0167). Thirty variants were shared between all six exomes of which twenty-nine were excluded because of a high MAF (>0.01) in 3 control databases ($n=16$) or because they did not co-segregate with the polyposis phenotype in the family ($n=13$). One missense variant (p.E333K) in the *BCAT1* gene remained, but was predicted to be benign based on five in silico prediction tools. Although we noticed a slightly increased expression of the p.E333K allele, the overall RNA expression levels of the *BCAT1* gene were not elevated in mutation carriers. Also the gene *KRAS,* located 250kb upstream of *BCAT1*, showed normal expression levels in patient-derived EBV cell lines compared to unaffected family members that were wild type for *BCAT1*.

Conclusion: We present a family with autosomal dominant inheritence of SPS. A causative genetic germline aberration was not found using our WES-based approach in this promising family. In our family two truncating variants in previously described *RBL1* and *PIF1* genes are unlikely to explain the serrated polyposis phenotype. We hypothesize that the causative genetic factor might be located outside the regions captured by the whole-exome sequencing approach, and requires whole-genome sequencing to be identified.

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OP435 EPIGENETIC CHANGES OF WNT SIGNALING PATHWAY GENES CONTRIBUTE TO COLORECTAL CARCINOGENESIS AND PROGRESSION TOGETHER WITH MUTATIONS OF APC KEY GENE

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Introduction: The WNT signaling pathway has an essential role in colorectal carcinogenesis and progression which involves a cascade of genetic and epigenetic changes.

Aims & Methods: We aimed to analyze the genetic and epigenetic alterations of WNT pathway genes in parallel during the normal-adenoma-carcinoma sequence using next generation sequencing methods.

Whole-methylome analysis was performed from 30 colorectal tissue samples (9 colorectal carcinoma (CRC), 15 adenoma (AD) and 6 normal adjacent tissue (NAT) samples) by next generation sequencing (Illumina) after enrichment of methylated DNA using MethylCap kit (Diagenode). WNT pathway genes were selected using KEGG pathway database. Differently methylated genes were identified, and promoters regions of these genes were determined according to the 'Integrative annotation of chromatin elements from ENCODE data'. Gene expression was studied using Affymetrix HGU133Plus2.0 microarrays (38 normal, 29 adenoma and 27 CRC biopsy samples). Gene expression data (GSE37364 and in silico using 6 GEO datasets) and promoter methylation results were analyzed to find potentially methylation-regulated genes. For confirmation, data of 5-aza-2'-deoxycytidine-treated colon carcinoma cell lines were also involved. Mutations of WNT genes (APC, CTNNB1) were analyzed by 454 sequencing on GS Junior platform.

Results: The most of the differentially methylated CpG sites were localized in gene body regions. Promoter regions of 32 from the 163 analyzed WNT pathway genes were found to be differentially methylated in CRC samples compared to NAT samples, including hypermethylated AXIN2, CHP1, PRICKLE1, SFRP1, SFRP2, SOX17 and hypomethylated CACYBP, CTNNB1, MYC. In AD vs. NAT comparison, altered promoter methylation of 42 WNT signaling genes was detected including hypermethylated APC, AXIN2, DAAM2, DKK4, PRICKLE1, SOX17, SFRP1,2 and 4 and hypomethylated CACYBP, FZD3. Forty-one genes were identified which showed different promoter methylation between CRC and AD samples. Hypermethylation of AXIN2, DKK1, VANGL1 and WNT5A gene promoters was increased in CRC compared to AD, while promoter methylation of SOX17, PRICKLE1, DAAM2 and MYC genes was found to be higher in AD than in CRC. Inverse expression of 26 genes was observed during the gene expression-methylation comparative analysis. Among others, CACYBP, DAAM2, PRICKLE1, PSEN1, SFRP2 and SFRP1 genes were identified as relevant methylation-regulated WNT pathway genes in colorectal normal-adenoma-carcinoma sequence. APC mutations were detected in 0% of NAT, 27% of adenoma and 29% of CRC samples, while only one AD sample showed CTNNB1 mutation.

Conclusion: Beside the frequent APC mutations, the robust, common epigenetic changes of WNT signaling pathway genes also contribute to the development and progression of CRC. Aberrant DNA methylation also appears in adenomas indicating that DNA methylation is an early event of colorectal carcinogenesis.

Disclosure of Interest: None declared

OP436 COLORECTAL CANCER ALARM SYMPTOM INTERRELATION WITH THE PARTICIPATION IN COLORECTAL CANCER SCREENING AND FAECAL OCCULT BLOOD TEST RESULTS

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Introduction: The purpose of screening programmes is to lower the burden of cancer in the population by discovering disease in its early latent stages before any symptoms appear. The objective of the study was to evaluate if colorectal cancer alarm symptoms correlate to the participation in screening.

Aims & Methods: A self-administered questionnaire was mailed to the colorectal screening target group (50-74 years old) of a randomised faecal occult blood test (FOBT) based pilot-study in Latvia. Questionnaire was sent to all responders and non-responders and it was asked if they had observed any of the listed health problems during the last year (multiple-choice question). Listed symptoms were abdominal pain, stool changes (diarrhoea or obstipation), weakness or fatigue, a lot of mucus in the stool, visible blood on the stool and weight loss.

Results: From 6023 questionnaires delivered to the responders of CRC screening pilot project - 5129 were returned (85.1%). While in non-responder group the response rate was only 14.6% (1195 people). Eligible to analysis were 4930 and 1121 questionnaires respectively.

In the responder group 54.1% had not observed any health changes, 31.8% mentioned one symptom, 10.1% two symptoms, others- more than two symptoms. The most common symptom was stool changes 23.9%, then abdominal pain 14.2% and fatigue 11.2%. The highest rate of the positive FOBT was for responders with visible blood in the stool 26.7%, for other symptoms correlation with positive FOBT was from 12.4-16.2%. In the group that hadn't observed any symptoms FOBT was positive in 10.2% of the cases. Relative risk (RR) of positive tests was significantly higher for patients having symptoms (at least one symptom RR = 1.33, at least two symptoms RR = 1.53, at least three symptoms RR = 1.73 and at least four symptoms 1.96, $p < 0.0001$). In the non-responder group 70.5% (significantly higher than in respondent group $p < 0.0001$) had not observed any health changes. Stool changes were mentioned by 17.8%, other symptoms- by less than 8.8% of non-responder group. At least one symptom was mentioned by 19.8%, at least two by 6.2%, and more symptoms by 3.6% in this group.

At the same time only 1% of responders said that symptoms was the motivator to perform FOBT test, but 35% of non-responders as the reason of non-compliance to screening mentioned feeling heathy.

Conclusion: Health problems related to colorectal cancer alarm symptoms influence the decision to participate in screening program. These symptoms and their quantity correlate with faecal occult blood test positivity.

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Disclosure of Interest: None declared

OP437 GREEN TEA EXTRACTS FOR THE PREVENTION OF COLORECTAL ADENOMA AND COLORECTAL CANCER

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Introduction: Colorectal adenomas are precursors to colorectal cancers, and experimental studies have shown the chemopreventive properties of green tea extract (GTE) on colorectal cancer.

Aims & Methods: The aim of this study was to determine the preventive effect of GTE supplements on metachronous colorectal adenoma and cancer by giving GTE tablets which are equivalent of 9 cup-of-green tea per day (0.9 g/day GTE, 0.6 g/day epigallocatechin gallate [EGCG]). The subjects who had undergone complete removal of colorectal adenomas by endoscopic polypectomy were enrolled. A sample size of 176 patients (88 per each group) considering 20% loss to follow-up was calculated to give the study 80% power to detect a difference, assuming a 2-sided significance test at the 0.05 level. They were then randomized into two groups: supplementation group (0.9 g GTE per day for 12 months) or control group without GTE supplementation. A structured 48-h recall at baseline and the 1-year follow-up was used to assess dietary factors. Follow-up colonoscopy was conducted 12 months later in 140 patients (71 in control group and 69 in the GTE group).
Results: Of the 140 patients completed in the study, the incidences of metachronous polyps at the end-point colonoscopy were 60.6% (43 of 71) in control group and 27.5% (19 of 69) in GTE group (relative risk [RR], 0.25; 95% confidence interval [CI], 0.12 - 0.50). Occurrences of metachronous adenoma showed a decrease in GTE group (24.6%, 17 of 69) compared to control group (42.3%, 30 of 71; RR, 0.45; 95% CI, 0.22 - 0.92); the number of relapsed adenoma was also decreased in the GTE group than in the control group (0.72 ± 1.12 *vs.* 0.33 ± 0.63, $P = 0.014$). There were no significant differences between the 2 groups in terms of body weight, body mass index, waist circumference, serum lipid profiles, fasting serum glucose and serum C-reactive protein levels.
Conclusion: This study of GTE supplement suggests a favorable outcome for the chemoprevention of metachronous colorectal adenomas in Korean patients (ClinicalTrials.gov number, NCT02321969).
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 11:00–12:30

NEW INSIGHTS INTO INFLAMMATION IN THE LOWER GI TRACT – ROOM E6

OP438 LARGE-SCALE DRUG SCREEN REVEALS BENZIMIDAZOLE ANTI-HELMINTHICS AS ANTI-TNF CO-THERAPY

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Introduction: Wound-healing and immunosuppressive macrophages are important players in the regulation of mucosal immunity. Anti-TNF compounds induce this type of macrophages in vitro and in vivo, indicating this as an effector mechanism for mucosal repair in IBD. We have previously shown that the clinical benefit of anti-TNF compounds in IBD patients correlates with their capacity to induce immunosuppressive macrophages in a mixed lymphocyte reaction, indicating this assay as a model system. This was further validated by the fact that addition of azathioprine to the assay resulted in an enhanced induction of regulatory macrophages, again in line with the clinical data showing superior efficacy for thiopurine and anti-TNF combination therapy. Given the relatively high proportion of patients who do not tolerate thiopurine therapy, identification of alternative compounds which can be used as anti-TNF co-medication would be valuable. The aim of this study was to use our culture system in order to screen a library of existing drugs for their potential in anti-TNF combination therapy.
Aims & Methods: A library of 1600 FDA-approved compounds were screened for their capacity to potentiate anti-TNF mediated induction of CD14 + CD206+ regulatory macrophages. For each compound, 4 concentrations were tested. Positive compounds were then selected based on clinical applicability in IBD. Selected drugs were further validated in functional studies including viability, extended dose-response titration and functionality of macrophages.
Results: The initial screen resulted in 154 compounds which potentiated anti-TNF effects in at least 1 concentration tested. Clustering of these compounds revealed significant enrichment in the drug classes of cytostatics (including the positive control thioguanin), steroids and anti-helminthics. In particular the family of benzimidazoles proved effective at inducing regulatory macrophages. This family includes albendazole and mebendazole, both compounds which have been in extensive clinical use with a good safety profile. We further validated these findings and confirmed that albendazole significantly increases the number of macrophages induced by anti-TNF therapy. Although albendazole monotherapy induced macrophages as well, the number of macrophages induced in this case was significantly lower than that seen in combination treatment. The concentrations of albendazole used in these experiment did not affect cell viability. Interestingly, macrophages induced in the presence of albendazole displayed enhanced immunosuppressive capacity compared to anti-TNF monotherapy induced macrophages on a per cell basis, suggesting enhanced functionality. Preliminary in vivo experiments in the T cell transfer model of colitis showed that albendazole and anti-TNF combination therapy resulted in faster endoscopic responses than anti-TNF therapy alone.
Conclusion: The anti-helminthic albendazole has a synergistic effect on anti-TNF in the induction of regulatory macrophages. Given the correlation between induction of these macrophages and clinical response in IBD and the extensive clinical experience with this drug, anti-TNF plus albendazole combination therapy may be a good option for IBD patients who do not tolerate thiopurines.
Disclosure of Interest: M. Wildenberg Lecture fee(s): Takeda, Falck, A. Levin: None declared, A. Ceroni: None declared, Z. Guo: None declared, D. Ebner: None declared, G. van den Brink Financial support for research: PPM services, Crucell and AbbVie, Lecture fee(s): Abbvie, Merck Sharp and Dome, Ferring pharmaceuticals, Consultancy: Abbvie

OP439 EFFECT OF HUMAN AMNION-DERIVED MESENCHYMAL STEM CELL TRANSPLANTATION IN RATS WITH RADIATION PROCTITIS

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Introduction: Mesenchymal stem cells (MSCs) have been reported to be a promising cell source in cell therapy, and large amounts of MSCs can easily be isolated from human amnion. Therapeutic irradiation for intrapelvic cancer often causes radiation proctitis; however, there is currently no effective treatment. We therefore investigated the effect of transplantation of human amnion-derived MSCs (AMSCs) in rats with radiation proctitis.
Aims & Methods: The Medical Ethical Committee of Hokkaido University Graduate School of Medicine, Sapporo, Japan approved this research, and all pregnant women gave written informed consent. Human fetal membranes were obtained during Cesarean deliveries, and amnion was manually separated from the chorion by peeling. AMSCs were isolated and expanded by digestion with collagenase type III. Seven-week-old male Sprague-Dawley rats were γ-irradiated (5 Gy/day) at the rectum for 5 days. Rats were anesthetized and placed in the supine position under a 6-mm thick lead shield with a 3×4-cm opening around the anus. On day 5, AMSCs (1×10^6 cells) were intravenously transplanted. Rats were sacrificed on day 8. Histological analyses were performed, and mRNA expression of inflammatory mediators was measured by quantitative RT-PCR. *In vitro*, after γ-irradiation of rat intestinal epithelial cells (IEC-6), the cells were cultured with AMSC-conditioned medium (CM). The effect of AMSC-CM was evaluated by measuring caspase-3/7 activity, p53 transcription activity, and quantitative RT-PCR for p53-target genes.
Results: Histological examination demonstrated that epithelial injury and infiltration of inflammatory cells in the rectum were significantly suppressed by transplantation of AMSCs. The expression levels of CXCL1, CCL2, TNF-α, and IL-6 were markedly increased by γ-irradiation and they all tended to be decreased by AMSC transplantation. *In vitro,* the cell injury in IEC-6 cells induced by γ-irradiation was inhibited by AMSC-CM, which also inhibited the upregulation of p53 transcription activity, caspase-3/7 activity, and p21 expression by γ-irradiation.
Conclusion: Transplantation of AMSCs improved radiation proctitis, possibly through inhibition of cell injury and inflammatory reactions. AMSC transplantation should be considered as a new treatment for radiation proctitis.

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Disclosure of Interest: None declared

OP440 PRE-CLINICAL PHARMACOLOGY FOR A HUMAN INTERLEUKIN-22 IG FUSION PROTEIN FOR THE POTENTIAL TREATMENT OF INFECTIOUS OR INFLAMMATORY DISEASES

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Introduction: Interleukin 22 (IL-22) belongs to the IL-10 cytokine family (Ouyang et al. 2011) and binds specifically to the IL-22 receptor (IL-22R) heterodimer, which is expressed on a variety of epithelial tissues, including the gastrointestinal (GI) tract epithelium, epidermal keratinocytes, liver hepatocytes, pancreatic epithelium, and renal tubular epithelium (Gurney 2004). IL-22 binding results in activation of the transcription factor STAT3, which further leads to the modulation of innate immunity through multiple different regenerative and protective mechanisms in epithelial tissues, including the GI tract mucosal epithelium (Wolk et al. 2004). Unlike more traditional immunosuppressive biologic therapeutics such as TNF-α inhibitors, IL-22 is not immunosuppressive, but instead has a protective effect in infections and inflammatory disease that has been linked to its ability to meditate innate immunity via multiple mechanisms in epithelial tissues (Wolk et al. 2004). IL-22Fc is a recombinant fusion protein that links the human cytokine IL-22 with the Fc portion of human immunoglobulin.
Aims & Methods: To assess the pharmacological activity of IL-22Fc, STAT3 activation was evaluated in primary hepatocytes isolated from human liver. The *in vitro* activity and potency of IL-22Fc were further evaluated using stably transfected epithelial cells expressing the human IL-22R, and human colonic epithelial cell lines. In vivo studies in the dextran sulfate sodium (DSS) induced mouse colitis model were performed to assess the impact of murine IL-22Fc (muIL22Fc) treatment on histologic colitis scores. Dose ranging *in vivo* efficacy studies were performed in the DSS colitis model and relevant pharmacodynamic (PD) markers were measured including REG3β, an antimicrobial peptide, and serum amyloid protein A (SAA), a STAT3-dependent anti-microbial protein. The pharmacokinetic (PK) and PD relationships of IL-22Fc were also assessed in healthy mice, rats, and cynomolgus monkeys.

Results: In HT29 and Colo205 human colon cell lines, as well as in primary human hepatocytes, IL-22Fc activated STAT3 phosphorylation in a concentration dependent manner with an EC50 of 1.56 ± 0.54 μg/mL for HT29 cells (n = 3), 3.29 ± 2.2 μg/mL for Colo205 cells (n = 3), and 2.89 ± 3.4 μg/mL for primary human hepatocyte from 5 donors. Cell lines also produced PD markers REG3A and SAA after stimulation with IL-22Fc under certain conditions. All muIL-22Fc – treated groups in the DSS colitis model had lower average histologic colitis scores than the control treated group; with the three highest muIL-22Fc dose groups (1.25, 6, and 30 μg) demonstrating a statistically significant decrease in severity of histologic colitis. These results were associated with a dose-dependent induction in PD markers REG3β and SAA in mice; and REG3A, SAA, and LBP in cynomolgus monkeys.
Conclusion: The combined data from the *in vitro* and *in vivo* studies confirm pharmacological activity of IL-22Fc including regenerative and protective mechanisms in epithelial tissues and efficacy in mouse colitis models.
Disclosure of Interest: E. Stefanich Shareholder: Roche, J. Rae Shareholder: Roche, J. Lutman Shareholder: Roche, X. Wang Shareholder: Roche, A. Lekkerkerker Shareholder: Roche, W. Ouyang Shareholder: Roche, J. Qiu Shareholder: Roche, D. Lee Shareholder: Roche, D. Danilenko Shareholder: Roche, K. Loyet Shareholder: Roche, M. Keir Shareholder: Roche, S. Sukumaran Shareholder: Roche, A. Herman Shareholder: Roche

OP441 COMBINATORIAL EFFECTS OF WESTERN DIET AND ADHERENT-INVASIVE E. COLI INFECTION ON INTESTINAL INFLAMMATION

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Introduction: Recent advances have shown that the abnormal inflammatory response observed in Crohn's disease (CD) involves an interplay between intestinal microbiota, host genetics and environmental factors. The escalating consumption of fat and sugar in Western countries parallels an increased incidence of CD during the latter 20th century.
Aims & Methods: The impact of a High-Fat/High-Sugar (HF/HS) diet in mice was evaluated for the (i) gut micro-inflammation (fecal lipocalin-2), (ii) selection of *E. coli* and impact on intestinal microbiota composition, (iii) susceptibility to a DSS-induced colitis, (iv) concentration of short-chain fatty acids (SCFA) and (v) expression and potential protective effect on gut inflammation of their free fatty acid receptor, G-protein-coupled receptor 43 (GPR43).
Results: HF/HS diet increased Lcn-2 level in stools from 5 weeks until 18 weeks of treatment, showing that HF/HS diet creates a specific inflammatory environment in the gut. This was correlated with intestinal mucosa dysbiosis characterized by reduction of bacterial richness, but also by an overgrowth of pro-inflammatory proteobacteria such as *E. coli* and a decrease in protective bacteria. In addition, the fecal transplantation from HF/HS treated mice to germ-free mice increased susceptibility to Adherent-Invasive *Escherichia coli* (AIEC) infection. Interestingly, HF/HS diet led to an exacerbation of gut inflammation following DSS-induced colitis, with an increase of DAI, histological score and release of pro-inflammatory cytokines. Moreover, a significantly decrease of SCFA concentrations in fecal samples from mice fed a HF/HS diet compared with mice fed a conventional diet was observed. The expression of SCFA G-protein coupled receptor 43 (GPR43) was reduced in mice treated with a HF/HS diet and reduced in CD patients compared with controls. Interestingly, mice treated with an agonist of GPR43 were protected against DSS-induced colitis.
Conclusion: Western diet creates a low-grade inflammation in the gut with a decrease of protective SCFA producing bacteria, favoring the overgrowth of opportunistic pathogenic *E. coli* which could aggravate the inflammatory process resulting in chronic inflammation. Moreover, activation of GPR43 receptor pathway could be used as a new strategy to treat CD patients abnormally colonized by AIEC bacteria.
Disclosure of Interest: None declared

OP442 INVOLVEMENT OF FLGM IN THE PATHOGENESIS OF ADHERENT-INVASIVE ESCHERICHIA COLI

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Introduction: AIEC strains (Adherent-Invasive *E. coli*) isolated from ileal lesions of Crohn's disease patients are flagellated bacteria able to invade intestinal epithelial cells and to survive into macrophages. Flagellin, major bacterial flagellum protein, is required for motility but is also recognized by innate immune receptors TLR5 and Naip5-Naip6/NlrC4/Caspase-1 leading to production of pro-inflammatory cytokines. Non-flagellated AIEC mutants presented a reduced ability to adhere to and to invade intestinal epithelial cells and to survive within macrophages. The function of FlgM is to couple flagellar assembly to appropriate temporal flagellar gene transcription.
Aims & Methods: We hypothesized that efficient modulation of flagellin expression is required for mucosa colonization and *in vivo* persistence, and permits AIEC to evade innate immune detection. To test this hypothesis, we constructed AIEC LF82 deficient in the anti-sigma factor *flgM*, which is unable to repress its flagella production and overproduce flagellin. This mutant was tested for its capacity to invade intestinal epithelial cells, to survive into macrophages and to aggravate a DSS induced colitis in a transgenic mouse model expressing human CEACAM6 necessary for AIEC mucosa invasion.
Results: Deletion of *flgM* gene did not alter growth of AIEC LF82 bacteria in Luria Broth (LB). However, this mutant show a decreased of motility and yeast agglutination titer compared to LF82 wild type, indicating that deletion of *flgM* impact type 1 pili and flagella expression. Electron microscopy examination showed a reduction in the number of flagella per bacteria and a shortening of the length of flagella at the surface of LF82-D*flgM* isogenic mutant compared to wild type LF82. This is associated with an increased secretion of flagellin in the culture supernatant of the mutant, suggesting that it could activate innate immunity via the recognition of transmembrane and cytoplasmic receptors. The loss of this anti-sigma factor leads to decrease of AIEC LF82 ability to adhere to and to invade intestinal epithelial TC7 and T84 cells. In addition, LF82-D*flgM* mutant shows reduced ability to survive within THP1 human macrophages. A preliminary study of the behavior of the AIEC-D*flgM* mutant in murine model demonstrate that the regulation of flagella expression and monomeric flagellin subunit released is required for AIEC persistence in the gut of CEABAC10 transgenic mice.
Conclusion: This work aims to better understand the pathogenicity of AIEC strains to develop specific inhibitors interfering with bacteria/cell interaction. Targeting FlgM bacterial factor could be an alternative therapeutic strategy to limit AIEC colonization on the gut mucosa of Crohn's disease patients.
Disclosure of Interest: None declared

OP443 CHROMOGRANIN-A REGULATES P53-UPREGUALTED MODULATOR OF APOPTOSIS (PUMA) AND B-CELL LYMPHOMA-2 (BCL-2) PRO-APOPTOTIC MEDIATORS IN EXPERIMENTAL COLITIS

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Introduction: The pathogenesis of ulcerative colitis (UC) involves increased apoptosis of intestinal epithelial cells. The extrinsic apoptosis pathway is induced by extracellular signals that result in the activation of death receptors and the activation of the TNF-related apoptosis-inducing ligand (TRAIL) / Caspase 8 apoptosis-related cysteine peptidase (CASP8) pathway. The intrinsic pathway is activated in response to stress conditions including DNA damage, oxidative stress through the activation of p53-upregulated modulator of apoptosis (PUMA), Bcl-2 associated X protein (BAX), Bcl-2 associated death promoter (BAD) and Bcl-2 antagonist/killer 1 (BAK1) proteins. Serum chromogranin-A (CgA), released by enterochromaffin cells, is increased in UC patients, and neuroendocrine differentiation represents an early event in the UC-neoplasia pathway in which p53 and CgA are both upregulated and considered as early markers. Therefore, we hypothesized that CgA is involved in the pathogenesis of colitis by mediating cell apoptosis induced through the intrinsic pathway.
Aims & Methods: Using an experimental model of colitis mimicking UC, the aim of this study was to investigate the association between CgA and the apoptotic/cell death markers in colitis.
Colitis was induced in CgA-C57BL/6-deficient ($CgA^{-/-}$) mice and wild type ($CgA^{+/+}$) mice by administration of dextran sulfate sodium (DSS 5%) in drinking water for 5 days. Disease activity index was evaluated daily and mice were sacrificed on day 5 post-DSS induction to assess the extent of colitis. At sacrifice composite macroscopic score were evaluated and tumor necrosis factor (TNF)-α was quantified in colon using ELISA and RT-qPCR. Colonic mRNA levels of TRAIL, CASP8, *PUMA*, *BAX*, *BAD* and *BAK1* were quantified using RT-qPCR.
Results: Delayed onset and reduced severity of clinical disease were observed in $CgA^{-/-}$ mice as compared to $CgA^{+/+}$ mice after induction of colitis. No rectal bleeding and no loose stools were observed in $CgA^{-/-}$ mice and weight loss was significantly decreased. Macroscopic inflammation scores were significantly decreased in $CgA^{-/-}$ mice as compared to $CgA^{+/+}$ mice. Colonic protein and mRNA expression levels of TNF-α were significantly decreased $CgA^{-/-}$ mice. In the colitic condition, *PUMA*, *BAX*, *BAD* and *BAK1* were significantly down-regulated in $CgA^{-/-}$ mice compared to $CgA^{+/+}$ mice. Conversely, the presence or absence of CgA did not affect TRAIL or CASP8 mRNA levels. In control mice groups the deficiency did not affect any inflammatory or apoptotic markers.
Conclusion: These results indicate that a lack of CgA contributes to the improvement of colitis by reducing the disease severity, TNF-α levels and abrogating apoptosis through the intrinsic pathway and not *via* the extrinsic pathway. CgA inhibition may offer a new potential way to protect against apoptosis and might be use as a novel therapeutic strategy in UC.
Disclosure of Interest: None declared

Abstract number: OP444 Table 1: Measurements of the ablated samples

Temperature (°C)	Layer	n	Mean ± SD (μ)	Thickness decrement (percentile)	Layer	n	Mean ± SD (μ)	Thickness decrement (percentile)	Layer	n	Mean ± SD (μ)	Thickness decrement (percentile)
Control	Muscularisthickness	13	177.2 ± 114.7	-	Mucosa (Crypts)thickness	12	338.6 ± 60.8	-	Total thickness	12	990.7 ± 230.5	-
50		29	165.7 ± 110.6	6.5		24	418.9 ± 335.4	-23.7*		24	1135.8 ± 509.1	-14.6*
60		47	123.6 ± 101.3	30.2		42	354.8 ± 177.2	-4.8*		42	924.0 ± 386.0	6.7
90		29	135.0 ± 142.4	23.8		25	314.2 ± 165.1	7.2		25	896.1 ± 521.5	9.5
97	6	108.8 ± 113.8	38.6	6	293.5 ± 105.9	13.3	6	790.5 ± 476.5	20.2			
Control	Submucosathickness	13	137.5 ± 80.3	-	Mucosa (Villi)length	12	295.6 ± 59.9	-				
50		28	146.1 ± 70.6	-6.3*		24	310.9 ± 67.3	-5.2*				
60		47	119.7 ± 78.9	13.0		42	251.9 ± 74.7	14.8				
90		29	130.7 ± 134.1	5.0		25	244.1 ± 96.7	17.4				
97	6	112.0 ± 104.2	18.6	5	186.0 ± 115.5	37.1						

*Increase in thickness

WEDNESDAY, OCTOBER 28, 2015 11:00–12:30

ENDOSCOPIC MANAGEMENT OF BENIGN PANCREATIC LESIONS – ROOM B3

OP444 EX-VIVO CYST ABLATION WITH A NEW EUS-NEEDLE PROTOTYPE DEVICE

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Introduction: Pancreatic cystic lesions (PCLs) are frequently diagnosed in asymptomatic patients. Currently, the only accepted treatment is surgical pancreatectomy which can carry severe complications. Therefore, new treatment strategies are needed.
Aims & Methods: To demonstrate the feasibility and evaluate the efficacy of radiofrequency ablation (RFA) in cystic models with a new EUS needle prototype.
Two centers were involved: Massachusetts General Hospital and Mayo Clinic. To create the cystic models, consecutive 2cm-sections of porcine small intestine were measured, tied off with surgical suture and filled with 2ml of saline. The prototype consisted of a modified EUS 22 gauge monopolar needle with a 1cm length active electrode shaft at the tip and an otherwise insulated needle shaft. The needle was connected to an ERBE Vio300 Electrosurgical unit (ERBE USA, Marietta, GA). Electrosurgical settings were soft coagulation mode with 10 watts and a hemostatic effect of 4. Each ablation was performed until a predetermined temperature was measured by a thermometer with an external sensor in contact with the cyst surface. Immediately after ablation, all samples were processed for histological H&E staining. Each layer was measured in at least two different sites of each sample using a micrometer. All measurements were compared with the corresponding control (unablated) sample.
Results: A total of 32 cystic models were ablated. The maximum temperatures reached were 50, 60, 90 and 97 degrees celsius(°C) in 8, 11, 11 and 2 cysts respectively. The ablation time increased as higher temperatures were reached (range 102-440 sec). The spectrum of macroscopic changes, starting at 60°C, were minimal color change, visible color/texture change, and total dehydration/thinning of the tissue. Overall, a decreased trend in the thickness of all the measured layers was observed as the temperature rose (table 1). However, to reproduce this effect, a temperature over 50°C was required for the muscularis, submucosa and villi of the mucosa, and over 60°C for the crypts of the mucosa.
Conclusion: RFA of a cystic model may be a feasible new management option that can be performed in regular endoscopy labs. The device has the advantage of using currently available needle and electrosurgical instruments. The ablated area appeared to be temperature-dependent with a temperature threshold of at least 60°C and a safe cyst margin below 97°C.
Disclosure of Interest: None declared

OP445 FEASIBILITY AND COMPLICATIONS RATE OF NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY (NCLE) IN PANCREATIC CYSTS : PRELIMINARY RESULTS OF A MULTICENTER PROSPECTIVE STUDY

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Introduction: Needle-based confocal laser endomicroscopy (nCLE) is an imaging technique, which enables observation of the inner wall of pancreatic cysts, in vivo and in real-time, during an EUS-FNA procedure.
An international multicentric study (INSPECT) on 66 patients reported a pancreatitis rate of 3%. The rate of technical issues was not mentionned. A prospective multicentric French study (CONTACT) aims at evaluating the accuracy of nCLE for the diagnosis of lonely pancreatic cysts.
Aim: Evaluate the feasibility and the complications rate of nCLE in pancreatic cysts in a multicenter prospective study.
Aims & Methods: Between June 2012 and March 2014, 182 patients have been included, in four French centers.
Following EUS examination, the AQ-flex miniprobe was introduced in a 19G needle and real-time video of the wall was recorded. Procedures were realized with a Cook needle (17% of the cases) or a Boston Flex (83% of the cases). A prophylactic antibiotic therapy was systematically given before each procedure. Causes of technical issues and complications rate were prospectively recorded.
Results: Procedures were technically feasible and satisfactory in 95% of the cases. The locations of the lesions in the pancreas were: uncinate process (n = 6), of the head (n = 94), of the body (n = 63) or of the tail of the pancreas (n = 19). Puncture was done per a transgastric (n = 98) or transduodenal (n = 78) approach, through the second part of the duodenum in 6 patients. Three technical failures of the puncture were reported (2% of the cases). In each of these three cases, puncture was considered only through the second part of the duodenum (one lesion in the uncinate process, two in the head). Cellvizio images have not been acquired due to software issues in seven procedures (4% of the cases). Three minor acute pancreatitis (1, 6%) were reported (48h hospitalization). There was intracystic bleeding without any extravasation in 10% of the cases, without any clinical consequence. No other complication happened.
Conclusion: In a large prospective study of nCLE in pancreatic cysts, the technical sucess rate is 95% and the pancreatitis rate is 1.6%. The main technical limitaion is observed for cysts, which require an approach through the second part of the duodenum (50% failure). The complications rate compares with the complications rate of EUS-FNA.
Disclosure of Interest: None declared

OP446 FEASIBILITY AND SAFETY OF A FULLY COVERED SELF-EXPANDABLE METAL STENT WITH ANTIMIGRATION PROPERTIES FOR EUS-GUIDED PANCREATIC DUCT DRAINAGE: EARLY AND MIDTERM OUTCOMES

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Introduction: Recently, EUS-PD has been used for patients on whom endoscopic retrograde pancreatography (ERP) has failed. Stent-related adverse events such as stent migrations, failures in stent placement, or pancreatic fluid leakages have been of concern in transmural plastic stenting procedures.
Aims & Methods: The aim of this study is to evaluate the feasibility and safety of EUS-PD with a fully covered self-expandable metal stent (FCSEMS) for patients with obstructive pancreatitis who failed ERPs. Twenty five consecutive patients with obstructive pancreatitis underwent EUS-PD with a FCSEMS after failed ERPs. Technical and clinical success, adverse events, and stent patency were assessed.
Results: EUS-PD was successful in all 25 patients (technical success rate, 100%), and symptoms improved in all patients (clinical success rate, 100%). EUS-guided pancreaticogastrostomy (n = 24), pancreaticoduodenostomy (n = 1) and pancreaticojejunostomy (n = 1) were performed. Pain scores improved significantly after FCSEMS placement ($P = 0.001$). Median stent patency duration was 123.5 days (Interquartile range 65.75 – 171.50). Early adverse events occurred in five (20%) patients, including four with self-limited abdominal pain and one with minor bleeding. No other adverse events related to FCSEMS-including stent migration, stent clogging, pancreatic sepsis and stent induced ductal stricture-were observed during follow-up periods.
Conclusion: EUS-PD with an FCSEMS may be technically feasible and relatively safe for patients failed conventional ERPs.
Disclosure of Interest: None declared

OP447 A NOVEL BIODEGRADABLE NON-COVERED SELF-EXPANDABLE STENT TO TREAT PANCREATIC DUCT STRICTURES IN CHRONIC PANCREATITIS; A PILOT STUDY

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Introduction: In chronic pancreatitis (CP), fibrotic pancreatic duct (PD) strictures are a common complication and a therapeutic challenge. Dilatation by

(progressive) plastic stent insertion requires multiple procedures and has limited success. Drainage with self-expandable metal stents seems more effective, but removal and migration problems limit their use. Biodegradable self-expandable stents (BD-SES) might be an attractive alternative, but have never been investigated in humans in this setting.
Aims & Methods: The aim of this prospective pilot study was to evaluate the safety of non-covered BD-SES's (ELLA-CS) in CP patients with a fibrotic PD stricture. Patients were included, in whom treatment with plastic stents for at least 6 months had failed and surgical intervention was considered. Efficacy was a secondary endpoint. The participating centers are university hospitals in Rotterdam, the Netherlands, and Leuven, Belgium. Stents were 6 mm in diameter, 3 or 4 cm in length, with an expected degradation time of 3-6 months. Patients were followed for one year. Stent and stricture resolution were evaluated by ERCP after 6 months.
Results: Stents were placed in 10 patients (median age 56, 6 male, median disease duration 4 years). The median stricture length was 1 cm (IQR 0.5-3.5 cm). All stents were placed successfully, 9 after sphincterotomy and 6 after balloon dilatation. Nine were placed transpapillary, of which two were pulled down with a balloon or forceps after deployment, to achieve an optimal position. One stent was positioned intraductally. No serious peri-procedural complications were encountered, but two patients were admitted shortly because of self-limiting pancreatic pain.
In the eight patients that have completed at least 6-months of follow-up, complete stent degradation was accomplished (stent resolution 100%). In six patients, ERCP demonstrated stricture resolution (technical success rate 75%). In two cases, stent related complications had occurred; ductal hyperplasia and stent migration, both of which were treated with plastic stents and eventually surgery. Two additional patients underwent a Whipple's procedure for other pancreatitis related problems, 9 and 11 months after stent insertion; one because of groove pancreatitis with a gastric outlet obstruction, the other for a CBD stricture and recurrent flares (neither had evidence of a recurrent PD stricture). The remainder four patients are still stricture and pain free after 1 year (clinical success rate 50%).
Conclusion: These preliminary results show that BD-SES's for fibrotic PD strictures in CP are easy and safe to place, degrade completely within 6 months, and may even resolve strictures, resilient to conventional plastic stent treatment. These encouraging results warrant further testing.
Disclosure of Interest: None declared

OP448 LONG-TERM OUTCOME OF ENDOSCOPIC THERAPY FOR CHRONIC PANCREATITIS IN CHILDREN

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Introduction: Chronic pancreatitis (CP) occurs rarely in children and the most frequent presentation is recurrent acute pancreatitis (RAP). Previous publications have shown that endoscopic therapy with ductal drainage, with or without extracorporeal shock wave lithotripsy (ESWL), is safe and efficient. However, long-term results are scarce or inexistant regarding the european population. The aim of this retrospective study was to evaluate the long-term effects of endoscopic therapy on pain relief in children with CP.
Aims & Methods: During a period of 21 years (1991-2012), 41 children with CP had endoscopic therapy. Clinical status was evaluated after therapy, based on the number of hospital admissions (for pain or subsequent endoscopic procedure) during follow-up (FU). Results were considered excellent if no other admission was required, satisfactory if < 5 admissions or ≥ 5 but with no pain or ongoing endoscopic therapy for minimum 12 months at the end of FU, and poor if surgery was required or ≥ 5 admissions were noted with ongoing endoscopic therapy at the end of FU.
Results: 41 patients (female: 25(61%)) were included (median age:10(2-17)). 15 (36.6%) were ≤ 7 years old. Eleven children (26.8%) had hereditary CP associated with cationic trypsinogen mutation. CP was characterized as severe according to the Cambridge classification in 28 (68.3%) children. Duration of disease before treatment was 27 (1-120) months. RAP was seen in 24 (58.5%) patients. Pancreas divisum was seen in 6 patients (14.6%). Endoscopic therapy consisted of pancreatic sphincterotomy of the major ($n = 35$) and/or the minor papilla ($n = 11$) for all patients. ESWL for pancreatic calcifications was required in 9 (22%) patients. Only 2 (4.9%) patients had pancreatic stent insertion during initial therapy. Mild post-ERCP AP occurred in 7 (17.1%) and median length of stay for initial therapy was 3 days (2-8). Median FU of 72 months (7-240) was obtained in 36 children. Subsequent endotherapy during FU was required in 30/36 (85.7%) patients and pancreatic stenting was necessary in 14 (40%), for a median period of 23 (5-148) months. Median frequency of admissions per year (0.66 (0-3.4)) was significantly decreased after therapy as compared to the frequency before therapy (3 (0.6-18))($p = 0.001$). Results were excellent in 5 (13.9%) and satisfactory in 26 (72.2%) patients. Finally, poor results were observed in 5 children (13.9%), who required surgery ($n = 1$) and/or frequent admissions for ongoing endoscopic therapy ($n = 4$).
Conclusion: Therapeutic ERCP in a pediatric population of CP can lead to clinical improvement and can be considered as the initial treatment of choice.
Disclosure of Interest: None declared

OP449 SURVEILLANCE OF LOW-INTERMEDIATE RISK INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

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Introduction: Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are potentially malignant epithelial neoplasms that involve the main duct, branch ducts, or both. Although a great majority of these lesions do not meet consensus criteria for resection and are therefore surveyed regularly, outcomes of long term surveillance are not known. Our goal was to understand the natural history and risk of progression of low-intermediate risk IPMNs that have been surveyed for > 4 years.
Aims & Methods: We conducted a retrospective review of radiology and endoscopy databases between 2001-2013. We included all cystic lesions that (1) met clinical IPMN criteria and, (2) had greater than four year cross sectional imaging (CT/MRI) or EUS follow-up. Data points such as demographics and cyst characteristics were collected. Progression was defined as one of the following: (1) increase in cyst diameter > 2 mm, (2) increase of 20% or more in the cyst's largest dimension, (3) development of such worrisome features as pancreatic duct dilatation, mural nodules, pancreatic atrophy.
Results: We identified a total of 2400 patients with cystic pancreatic lesions of whom 268 patients were followed for > 4 years and 135 met clinical criteria for the diagnosis of IPMN (44% M, 56% F, average age 73). 60 patients (44%) had interval cyst progression of greater than or equal to 20% with an average increase of 69% in the single largest dimension. Of these 60 patients, 15 developed worrisome features. 18 patients (13%) had interval cyst progression less than 20%, of whom two developed worrisome features. 32 patients (23.7%) had cysts with no demonstrable growth in the greatest diameter, however three developed worrisome features. There were no significant differences in age, gender, baseline cyst measurement, CEA or amylase values among progressors and non-progressors.

Table 1: IPMN Characteristics

Baseline Cyst Size	N	No Change	Cyst Size Increase > 2 mm	Cyst Size Increase $> 20\%$	Developed Worrisome Features
< 10 mm	54	20	23	25	6
11-20 mm	58	10	31	27	8
21-30 mm	12	1	9	5	6
> 31 mm	10	0	5	3	3

Conclusion: In a large retrospective cohort of patients with suspected low to intermediate risk IPMNs, nearly half progressed during four-year follow-up as defined by 20% or more growth in the single largest dimension, however only a minority ultimately met resection criteria. There were no significant differences in demographics or baseline cyst characteristics among progressors and non-progressors.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 14:00–15:30
COMPLICATIONS OF CROHN'S DISEASE (AV) – ROOM F1

OP450 THE CLINICAL OUTCOMES OF 165 ENDOSCOPIC BALLOON DILATATION FOR ILEOCOLONIC OR CAECAL STRICTURES IN PATIENTS WITH CROHN'S DISEASE

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Introduction: In Japan and most other developed nations, the prevalence of Crohn's disease (CD) is on an increasing trend. CD is characterized by patchy, transmural, progredient inflammation along the intestine with stricture formation in approximately one-third of all CD patients. Strictures are a major cause of morbidity, hospitalisation and surgery. Strictures are caused by transmural inflammation, uncontrolled cell proliferation, tissue remodeling, and have as yet unknown biochemical mediators. Further, while new therapeutic options are aimed at suppressing inflammation, hitherto developed stenotic lesions often require surgical intervention. Endoscopic balloon dilation (EBD) has been expected to be a nonsurgical approach for the management of intestinal strictures.
Aims & Methods: We were interested to assess the true clinical outcome in CD patients who undergo EBD for intestinal strictures; caecal or ileocolonic. Additionally, we wished to identify factors associated with complications, compromising the long-term prognosis after an EBD procedure. From January 2006 to March 2015, 165 EBD sessions for strictures in the lower gastrointestinal tract were undertaken in 71 CD patients. EBD was done in patients who either presented with ileocolonic or caecal stenosis experiencing obstructive symptoms. EBD was carried out by using high-pressure Through-The-Scope Balloons with a diameter of 8-20 mm and a length of 5.5cm, depending on the size of the strictured lumen and the endoscopists' discretion. The primary success was defined as free passage of the scope through the strictured site after the EBD procedure.

Results: The rate of primary success was 79% (130 of 165 EBD procedures). However, during the time course of this study, 47 of the 71 patients (66%) returned for re-EBD or operations due to re-stenosis. Eighteen of the 71 patients (25%) needed surgical intervention for complications related to strictures. The rate of perforation was 1.4% (2 of 165 EBD procedures). We compared demographic features between the operation and the non-operation subgroups including ulcers at the stenotic lesions, duration, and the location of colitis, medications including 5-aminosalicylates anti-tumour necrosis factor (TNF)-α, immunomodulators, nutritional therapy, past surgical interventions, the length of stenosis, and the expansion diameter. In the subgroup who needed surgical interventions, there were significantly higher cases complicated with ulcers at the stenotic lesions ($P = 0.001$). Anti-TNF-α therapy and other medications mentioned above did not influence re-stenosis or the need for operation.
Conclusion: In this study, EBD of intestinal strictures in CD patients was an effective and safe alternative to surgical interventions in the majority of cases. It is believed that long-term anti-TNF-α therapy may promote intestinal strictures, but, anti-TNF-α, immunomodulators or 5-aminosalicylates did not appear to influence re-stenosis or the need for surgical interventions. Likewise, the length of stenosis and the expansion diameter were not associated with complications requiring surgery. Instead, we found that ulcers complicating the stenotic lesions were a significant risk factor for surgery following EBD. Accordingly, we believe that treatment of ulcers at the stenotic lesions prior to an EBD should increase the clinical outcome of EBD in CD.
Disclosure of Interest: None declared

OP451 BIOLOGICAL THERAPY IS ABLE TO MODIFY THE DISEASE PROGRESSION OF CROHN'S DISEASE PREVENTING ITS LONG-TERM ASSOCIATED DISABILITY – A STUDY PERFORMED USING THE LÈMANN SCORE

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Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disorder characterized by an alternation of remission and relapse phases. Even during periods of clinical remission a subclinical inflammation persists, reflecting a progressive, destructive disease course in the later phases of the disease. Surgical resection of the bowel can be considered the ultimate manifestation of bowel damage. Recently a new score, the Lèmann Score (LS), has been proposed in order to assess the cumulative structural damage to the bowel in different CD patients. Limited data are present assessing the value of this instrument in measuring the effect of various medical therapies on the progression of bowel damage.
Aims & Methods: The aim of our study was to evaluate the effect of various medical therapies on the progression of bowel damage using the LS. In this retrospective study we included 87 CD patients who were followed up at our IBD Unit. All patients underwent clinical assessment with measurement of disease status based on HBI index every three months, and bowel magnetic resonance imaging and a colonoscopy every year, or earlier, in case of disease relapse. Patients were divided on the basis of the drug administered during the follow-up: i) biological mono-therapy; ii) azathioprine; iii) mesalazine, and the LS was calculated both at baseline and at the end of follow-up in each group.
Results: We included 87 patients (49 males, mean age 43.5 years, range 19-79) with a median follow-up of 26 months. Among the 35 (40.2%) patients on biological mono-therapy the median LS was 7.1 (range, 2.5-292.3) at baseline and 9.7 (range, 1.3-292.3) at the end of the follow-up ($P = 0.34$). The median LS in azathioprine group (16 patients, 18.4%) was 3.5 (range, 0.6-159.6) and 7.6 (range, 0.6-209.6) at baseline and at the end of follow-up, respectively ($P = 0.0017$). In the mesalazine group (36 patients, 41.4%) the median LS at baseline and at the end of follow-up was 3.2 (range, 0.6-202.6) and 4.3 (range, 1-206.5), respectively ($P < 0.0001$). As far as the proportion of patients who showed a worsening in the LS is concerned, the azathioprine group showed the highest proportion of patients with increased scores (13/16, 81.3%) followed by the group treated with mesalazine (20/36, 55.6%), and patients treated with biological mono-therapy (8/35, 22.9%) ($P = 0.0002$).
Conclusion: Our data suggest that the use of biological therapy rather than azathioprine or mesalazine may change the cumulative structural damage to the bowel and, therefore, is able to modify disease progression in CD patients, preventing its long-term associated disability.
Disclosure of Interest: None declared

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MONDAY, OCTOBER 26, 2015 09:00–17:00
LIVER & BILIARY I – HALL 7

P0001 SYSTEMIC ADMINISTRATION OF XENOGENIC HUMAN ADIPOSE-DERIVED STROMAL CELLS COMBINED WITH ADENOVIRUS-HUPA IMPROVES EXPERIMENTAL LIVER FIBROSIS

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Introduction: In animal models of liver fibrosis transplant of hADSCs (adipose-derived stromal cells) improved hepatic function and reduced fibrotic tissue. Besides, systemic administration of Ad-huPA diminished liver fibrosis and increased tissue regeneration.
Aims & Methods: The aim of this study was to evaluate if the simultaneous administration of both therapies shows an enhanced antifibrogenic effect in cirrhotic rats. ADSCs were isolated from human fat tissue, expanded and characterized by expression of cellular markers ($CD105^+$, $CD73^+$, $HLA\text{-}ABC^+$, CD45, $CD34^-$,$HLA\text{-}DRII^-$) and cell differentiation to osteogenic, adipogenic and hepatogenic linage. Ad5-huPA vector was generated under CMV promoter control. CCl_4-cirrhotic rats via ileac vein were administered with $2X \times 10^6$ cells/rat hADSCs or $3x10^{11}$ vp/rat Ad-huPA or both therapies. One day before treatment, all animals begin immunosuppression with 10mg/kg/day of Cyclosporine A until sacrifice 10 days later. Fibrotic tissue, Collagen fibers and α-SMA immunoreactivity as well as expression of TGF-β1, collagen α1, CTGF, PAI-I and α-SMA were evaluated. Also, serum levels of ALT, AST and albumin, biodistribution of hADSCs and liver levels of huPA protein were examined.
Results: Administration of hADSCs, Ad-huPA and Ad-huPA/hADSCs reduces ($p < 0.01$) liver fibrosis in 78.9%, 65.2% and 72% respectively, compared to cirrhotic controls and diminishes Collagen α1, CTGF and α-SMA mRNA liver levels ($p < 0.05$). Furthermore, TGF-β1 and PAI-I liver mRNA levels ($p < 0.05$) decreases in animals treated with Ad-huPA and hADSCs. ALT and AST serum levels showed a significant decrease in hADSCs group ($p < 0.05$). Serum levels of albumin increased in the Ad-huPA, hADSCs and Ad-huPA/hADSCs groups ($p < 0.05$) compared with control group. hADSCs, Ad-huPA and hADSC/Ad-huPA administration reduced 4.3, 2.4 and 2.7 fold respectively ($p \leq 0.001$) collagen staining, compared to cirrhotic controls. hADSCs were mainly detected in liver and few of them in lung and spleen. huPA protein was expressed in similar levels in liver homogenates of Ad-huPA and Ad-huPA/hADSCs groups.
Conclusion: The combination of Ad-huPA and hADSCs reduced liver fibrosis and expression of pro-fibrogenic molecules in CCl_4-cirrhotic animals; however, it does not improve antifibrogenic effects of individual treatments.
Disclosure of Interest: None declared

P0002 THE DIAGNOSTIC PERFORMANCE OF NON-INVASIVE SERUM MARKERS TO IDENTIFY SIGNIFICANT LIVER FIBROSIS IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS AND PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Development of models and indexes incorporating non-invasive markers of liver fibrosis in chronic cholestatic liver diseases, namely primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC), is essential to facilitate the assessment of liver fibrosis progression and the effectiveness of new therapies.
Aims & Methods: The aim of this study was to evaluate the ability of indirect serum markers for discriminating between mild and significant fibrosis in patients with PBC and PSC. Data from 82 patients with PBC and 22 patients with PSC were analyzed retrospectively (admitted between 2008 and 2014). Forns index, Fibrosis 4 score (FIB4), aspartate aminotransferase (AST)/alanine aminotransferase (ALT) (AST/ALT) ratio index, AST to the platelet ratio index (APRI) and platelet count/spleen diameter ratio index were calculated based on results of blood analyses and abdominal ultrasound. Results of the histological study of the liver with the histology activity index (according the Knodell score) and stage of fibrosis assessment (according the METAVIR score) were used as a reference method and were available for all included patients. Receiver operating characteristic curve (ROC) analysis was conducted to determine diagnostic performance of these indexes for identification of significant liver fibrosis in patients with PBC and PSC.
Results: Among all the patients with PBC (n = 82; median age [25th – 75th interquartile range] 54.5 years [48.75-60.25]; 95.12% were female) 52.4% (n = 43) had significant fibrosis ($F \geq 2$) and 23.17% (n = 19) had cirrhosis. In PSC group (n = 22; median age 38 years [26.5-48.5]; 27.2% were female) 50% (n = 11) and 31.8% (n = 7) of patients had significant fibrosis ($F \geq 2$) and cirrhosis, consequently. Platelet count/spleen diameter ratio index (AUROC = 0.761) was superior to APRI, AST/ALT ratio index, FIB4, and Forns index at distinguishing between mild and significant fibrosis in patients with PBC. With a cut-off of > 19.8, the presence of significant fibrosis could be excluded with a 74.4% negative predictive value (NPV) and 78% specificity. In patients with PSC FIB4 index (AUROC = 0.843), platelet count/spleen diameter ratio index (AUROC = 0.752), and APRI (AUROC = 0.744) were superior to Forns index and AST/ALT ratio index at distinguishing between mild and significant fibrosis. With a FIB4 index cut-off value of < 0.76, the presence of significant fibrosis could be excluded with a 85.7% NPV and 90.9% specificity.
Conclusion: Application of platelet count/spleen diameter ratio index in patients with PBC enabled correct classification of 74% of patients included in this study. Overall 73% of patients with PSC could be correctly classified by using FIB4 index. Thus, application of tests, incorporating indirect serum markers of live fibrosis, could help to decrease the need for liver biopsy in these patients.
Disclosure of Interest: None declared

P0003 EXPRESSION ANALYSIS OF PLASMA APOLIPOPROTEINS IN HEPATOCELLULAR CARCINOMA: A PROTEIN-BASED HCC-ASSOCIATED STUDY

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Introduction: Hepatocellular carcinoma (HCC) is the 6th cancer in incidence worldwide and the 3rd leading cause of cancer death. We aimed to identify new markers of HCC using a protein-based analysis.
Aims & Methods: To find out differential expression of apolipoproteins- ApoA1 and ApoAIV in HCC and controls without HCC. 30 Patients with HCC and 30 liver cirrhosis were included in the study. Target apolipoproteins were separated by SDS PAGE from blood plasma and the expression changes of ApoA1 and ApoA4 were confirmed by Western blotting followed by densitometric protein semiquantitaion estimation along with ELISA-based protein quantification.
Results: Western blotting densitometry image analysis of the plasma samples following CDC protocol and the comparison between patients with and without HCC revealed differential expression of ApoA1 and ApoA4. Levels of Apo-A4 were significantly higher in patients of liver cirrhosis and chronic hepatitis without HCC than in patients with HCC (0.208 ± 0.07 & $0.119 \pm .016$ $_{VS}$ 0.119 ± 0.005; $P < 0.01$). Levels of Apo-A1 were significantly higher in patients with HCC than in controls without HCC (0.279 ± 0.003 $_{VS}$ 0.171 ± 0.034 & $0.199 \pm .014$; $P < 0.01$).
Apo-A1 and ApoA4 were further tested whether quantitative measurement could be utilized as a diagnostic tool to distinguish patients with HCC from the controls without HCC by ELISA. Once calibration curves were proven to be analytically optimal, Apo-A1, ApoA4 and AFP were measured in blood plasma samples by ELISA according to the manufacturer's protocol. The result showed significant increased Apo-A1 expression in HCC group ($P < 0.01$).
Mean ApoA1 concentration in human blood plasma: HCC- 81726.61 ng/ml; LC-16388.09 ng/ml; chronic hepatitis – 22172.30 ng/ml; Mean ApoA4 concentration in human blood plasma: HCC-307.79 ng/ml; LC- 614.86 ng/ml; chronic hepatitis – 495.13 ng/ml. ELISA Assays revealed that there was a deregulation in expression of both ApoA1 and ApoA4 proteins deflected from the normal levels in healthy controls. It showed that the plasma levels of ApoA1 were higher in HCC than both the healthy and disease controls. On the other hand plasma levels of ApoA4 were lower in HCC than controls with liver cirrhosis and chronic hepatitis but without HCC. Plasma levels of ApoA4 were significantly higher in liver cirrhosis than that of HCC as well as healthy control. Plasma levels of AFP were higher in HCC than that of healthy control and liver cirrhosis along with chronic hepatitis.
Conclusion: Apolipoprotein A1 is highly expressed in HCC in comparison to cirrhosis and may be used as future diagnostic tool in addition and associated with other conventional biomarkers for HCC after further analysis of a higher number of population.

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Disclosure of Interest: None declared

P0004 RIFAXIMIN PREVENTS THE DEVELOPMENT OF STEATOHEPATITIS BY INHIBITING NF-KB AND TNF ALPHA IN RATS FED WITH HIGH FRUCTOSE

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Introduction: Non alcoholic fatty liver disease is the most common liver disease in the world. In addition it is commonly associated with the methabolic syndrome. There is possibility that the disease may be associated with the increase fructose consumption
Aims & Methods: In this study, we investigated the preventive effect of rifaximin in steatohepatitis induced by fructose in rats. In this study, 42 male Sprague-Dawley rats were divided in 6 groups with an equal number. Normal diet was given to Group 1. Fructose was given to Group 2, fructose + rifaximin once a week was given to Group 3, fructose + rifaximin three days a week was given to Group 4, normal diet + rifaximin once a week was given to Group 5 and normal diet + rifaximin three days a week was given to Group 6. Rifaximin was administered at a dose of 15 mg/kg by orogastric catheter. 50% fructose was added to drinking water. The rats were decapitated at the end of 8 weeks. At the end of 8 weeks, hepatic tissue samples were obtained from the rats for histopathological examination and MDA, TNF-α, NF-kB, Nrf-2 and HO-1 levels. Biochemical examination was performed and plasma glutathione peroxidase, TNF-α, 4-hydroxynonenal levels were measured.
Results: The body and liver weights were increased in all rats fed with fructose compared to the control group. On histopathological examination, balloning degeneration, inflammation and grade 1 steatosis developed in the rats who were given 50% fructose. Steatosis Grade 2 and above and fibrosis was not found in any rat. Ballooning degeneration and inflammation were found with a significantly lower rate in rates who received rifaximin. No significant difference was found between different doses of rifaximin. Plasma and tissue TNF-α levels and NF-κB were found to be significantly lower in the groups who received rifaximin compared to the group who received fructose. In addition, GSH-Px, Nrf-2, HO-1 levels were found to be high in the group who received rifaximin. No significant difference was found between different doses of rifaximin.
Conclusion: Rifaximin protects aganist steatosis, ballooning degeneration and inflammation induced by high fructose diet in rats. It was thought that rifaximin may be prevent the steatohepatitis inhibiting NF-kB, TNF-α, with decreasing intestinal translocation of endotoxin. New studies on this subject are needed.
Disclosure of Interest: None declared

P0005 CELECOXIB AMELIORATES INTESTINAL INFLAMMATORY INFILTRATION ALONG THE GUT-LIVER AXIS VIA RESTORATION OF INTESTINAL EPITHELIAL BARRIER IN CIRRHOTIC RAT

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Introduction: Liver cirrhosis is an inevitable outcome triggered by chronic inflammation. However, the mechanism of inflammatory infiltration in the liver is largely unknown. It is accepted that intestinal epithelial barrier dysfunction might contribute to liver cirrhosis by facilitation of inflammatory infiltration along the gut-liver axis. In the present study, we characterize the effects of celecoxib on inflammatory infiltration and intestinal epithelial barrier of cirrhotic rats.
Aims & Methods: Liver cirrhosis was induced by peritoneal injection (i.p.) of thiacetamide (TAA, 200 mg/kg every 3 days for 16 weeks). 36 male Sprague-Dawley rats were randomized into control, TAA and TAA + celecoxib groups with 12 animals in each group. TAA + celecoxib group received TAA plus celecoxib (20mg/kg/day) from the initiation of TAA administration. TAA group received TAA plus placebo and control group received normal saline (i.p.). The parameters for fibrosis (Collagen III and a-SMA), inflammatory infiltration (TNF-α, IL-6, and CD3/CD4/CD8 lymphocytes), barrier function (ZO-1, claudin-4 and E-cadherin) and integrated signal pathways (cyclooxygenase-2 (COX-2), p-Akt, p-ERK and NF-kB) were determined. Moreover, the content of TNF-α, IL-6 and lipopolysaccharide (LPS) was quantified. *In vitro*, human colorectal adenocarcinoma cells Caco-2 was treatment with vehicle, celecoxib, PGE2, PGE2 antagonist, EP-2 antagonist, ERK inhibitor and Akt inhibitor, respectively. Afterwards, ZO-1, claudin-4 and E-cadherin, Akt/p-Akt and ERK/p-ERK were evaluated by immunocytofluorescence and Western blot.
Results: *In vivo*, compared with TAA group, fibrotic areas and Ishak's scoring in TAA + celecoxib group were remarkably decreased by 40.4% and 36.1%. The mRNA levels of a-SMA and collagen III in TAA + celecoxib group were also reduced. Moreover, hepatic and intestinal inflammatory infiltration, which express as increased mRNA and protein level of TNF-α, IL-6, LPS and decreased portal venous CD3+, CD3+/CD4+, CD3+/CD8+ and CD3+/CD4+/CD8+ T cell, were observed in TAA group when compared with those in control group. Interestingly, the hepatic and intestinal inflammatory infiltration was attenuated after treatment with celecoxib. Disruption of intestinal barriers that induced by TAA, which was verified by ultrastructure and decreased mRNA and protein of junction molecular (ZO-1, Cluadin-4 and E-cadherin), was partly restored after treatment with celecoxib. Moreover, activation of p-Akt, p-ERK and NF-kB in TAA group was significantly inhibited by celecoxib treatment. *In vitro*, compared with vehicle treated Caco-2 cells, the protein levels of ZO-1, Cluadin-4, E-cadherin were obviously increased by celecoxib, PGE2 antagonist, EP-2 antagonist and ERK inhibitor treatment but not by Akt inhibitor.
Conclusion: Long-term treatment with celecoxib attenuates liver cirrhosis via blockage of inflammatory infiltration along the gut-liver axis and restoration of intestinal epithelial barrier. This effect afforded by celecoxib may attribute to its modulation on COX-2 – PGE2 – p-ERK integrated signal pathways. Our results suggest that celecoxib might be considered as a potential therapeutic agent in the preventive strategy for the patients suffering from liver cirrhosis.
Disclosure of Interest: None declared

P0006 EFFECTS OF URSODEOXYCHOLIC-ACID AND RIFAMPICIN ON AUTOPHAGY IN THE LIVER

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Introduction: Bile acids and activation of the bile acid receptor FXR inhibit autophagy, a cellular self-digestion process necessary for cell homeostasis and regeneration. The effects of chronic bile acid accumulation in chronic cholestatic liver disease on autophagy have not been studied in detail. However, indirect evidence (e.g. accumulation of Mallory-Denk bodies in primary biliary cirrhosis) indicate that autophagy may be impaired in human cholestasis.
Aims & Methods: We aim to determine whether ursodeoxycholic-acid (UDCA) and Rifampicin (Rifa), two drugs for the treatment of human cholestatic liver disease, may activate autophagy as a potential mode of drug action.
Markers of autophagy (LC3, p62, ATG5, 7, 12) and the upstream mTOR signaling pathway (Raptor, ULK1, pS6K) have been studied by Western blot and immunofluorescence in liver biopsy from patients treated with UDCA and Rifampicin. Mechanistic details of UDCA and Rifa action have further been studied in human HepG2 cells and primary hepatocytes.
Results: Both UDCA and Rifampicin induce LC3 as the main autophagy readout in human biopsies. UDCA activates autophagy via mTOR-ULK1 signaling whereas Rifampicin induces autophagy on transcriptional levels (LC3C, LAMP1, ATG10) without impacting on mTOR signaling. Knockdown of the Rifampicin activated transcription factor PXR significantly represses autophagy already under basal conditions on mRNA and protein levels. In addition, PXR knockdown prevents Rifampicin induced autophagy induction.
Conclusion: UDCA and Rifampicin induce autophagy in the liver via different mechanisms. UDCA induces autophagy via mTOR signaling pathways and Rifampicin induces autophagy mTOR independently via the transcription factor PXR. Part of the beneficial effects of UDCA and Rifampicin in the treatment of cholestatic liver disease may be attributed to an induction of autophagy. Both compounds, UDCA and Rifampicin may have additional beneficial effect by inducing autophagy on other hepatological as well as non-hepatological diseases.
Disclosure of Interest: None declared

P0007 INDUCTION OF CB2 EXPRESSION, HSC APOPTOSIS AND CB1 INHIBITION BY QUERCETIN ADMINISTRATION IN AN ANIMAL MODEL OF LIVER FIBROSIS

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Introduction: Cirrhosis is a distortion of normal tissue architecture which develops when the liver is chronically damaged. Activated hepatic stellate cells (HSC) participate actively in liver fibrosis development where endocanabinoids receptors CB1 and CB2 regulate this process. Quercetin, a flavonoid with antioxidant properties has shown prevent liver fibrosis.
Aims & Methods
Aim: To elucidate the effect of quercetin on CB1 and CB2 expression and on HSC activation in an experimental model of cirrhosis.
Methods: Wistar rats were intoxicated with CCl_4 for eight weeks and concomitantly treated with quercetin (150mg/Kg/day). Animals were sacrificed, livers were taken for histology (Masson, Sirious red, immunohistochemistry (IHC) for a-sma and TUNEL for apoptosis), for gene expression (Col-1 TGF-b, CTGF, CB1 and CB2) and for western blot (CB1 and CB2).
Results: Expression of Col-1, TGF-b1 and CTGF significantly increased in CCl_4 cirrhotic rats compared to healthy rats. Tretament with quercetin significantly decreased expression of all these genes. Liver fibrotic rats presented a fibrosis index of 22.5% while rats with quercetin treatment had a fibrosis index of 10.76%. Activated HSC determined by IHC for a-sma and quantity of apoptotic cells were 40% less and 17 times more respectively in quercetin group respect to control. CB1 expression was 20% decreased where CB2 was 47% increased with quercetin treatment respect to group without quercetin treatment.
Conclusion: Quercetin administration prevents liver injury in an animal model of cirrhosis increasing CB2 expression and reducing CB1 expression. In the

same way, quercetin promotes HSC apoptosis decreasing activated hepatic stellate cells number.

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P0008 THE LEVEL OF TGF-β1 AND TIMP-1 IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: As chronic liver disease progresses, an imbalance between synthesis and breakdown of extracellular matrix (ECM) occurs. Matrix metalloproteinases (MMPs) are involved in ECM degrading while tissue inhibitors of metalloproteinases (TIMPs) prevent their fibrolytic action. Circulating levels of tissue inhibitor of metalloproteinase (TIMP)-1 was investigated as parameters for the diagnosis of fibrosis in chronic liver disease. Removal of excess collagen after cessation of liver injury is regulated by TIMP-1 and TGF-β1 (transforming growth factor-β1). Among growth factors, TGF-β1 appears to be a key mediator in human fibrogenesis.
Aims & Methods: The aim of research was to assess the level of TGF-β1 and TIMP-1 in patients with liver cirrhosis (LC).
Materials and methods: 80 patients with LC of nonviral etiology were examined. Classification of the International Working Group and the World Congress of Gastroenterology (Los Angeles, 1994) was used for the diagnosis of LC. Diagnosis was based on anamnestic, clinical and laboratory data, ultrasound evidence of liver damage, detection and absence of serological markers of viral hepatitis and alcoholic origin of the disease. Parameters of free-radical oxidation and antioxidant system (malonaldehyde, diene conjugates, the activity of ceruloplasmin, transferrin saturation with iron) and medium molecular weight peptides as manifestation of endogenous intoxication were determined in the patients' the blood. For all patients ^{13}C-metacetin breath test was performed to assess the functional capacity of hepatocytes. TIMP-1, TGF-β1 and bacterial endotoxin were determined with the ELISA method. The investigated group included the patients with LC at stage A and B according to Child-Pugh.
Results: Examined patients included 71 men (88.7%) and 9 women (11.3%). Age of patients ranged from 34 to 64 years on average (47.7 ± 0.82) years. Disease duration in patients ranged from 2 to 9 years.
The level of TIMP-1 in patients with LC was (523.5 ± 6.5) pg/ml and significantly different from healthy persons - (164.6 ± 8.50) pg/ml ($p < 0.05$). TGF-β1 levels in patients with LC was 437.7 ± 5.9 pg/ml and 166.98 ± 6.73 pg/ml ($p < 0.05$) in healthy persons. The level of bacterial endotoxin in patients with LC was 79.32 ± 2.1 pg/ml and significantly different from healthy persons – 23.6 ± 0.91 pg/ml ($p < 0.05$). Endotoxin was positively correlated with TGF-β1 ($r = 0.338$, $P < 0.05$), and positively correlated with medium molecular weight peptides ($r = 0.413$, $P < 0.05$).
Conclusion: Cytokines are released under the influence of bacterial endotoxin from Kupffer cells causing the production of fibrogenic factors (such as TGF-β1), and leading to stimulation of fibrogenesis and progression of disease.
Disclosure of Interest: None declared

P0009 ADMINISTRATION OF ANTISENSE OLIGODEOXYNUCLEOTIDES TO NERVE GROWTH FACTOR ATTENUATES INFLAMMATION AND LIVER DAMAGE IN ACUTE LIVER DAMAGE MODELS

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Introduction: Nerve growth factor (NGF) has pro-inflammatory effects in lung and skin inflammatory diseases. During liver regeneration, NGF secreted by hepatocytes induces hepatic stellate cell apoptosis. However, NGF involvement in models of liver damage and inflammation has not yet been assessed.
Aims & Methods
Aim: We investigated the possible inflammatory effects of NGF on isolated hepatic stellate cells (HSC), as well as the *in vivo* effect of silencing NGF on acute liver damage and inflammation.
Methods: Primary HSC from rats and mice were isolated and cultured for 7d and 14d to obtain activated and fully activated HSC, respectively. HSC were treated with 100ng/ml NGF and proNGF and inflammatory cytokine expression was assessed by qRT-PCR and ELISA. Acute liver damage was induced by two i.p. injections of CCl_4 (1ml/g body weight) or by bile duct ligation (BDL) and mice received daily treatment with antisense oligodeoxynucleotide to NGF (ODN)(25mg/kg body weight).
Results: Both NGF and proNGF induced expression of pro-inflammatory cytokines TNFa and IL-6 in activated and fully activated primary rat and murine HSC. Administration of antisense ODN to NGF in the acute CCl_4 and BDL models reduced liver damage, as demonstrated by significantly reduced serum liver enzymes. In addition, antisense ODN to NGF resulted in dramatically reduced (6- fold) hepatic mRNA expression of pro-inflammatory cytokines IL-6, TNFa and MCP1 in the acute CCl_4 acute model. In the BDL-induced acute liver injury, administration of ODN resulted in a two-fold reduction in TNFa, MCP-1 and CXCL1expression.
Conclusion: Silencing NGF may have a beneficial, anti-inflammatory and protective effect in acute hepatotoxicity models.
Disclosure of Interest: None declared

P0010 FERMENTED SOYMILK PREVENTS FREE FATTY ACID-INDUCED LIPOGENESIS AND PRODUCTION OF REACTIVE OXYGEN SPECIES IN HEPATOCELLULAR STEATOSIS MODEL

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Introduction: Ingredients of soy and fermented products have been widely utilized as food supplement for health-enhancing properties, such as reducing the risk of osteoporosis, protection from cardiovascular diseases, and prevention of prostate and breast cancer. This study was carried out to examine the effects of fermented soymilk (FSM) on the free fatty acid-induced lipogenesis in an in vitro model of hepatocellular steatosis model.
Aims & Methods: HepG2 cells were incubated with 0.2 mM of palmitic acid (PA) for 24 h to induce lipogenesis and to accumulate the intracellular lipid accumulation, which was observed by oil red O and Nile red staining. The PA-treated cells were co-incubated with 0.04~1.0% of lyophilized FSM, 0.05 mM of genistein, and 50 nM of estrogen, respectively. Western blot analysis of sterol regulatory element-binding protein-1 (SREBP-1) and nuclear factor erythroid 2-related factor-2 (NRF-2) were performed to examine the lipogenesis related extracellular signal-regulated kinase (ERK) pathway. Cellular reactive oxygen species (ROS) was measured by the DCFDA assay kit.
Results: Lipid accumulations in the PA and FSM co-incubated cells were significantly decreased by 0.5% and 1.0% of FSM without cytotoxicity. Treatments of PA and combining with genistein and estrogen significantly increased the expressions of SREBP-1. However, FSM co-incubation significantly attenuated the expression of SREBP-1 in the PA treated cells. In addition, expression of NRF-2 and phosphorylation of ERK were significantly increased in the PA and FSM co-incubated cells. PA-induced ROS production was significantly reduced by 1.0% of FSM. Meanwhile, genistein or estrogen alone did not lead to significant differences in ROS production.
Conclusion: Our results show that bioactive components, except genistein and phytoestrogen, in fermented soymilk protect hepatocytes against lipid accumulation and ROS production induced by free fatty acid. These effects may be mediated by inhibition of SREBP-1 and activation of NFR-2 via ERK pathway in hepatocytes.
Disclosure of Interest: None declared

P0011 NOD2 MUTATIONS AND ALCOHOLIC LIVER CIRRHOSIS: IS THERE A LINK?

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Introduction: Classically linked with increased risk of Crohn's disease, the polymorphisms of the *NOD2*, a gene involved in the immune response regulation, have been associated, more recently, with a higher risk of some infections and neoplasms. In liver cirrhosis, carriers of *NOD2* variants have been related with an increase in the risk of spontaneous bacterial peritonitis (SBP) because of impaired intestinal mucosa barrier function.
Aims & Methods: The aim of this study was to assess whether *NOD2* mutations are risk factors for alcoholic liver cirrhosis (ALC) and whether there are genotype-phenotype correlations in these patients.
Methods: Case-control study involving the research of the 3 main *NOD2* mutations (3020insC, R702W e G908R) in 202 patients with ALC and in 202 healthy controls.
Results: *NOD2* mutations were found in 43 patients (21.3%) and in 27 controls (13.4%) ($p = 0.064$). The mean age of patients was 59.3 ± 12.6 years old and 79.8% were males. The average age at diagnosis of ALC was significantly lower in patients with mutation (48.3 ± 11.8 *vs.* 58.2 ± 12.4 years old; $p = 0.008$). The incidence of *NOD2* mutations, especially of the R702W variant, was significantly higher in patients with SBP (38.0% vs 13.7%; $p = 0.022$). No significant associations were detected between *NOD2* mutations and hepatocellular carcinoma (22.2% vs 19.7%, $p = 0.603$), hepatorenal syndrome (28.5% vs 19.7%, $p = 0.454$), hepatic encephalopathy (22.5% vs 20.0%, $p = 0.727$), gastroesophageal variceal bleeding (17.6% vs 23.1%, $p = 0.775$), acute alcoholic hepatitis (31.2% vs 20.4%, $p = 0.403$) or other infectious intercurrences (18.7% vs 22.9%, $p = 0.674$).

Conclusion: In this study, the *NOD2* mutations are associated with a trend for increased risk of ALC, earlier onset of the disease and showed to be a risk factor for PBE.
Disclosure of Interest: None declared

P0012 HEPATIC EXPRESSION OF SOMATOSTATIN RECEPTOR 2 MAY BE REGULATED BY CYCLOOXYGENASE-2 IN RAT MODEL OF LIVER CIRRHOSIS

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Introduction: Somatostatin has been used in liver cirrhosis for several decades. Its effects are mediated through binding to its 5 receptors, somatostatin receptor 1-5 (SSTR1-5), among which SSTR2 takes part in an interesting physiopathological process. Hepatic expression of Somatostatin receptor 2 (SSTR2) is upregulated in liver cirrhosis. However, its regulatory mechanism during liver cirrhosis remains obscure.
Aims & Methods: The present study aimed to examine the mechanisms of SSTR2 regulation in liver tissue during the development of liver cirrhosis. Eighteen rats were randomly assigned into control group, cirrhosis group and cirrhosis + celecoxib group, with 6 in each group. Liver cirrhosis was induced in rats by injection of thioacetamide (TAA) intraperitoneally. Expressions of SSTR2, Cyclooxygenase -2 (COX-2) were assessed by western blot and real-time PCR. DNA methylation level of SSTR2 was investigated by bisulfite sequencing. To explore possible regulation effect of COX-2 on the expression of SSTR2, COX-2 was induced in L02 cell lines by transfection of COX-2 and addition of TAA with final concentration from 20mg/L to 80mg/L.
Results: Hepatic expression of SSTR2 and COX-2 were upregulated in liver cirrhosis group compared with control group, both of which were inhibited by the addition of celecoxib. Celecoxib (20uM and 40uM) inhibited the upregulation of SSTR2 in L02 cell line transfected with COX-2 gene or treated with TAA, in which COX-2 was induced, compared with control group. DNA methylation level in promoter region of hepatic SSTR2 is similar between liver cirrhosis group and control group (3.7% VS 3.9%, $p > 0.05$).
Conclusion: Hepatic expression of SSTR2 is upregulated in liver cirrhosis which may be regulated by COX-2 but not DNA methylation.
Disclosure of Interest: None declared

P0013 CHANGES IN GUT MICROBIOTA COMPOSITION ACCORDING TO NUTRITIONAL STATUS IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Gut microbiota (GM) contributes to host metabolism and energy balance, and significant modifications have been reported in malnourished populations. Liver cirrhosis is often associated with malnutrition and sarcopenia but GM changes in this setting have not been investigated yet.
Aims & Methods: The aim of this study was to assess whether GM composition may change in relation to nutritional status in cirrhotic patients. Fecal samples of cirrhotic patients without exposure to antibiotics, pre-/pro-biotics and bowel colonoscopy preparation for at least one month were collected. Nutritional status was assessed by two questionnaires including clinical and anthropometric parameters (Subjective Global Assessment, SGA, and Mini Nutritional Assessment, MNA). GM composition was assessed by a metagenomic gene-targeted approach (16S rRNA) using the Roche 454 GS Junior, following DNA isolation from stool samples stored at –80°C. Data were analyzed in Qiime. Biostatistic analysis was performed using R-statistics packages.
Results: Eighteen cirrhotic patients provided fecal samples. Median age was 60 years, Child-Pugh A/B/C 9/3/6, 3(66%) were well-nourished, 12(17%) at risk of malnutrition and 3(17%) severely malnourished according to MNA; 13(72%) were well-nourished, 2(11%) presented mild to moderate malnutrition and 3(17%) severe malnutrition according to SGA. PCoA of weighted-Unifrac distance evidenced samples clustering according to MNA and SGA rather than to Child-Pugh score ($p = 0.004$, $p = 0.002$ and $p = 0.284$ respectively; PERMANOVA). Malnutrition was associated to the reduction of several taxa, mainly related to the genus Bacteroides, Parabacteroides, Prevotella, Streptococcus, Faecalibacterium, Veillonella (adj. p-value < 0.05). These changes were not related to Child-Pugh score.
Conclusion: Changes in GM composition are strictly associated with nutritional status in cirrhotic patients. Metabolomic analyses should be performed to reveal the significance of these alterations and to evaluate potential therapeutic approaches.
Disclosure of Interest: None declared

P0014 THE ROLE OF HEPATITIS C VIRUS CORE ANTIGEN IN DIAGNOSIS OF HEPATITIS C VIRUS INFECTION

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Introduction: Hepatitis C virus (HCV) infection is a major public health problem worldwide. The prevalence of infection is nearly 3% worldwide. Egypt has one of the highest prevalence rates of HCV infection in the world, about 16-18%. Blood donations screening, achieved mainly by serological identification of HCV-Antibody (Ab), has largely reduced HCV transmission. However, Ab detection is not a reliable marker in the pre-seroconversion phase of infection, infection stage assessing or/for monitoring individuals on anti-viral therapy. HCV Core Antigen (CAg) tests have been introduced to supplement anti-HCV tests and HCV PCR analyses. It may be a useful test for identifying window phase blood donations from Ab negative donors infected with HCV and for the monitoring of antiviral therapy.
Aims & Methods: In this study we aimed to analyze the clinical performance of a commercially available enzyme linked immunosorbent assay (Cell Biolab, Diagnostic. Inc. USA) for HCV CAg and compare the performance of it with reverse transcription polymerase chain reaction (RT-PCR).
This study was done on 88 persons who were divided into two groups. Group 1 included 44 persons diagnosed as anti HCV antibody positive and group 2 included 44 persons diagnosed as anti HCV antibody negative. Sera from all patients were analyazed for both HCV (CAg) and PCR tests. The positive cases to HCV infection in both groups and could be treated by anti HCV therapy reanalyzed by both HCV (CAg) and PCR tests after 12 week.
Results: Out of 88 patients; 26 patients were positive by both CAg and PCR; 5 patients were positive by CAg and negative by PCR while 2 patients were positive only by PCR test. The diagnostic sensitivity, specificity, and positive and negative predictive values of the HCV (CAg) test compared to the HCV RNA test were 92.9%, 91.7%, 83.9%, and 96.5%, respectively. There was statistically positive correlation ($n = 26$, $r = 0.4$) between of the patients HCV (CAg) titer and HCV RNA levels by RT-PCR in ($P < 0.01$). 12 cases (from 26 patients positive to HCV infection from both groups) that could be treated by antiviral therapy using interferon (IFN) and ribavirin (RBV) were reanalyzed by (CAg) and PCR tests after 12 week of therapy and there was a positive correlation ($r = 0.7$) between of the patients HCV (CAg) titer and HCV RNA levels by RT-PCR in ($P < 0.02$).
Conclusion: HCV core antigen testing can be a reliable test used to identify current HCV infection and follow up of treatment especially in areas with poor facilities.

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Disclosure of Interest: None declared

P0015 PATHOGENETIC ROLE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN NONALCOHOLIC STEATOHEPATITIS

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Introduction: Among the various potential contributions of the microbiota to liver disease, small intestinal bacterial overgrowth (SIBO) has historically been shown to be common in chronic liver disease, to correlate with its severity, to be linked to minimal and overt encephalopathy and increased risk of spontaneous bacterial peritonitis. Most recently, more credence has been given to a suggestion that the gut microbiota might play a role in the pathogenesis or progression of certain liver diseases, including alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) through the direct effects of bacteria or their products, via nflammatory mediators such as tumor necrosis factor-α.
Aims & Methods: Our aim was to evaluate the frequency of SIBO in patients with NAFLD/NASH and the influence of eradication of SIBO on clinical course of NASH. We investigated 104 obese patients (66 male, mean age – 54 years, mean BMI – 30.5 ± 3 ,9) who were categorized into two groups: 54 patients with liver steatosis and 50 patients with NASH. Diagnosis of NALFD was confirm by use of ultrasonography or/and computed tomography. Diagnosis of NASH was based on increasing level of ALT (1.26 ± 0.18 mmol/l) and/or positive results of NASHTest (Poynard *et al.*, 2006). In patients with NASH the evaluation of liver function with ^{13}C-methacetine breath test (^{13}C-MBT) also was performed (IRIS by WAGNER, Germany). The presence of SIBO was diagnosed by using a hydrogen glucose breath test (EC60

Gastrolyzer 2, Bedfont Scientific Ltd, Rochester, UK). All patients with positive results of hydrogen glucose breath test (H_2-GBT) were treated with rifaximine (1200 mg/day during 10 days). The efficacy of treatment was controlled with repeated biochemistry, H_2-GBT and ^{13}C-MBT (after 1 month).
Results: Overall, positive results of H_2-GBT and presence of SIBO were found in 12 pts (22.2%) with liver steatosis and 28 (56%) with NASH ($P < 0.005$). Abnormal results of ^{13}C-MBT were occurred in 2 pts with liver steatosis and SIBO (16.6%) versus 12 pts with NASH and SIBO (42.9%, $P < 0.005$). Eradication of SIBO was achieved in 34 of 40 pts (85%) after use of rifaximine (1200 mg/day during 10 days). Obvious improvement of the level of ALT (0.48 ± 0.06, $P < 0.005$) and liver function with repeated biochemistry and ^{13}C-MBT (after 1 month) was occurred in 22 pts (64.7%) and 18 pts (52.9%), accordingly.
Conclusion: We concluded that the changes of intestinal microbiota, including SIBO, plays an important pathogenetic role in initiation and progression of NASH. The modulation of intestinal microbiota and eradication of SIBO with antibiotics (rifaximine) decreased the level of liver inflammation, improved biochemical and liver functional indicators and can be considered as an effective and prospective method of treatment of NASH.
Disclosure of Interest: None declared

P0016 TRANSPLANTED HEPATIC STELLATE CELLS STIMULATE RAT LIVER REGENERATION AFTER PARTIAL HEPATECTOMY AND 2–ACETYLAMINOFLUORENE INJECTION

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Introduction: In cases of insufficient efficacy of conventional therapy of chronic hepatitis and cirrhosis, the search for cellular sources of liver regeneration is becoming more and more urgent. One of the cell types claiming the role of liver regional stem cells (RSC) is hepatic stellate cell (HSC). The aim of our study was to investigate the influence of HSC transplantation on liver regeneration in rats after partial hepatectomy (PH) and administration of 2-acetylaminofluorene (AAF).
Aims & Methods: HSC were isolated from the intact rat livers by the collagenase-pronase perfusion method and then transfected with the green fluorescent protein gene (GFP). Isolated cells were injected immediately after performing PH into the portal vein of operated rats, which were administered with intraperitoneal injection of AAP for 5 days before PH and after PH till sacrifice date at a dose of 12 mg/kg per day. Animals were euthanized after HSC transplantation. Liver paraffin sections were stained immunohistochemically with antibodies against GFP, α-fetoprotein (a-FP) – marker of hepatoblasts, cytokeratin 19 (CK19) – marker of hepatoblasts and cholangiocytes.
Results: After the 1st day of HSC transplantation GFP-positive cells were not detected. After 2 days there were single GFP-positive hepatocytes. Their number reached maximum at 2–3 days after surgery and then rapidly decreased. At the early experimental stages CK19 was present only in the cells of intrahepatic bile ducts and in individual small cells in the periportal areas, the number of which had increased gradually till the 5th day, and up to this moment in the liver developed the evident ductular reaction: the number of bile ducts was increasing, their branching signs and holangioblasts' migration were noted. Further, the evidence of the ductular reaction decreased, but there was also noted decrease of interportal distances indicating the formation of new liver lobules by dividing of existing ones. After the 1st day of PH and injection of native HSC, morphological analysis revealed multiple α-FP + hepatocytes. Besides, many hepatocytes had two cell nuclei. At the same time at all experimental dates we identified GFP + sinusoidal cells and small round α-FP + cells located in periportal sinusoids, which obviously were hepatoblasts. After the 2nd postoperative day the number of α-FP + hepatocytes sharply decreased, α-FP + binuclear hepatocytes and sinusoidal cells were still visible in parenchyma and periportal areas. After 2 weeks only single α-FP + sinusoidal cells were observed in the liver of HSC recipients.
Conclusion: We concluded that at the early stages of our experiment transplanted HSC stimulate activation of RSC in recipients' liver presumably by releasing a variety of growth factors. This leads to expression of hepatoblasts markers cytokeratin-19 and α-FP by RSC localized in liver sinusoids. Later transplanted HSC begin to differentiate into the hepatocyte linage direction which is less pronounced. This probably occurs both due to the direct differentiation of transplanted cells and their fusion with host liver hepatocytes which is indirectly evidenced by the large number of GFP-positive binucleated hepatocytes.
Disclosure of Interest: None declared

P0017 ROLE OF HUMAN UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS IN MANAGEMENT OF CARBON TETRACHLORIDE-INDUCED HEPATIC FIBROSIS IN SPRAGUE DAWELY RATS

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Introduction: Hepatic fibrosis is a reversible wound-healing response to either acute or chronic cellular injury that reflects a balance between liver repair and scar formation. During acute injury, the changes in liver architecture are transient and reversible. With chronic injury, there is progressive substitution of the liver parenchyma by scar tissue. Advanced liver fibrosis results in cirrhosis, liver failure, and portal hypertension and often requires liver transplantation.
Chronic HCV is a major health problem in Egypt with a 10% prevalence of chronic HCV infection among persons aged 15-59 years, which, if left untreated, can result in cirrhosis and liver cancer.
Aims & Methods
Aim of work: To study the antifibrotic effect of umbilical cord mesenchymal stem cells (UCMSCs) and their ability for differentiation into functioning hepatocytes in early and late carbon tetrachloride(CCL4) induced hepatic fibrosis.
Methods: The study was conducted on 40 rats with average weight 180-200 gm, rats were housed under $25^{\circ}C \pm 2^{\circ}C$ and a 12-h light/dark cycle in clean cages with access to food and water ad libitum.
Rats were divided into 2 main groups (control group and UCMSCs-treated group) and each one of them was subdivided into 2 subgroups:
Control group : consists of 20 rats and subdivided into 2 subgroups A) Negative control group (control vehicle (CV) group) : injected by olive oil intraperitonealy equivalent to their body weight and they were scarificed at 2and 6 weeks , blood samples and liver were taken for histopathological examination. B) Positive control group: Rats were injected by carbon tetrachrolide (CCl4) by dose 0.5 mg/kg in olive oil in ratio of 1:1 intraperitonially twice per week for 2 weeks (early fibrosis) and 6 weeks (late fibrosis).
UCMSCs-treated group: they were treated by UCMSCS after 2 weeks and 6 weeks of CCL4 injection in a dose of one million cells/cm3 medium by single injection into the inferior pole of the spleen under general anasthesia using mixture of valium (5mg/kg) and ketamine (5 mg/kg). Then, we closed the wound layer by layer using interrupted sutures by vicryl 3/0. Injection of subcutaneous saline into the rat to avoid its dehydration. Rats were sacrificed 2 weeks after treatment.
Results: As regard laboratory parameters, there was significant reduction in AST & ALT levels in UCMSCs-treated group when compared with the control group with minimal statistical difference in both albumin and INR with significant reduction in area of fibrosis and effective tracing of human albumin gene in the rat's liver by RT-PCR technique in early and late fibrosis.
Conclusion: UCMSCs have both antifibrotic and regenerative powers in treatment of CCL4-induced liver fibrosis in rats at early and late stages.
Disclosure of Interest: None declared

P0018 GLUCAGON-LIKE PEPTIDE - 1 ANALOGUE LIRAGLUTIDE DOES NOT WORSEN CELL VIABILITY AND OXIDATIVE STRESS IN PRIMARY CULTURES OF RAT HEPATOCYTES ISOLATED FROM LEAN AND STEATOTIC LIVERS

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is one of the most common liver diseases in western countries, affecting 20-30% of adult population. This condition can progress to more severe liver diseases - nonalcoholic steatohepatitis, cirrhosis or hepatocellular carcinoma (1). Incretin hormone glucagon-like peptide-1 (GLP-1) exerts beneficial effects on liver functions and liver metabolism, especially in NAFLD condition. In our previous experiment we described a diminishing effect of GLP-1 analogue Liraglutide (LIRA) on an early phase of liver regeneration after partial hepatectomy in rats. In our present work we evaluated an effect of LIRA on cell viability and oxidative stress parameters in primary cultures of rat hepatocytes isolated from lean and steatotic livers.
Aims & Methods: Primary cultures of hepatocytes were obtained from male Wistar rats fed a standard laboratory diet (ST1-group, 10% of energy from fat) or a high-fat diet (HF-group, 71% of energy from fat) for 6 weeks. Hepatocytes were isolated by a two-step collagenase perfusion of rat liver, cell viability was >90%. After the establishment of monolayers, hepatocytes were incubated in supplemented Williams' E medium containing LIRA at concentrations of 0.1-1000 nmol/l for 24 hours. After this period the medium was collected for biochemical assays. We assessed cell viability (leakage of lactate dehydrogenase (LDH) and activity of cellular dehydrogenases - WST-1 assay), synthetic capacity of the hepatocytes (production of albumin determined by ELISA) and markers of oxidative stress (malondialdehyde concentration (MDA), and DCFDA assay).
Results: HF-groups vs. ST1-groups showed lower cell viability (lower cellular dehydrogenases activity, higher LDH leakage, $p < 0.001$) and increased MDA production ($p < 0.001$). LIRA increased activity of cellular dehydrogenases in

ST1-groups ($p < 0.01$), decreased oxidative stress in steatotic hepatocytes (DCFDA assay, $p < 0.05$) and showed no negative effects on other parameters.
Conclusion: In conclusion, GLP-1 analogue Liraglutide does not exhibit negative effects on cell viability and oxidative stress in primary cultures of rat hepatocytes isolated from lean and steatotic livers.
This work was supported by grants GAUK 1488213 and PRVOUK P37/02.

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Disclosure of Interest: None declared

P0019 THE ROLE OF ALBUMIN AND HEPATIC ELASTOGRAPHY LEVELS ON VITAMIN D DEFICIENCY

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Introduction: Liver is the major organ involved in vitamin D metabolism. Recent studies described a high prevalence of vitamin D deficiency in patients with different liver diseases and portal hypertension.
Aims & Methods
Aims: The authors propose to assess vitamin D deficiency in patients with liver disease and its association with clinical and analytical parameters related to hepatic and phospho-calcium metabolism.
Methods: Retrospective analysis of clinical records of patients followed on Hepatology Clinic in a single center. A vitamin D level <20ng/mL was considered as deficiency, according to guidelines. FibroScan transient elastography was used to estimate liver stiffness.
Results: In this study were included 250 patients: 156 men with a median age of 54 years, of which 38% patients had liver cirrhosis. The most common etiologies were VHB infection (31%), alcohol (18%) and VHC infection (16%). Median vitamin D levels were 16 (IQR: 15) ng/mL. Vitamin D deficiency was detected in 60% of total sample, 71% in those with cirrhosis and 53% in those without cirrhosis. Patients with vitamin D deficiency had lower calcium serum levels ($p = 0.004$) and increased hepatic elastography ($p = 0.013$). In multivariate analysis, using logistic regression, vitamin D deficiency was independently associated with liver cirrhosis (OR = 2.2, $p = 0.005$) and the albumin levels were a protective factor (OR = 0.86, $p = 0.002$).
Conclusion: Vitamin D deficiency is very common in liver disease, even without cirrhosis. This deficiency can lead to hypocalcemia, and should be prevented. Our results suggest that this deficiency may be primarily related with the severity of hepatic disease as reflected by the protective role of albumin levels and the association with cirrhosis and increased hepatic elastography.
Disclosure of Interest: None declared

P0020 THROMBOXANE A2 RECEPTOR SIGNALING PROMOTES LIVER REPAIR THROUGH PLATELET ADHESION TO THE SINUSOIDS DURING CHEMICAL-INDUCED HEPATOTOXICITY

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Introduction: Thromboxane A2 (TxA2) contributes to liver repair after acute liver injury as well as to tumor-associated angiogenesis.
Aims & Methods: The present study was to examine whether TxA2 receptor (TP) signaling in platelets facilitates sinusoidal restoration to repair the injured liver from chemical hepatotoxicity.
Treatment with carbon tetrachloride (CCl4) (1.0 mg/kg, ip) was used to induce acute liver injury in male TP knock out mice (TP-/-) and their wild counterparts (WT). At 0, 12, 24, 48, 72, and 96 h after CCl4 administration, plasma activity of ALT, necrotic area, proliferating cellular nuclear antigen (PCNA) index, and hepatic mRNA levels of growth factor relevant to angiogenesis were determined. Liver microcirculation was assessed by intravital microscopy.
Results: Both of WT and TP-/- experienced the maximal liver injury as evidenced by ALT levels at 24 h, and ALT levels were gradually decreased to basal levels at 96 h. Hepatic necrotic area in WT peaked at 48 h, and reduced thereafter, while that at 48 h in TP-/- was greater and remained high thereafter. The PCNA expression in WT peaked at 48 h, while that in TP-/- mice delayed and peaked at 72 h. Liver microcirculation was impaired and reached at nadir at 48 h, and delayed restoration in TP-/- compared with WT. Liver sinusoidal endothelial cell functional recovery was impaired in TP-/-. Platelets adhesion to the sinusoids was enhanced in WT at 48 and 72 h compared with TP-/-. This was associated with reduced mRNA levels of HGF, VEGFR2, basic FGF, and CD31 in liver from TP-/-. HGF levels in platelets from TP-/- treated with CCL4 for 48 h were lower than WT.
Conclusion: TP signaling promotes liver repair and sinusoidal restoration through enhancement of hepatic pro-angiogenic factors including HGF derived from platelets.
Disclosure of Interest: None declared

P0021 BACTERIAL INFECTION IN PATIENTS WITH LIVER CIRRHOSIS USING ACID SUPPRESSIVE MEDICATION: AN EXPERIENCE OF A SINGLE TERTIARY HOSPITAL IN QATAR

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Introduction: The association between bacterial infections and acid suppressive medications (i.e., proton pump inhibitors, PPIs) has been recently studied with debatable results.
Aims & Methods: The aim of this study was to investigate the relationship between PPIs and the development of bacterial infections in cirrhotic patients. Consecutive cirrhotic patients above 18 years old hospitalized from 2007 through 2012 to Hamad General Hospital-Qatar were enrolled. We specifically inquired for PPIs consumption in the last 90 days prior to hospitalization and classify as PPIs-users and non-users. Cirrhosis diagnosis was established either with a liver biopsy or the combination of physical, laboratory and ultrasonography findings. Cirrhotic patients with active gastrointestinal bleeding, using immunosuppressive therapy or using antibiotics in the previous two weeks prior to hospitalization were excluded.
Results: A total of 333 patients were included, 171 (51.4%) with and 162 (48.6%) without PPIs. The PPIs-users were significantly older in age ($p = 0.001$). There was no statistical difference between the two groups in sex distribution and etiology of cirrhosis ($p > 0.05$ for both parameters). The PPIs-users had a significantly higher incidence of overall bacterial infection rate (25.7%) than non-PPIs-users (13.5%), $p = 0.005$. On the multivariate analysis, older age >60 years, ($p = 0.02$), and PPIs-use ($p = 0.01$) were independent predicting factors for overall bacterial infection. The indication for PPIs use was undocumented in 43% of patients.
Conclusion: The present study shows that PPIs use, as well as older age >60 years, were independent predicting factors for the development of bacterial infection in hospitalized cirrhotic patients. Unless it is indicated, PPI therapy should be avoided in this group of patients, in particular those older than 60 years of age.

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P0022 PREVALENCE OF MALNUTRITION IN ADVANCED CIRRHOSIS – A PROSPECTIVE NUTRITIONAL ASSESSMENT IN HOSPITALIZED PATIENTS

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Introduction: Malnutrition is a risk factor for increased morbidity and mortality in liver cirrhosis. Nutritional assessment has been recognized as an important step to identify cirrhotic patients at greater risk of complications in clinical practice.
Aims & Methods
Aim: To evaluate nutritional status of hospitalized patients with decompensated liver cirrhosis.
We performed a prospective six-month study in a gastroenterology unit. All consecutive patients hospitalized due to decompensated liver cirrhosis were submitted to nutritional assessment by the following methods: anthropometric parameters (body mass index-BMI, skinfolds and circumferences), biochemical parameters, dynamometry and questionnaires. Demographic and relevant clinical data were also collected.
Results: A total of 50 patients were included, with a mean age of 60.9 ± 12.1 years, predominantly male gender (80.0%) and alcoholic cirrhosis (90.0%). Main admission causes: ascites and edema 24.0%, hepatic encephalopathy 20.0%, digestive hemorrhage 18.0% and spontaneous bacterial peritonitis 10.0%. All patients except two were classified as Child-Pugh B or C (B-36.0%; C-58.9%) and presented high MELD scores (mean 19.2 ± 7.3). The prevalence of malnutrition, according to the different methods used, was: BMI 22.0%, triceps skin thickness 86.0%, midarm circumference 78.0%, midarm muscle circumference 78.0%, Mini Nutritional Assessment 32.0% (with 62.0% of patients at risk), Subjective Global Assessment 86.0% and the Royal Free Hospital Global Assessment 86.0%. Malnutrition in Child-Pugh C patients was significantly higher comparing with Child-Pugh B, with all the methods used ($p < 0.05$), except for BMI ($p > 0.05$). MELD score was significantly higher in malnourished patients, compared with non malnourished patients (27 versus 13), independently of the method ($p < 0.05$).
Conclusion: Prevalence of malnutrition in advanced cirrhosis was superior to 70% with all the evaluation methods, except for BMI. Greater severity of disease was associated with higher prevalence of malnutrition.
Disclosure of Interest: None declared

P0023 CIRRHOTIC CARDIOMYOPATHY DOES NOT INFLUENCE MORTALITY OR MORBIDITY IN A PROSPECTIVE COHORT OF CIRRHOTIC PATIENTS

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Introduction: Cirrhotic cardiomyopathy (CCM) is a clinically silent complication of liver cirrhosis that becomes overt after stressful events such as infections, placement of transjugular intrahepatic portosystemic shunts or liver transplant. Diagnostic criteria as well as clinical relevance of this entity in patients suffering from cirrhosis are currently under debate.
Aims & Methods: We aimed to determine the impact on survival and disease-related adverse events in a cohort of consecutive patients with liver cirrhosis.
Seventy cirrhotic patients examined in our tertiary referral centre were enrolled in a prospective observational study. Prior history of cardiovascular disease, diabetes, acute renal failure, severe anaemia, obesity or cachexia, active malignancy, infections were considered exclusion criteria.
Full physical examination, routine blood work, N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, 12-lead electrocardiograms and transthoracic echocardiography examination with tissue Doppler imaging were performed in all patients. CCM was diagnosed according to the consensus criteria [1] in the presence of left ventricular ejection fraction $<55\%$ and/or diastolic dysfunction (E/A <1, E wave deceleration time >200ms, isovolumetric relaxation time >80ms). Patients were contacted by telephone every 3 months and invited for a study visit one year after enrollment. Disease-related adverse events (gastrointestinal bleeding, encephalopathy, new-onset or worsening of ascites, severe infections, hepatocarcinoma) and death were the main outcomes reported. Patients were stratified according to the presence of CCM and hypothesis testing was two-tailed with $p < 0.05$ considered significant. Survival analysis was performed by Kaplan-Meier curves.
Results: According to consensus criteria cirrhotic cardiomyopathy was diagnosed in 31 patients (44%). 3 patients were lost to follow-up. There was no difference in etiology or severity of cirrhosis amongst the groups. NT-proBNP levels and length of rate adjusted QT interval did not differ significantly according to the presence or absence of CCM (189 vs 238 pg/mL and, respectively, 414 vs 420 ms). During follow-up (range:3-15 months) there were 10 deaths and 31 patients experienced at least one disease-related adverse event. The median time to appearance of decompensation was 9 months. There were no significant differences between patients with and without CCM in rate of death (4 vs 6 patients, $p=0.9$), risk of adverse-event (14 vs 17 patients, $p=0.1$). There was a statistically insignificant trend towards earlier decompensation in the CCM group (8.8 vs 10.2 months, $p=0.2$). Higher MELD score was the only risk factor for earlier decompensation.
Conclusion: Cirrhotic cardiomyopathy has a high prevalence in the general population of patients with cirrhosis when consensus criteria are used for diagnosis. The presence of cirrhotic cardiomyopathy did not influence survival or time to first decompensation during up to 15 months follow-up in this cohort.

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Disclosure of Interest: None declared

P0024 MEAN PLATELET VOLUME AS A NONINVASIVE MARKER FOR PREDICTION OF INFLAMMATION AND INFECTION OF ASCITIC FLUID IN DECOMPENSATED CHRONIC LIVER DISEASE

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Introduction: One of the most important complication of cirrhosis is ascitic fluid infection (AFI) and occurs in up to 25% of patients. Current literature suggests that ascitic fluid analysis by paracentesis should be done for all patients with ascites that are admitted to the hospital to exclude AFI. Beside membrane inflammation, AFI is also associated with increased systemic inflammation. The mean platelet volume (MPV) as an indicator of larger, active platelets, is being widely studied as a marker for systemic inflammation in areas like Cardiology and Rheumatology, because of its low cost and availability in routine analysis (platelet count).
Aims & Methods: To evaluate the value of MPV as (1) an inflammation marker in decompensated chronic liver disease (2) its ability to exclude AFI.
Retrospective analysis of all patients admitted to our center with the diagnosis of decompensated chronic liver disease, between the period of 2010 and 2014. We excluded admissions for gastrointestinal bleeding and those where paracentesis was not done. At admission, patients were divided in 3 groups: with active infection, infected without AFI and with AFI. A receiver operating characteristics (ROC) curve was obtained, and sensitivity and negative predictive value were calculated for MPV as a predictive marker for AFI exclusion.
Results: We identified 434 patients, 232 with active infection and 99 with criteria for AFI.
The MPV was statistically higher in the group of patients with active infection compared to not infected (10.84 vs 10.43 fL; $p = 0.000$). Within the group of patients with active infection, those with criteria for AFI presented higher values of MPV (11.28 vs 10.49 fL; $p = 0.000$) compared to the other infections.
When compared, the MPV of patients with criteria for AFI versus the rest of the patients, the variables MPV (10.45 fL vs. 11.28; $p = 0.000$), leukocyte count (11.3 vs $8.7x10^9$ /L, $p = 0.003$) and CRP (65.30 vs 34.15 mg/L; $p = 0.00$) were significantly higher; no statistically significant differences were found for the variables number of platelets and platelet distribution width (PDW).
The ROC curve analysis suggested that the optimum MPV level cut-off point for cirrhotic patients with AFI, was 9.75 fL with a sensitivity of 92% and a negative predictive value of 91% (area under the curve: 0.701).
Conclusion: Our results show that MPV is significantly increased in patients with active infection, and represents a good marker for inflammation. We propose the MPV as a noninvasive useful marker for AFI exclusion, with an average discriminating power.
Disclosure of Interest: None declared

P0025 THE ROLE OF BIOMARKERS AND SYSTEMIC INFLAMMATORY RESPONSE SYNDROME IN THE EXCLUSION OF BACTERIAL INFECTION IN PATIENTS WITH DECOMPENSATED CHRONIC LIVER DISEASE

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Introduction: It is estimated that up to 35% of patients hospitalized for decompensated chronic liver disease have a bacterial infection [(1-2)]. The usual biomarkers (C reactive protein- CRP, leukocyte count and mean platelet volume - MPV), together with criteria for systemic inflammatory response syndrome (SIRS), do not behave like in healthy population.
Aims & Methods: We sought to evaluate the diagnostic role of SIRS, CRP, leukocyte count and MPV as predictors of infection at admission in patients with decompensated chronic liver disease.
Retrospective study conducted from 2010 to 2014, which evaluated patients admitted to our center for decompensated chronic liver disease. We excluded gastrointestinal bleeding and those that had not had paracentesis. The patients were divided according to the presence or absence of active infection. We recorded demographic, clinical and laboratory data and assessed the effectiveness of SIRS, CRP, leukocyte count and MPV in predicting infection by using areas under the curve (AUCs).
Results: We identified 434 patients with a mean age of 60 years (80% male). Alcohol was identified as a causative agent for liver disease in 90% of patients and in 24% there was chronic viral infection. About 52% of patients were classified as Child-Pugh C and 13% had criteria for SIRS.
The variables CRP (57 versus 27 mg/L; $p = 0.000$), MVP (10.85 versus 10.42 fL; $p = 0.000$) and leukocyte count (10.54 versus $7.33x10^9$/L; $p = 0.000$) were significantly higher in the group of patients with active infection compared to uninfected. In univariate analysis, the presence of SIRS was associated with infection (X^2: 55.6; $p = 0.000$, OR = 68). Regardless of the Child-Pugh score, when compared, the variables CRP (AUC: 0.754), leukocyte count (AUC: 0.633), SIRS (AUC: 0.621) and MPV (AUC: 0.600), CRP presented the highest discriminating power, and was statistically superior when compared to other variables (respectively, $p = 0.0006$; $p < 0.0001$; $p < 0.0001$). This superiority is still maintained whether is analyzed only Child-Pugh B patients or in Child-Pugh C patients.
Conclusion: The set of our results, only identified CRP as a good marker for exclusion of infection in patients with decompensated chronic liver disease. SIRS and the biomarkers MPV and leukocyte count showed an average discriminatory power (AUC <0.75).

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Disclosure of Interest: None declared

P0026 PREVALENCE AND PREDICTORS OF MORTALITY IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE

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Introduction: Acute-on-chronic liver failure (ACLF) is characterized by acute hepatic insult manifesting as jaundice and coagulopathy, complicated within 4 weeks by clinical ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease/cirrhosis, and is associated with high 28-day mortality.

Aims & Methods: To determine the prevalence of ACLF in patients with chronic liver disease and variables which predict mortality in the former condition. Consecutive patients with known or unknown chronic liver disease (CLD), admitted to Kasturba Hospital, Manipal, between May 2014 and February 2015 were included. ACLF was diagnosed at baseline in patients based on Asia Pacific Association for the Study of Liver (APASL) definition and all were given standard intensive care. All patients were followed up for 28 days or till mortality whichever was earlier. Univariate analysis and subsequently multivariate analysis was done to determine the factors which predict mortality in ACLF.

Results: 115 (male = 109) patients with CLD were included prospectively of whom 37 (32.2%) had ACLF. Alcohol was the most common cause of underlying chronic liver disease (80%) followed by cryptogenic (13.9%). Alcohol (62.16%), Hepatitis E infection (27.03%) and Reactivation of Hepatitis B virus (5.41%) were the most common acute insults. The 28-day mortality was 56.7% among those with ACLF and 23.1% in those without. On multivariate analysis, high serum creatinine ($p = 0.043$) and high C-reactive protein (CRP) ($p = 0.044$) were found to be independent predictors of mortality. Among the severity scores studied, Model for end-stage liver disease (MELD) score was individually able to differentiate between survivors and non-survivors ($p = 0.004$) and fared better than Child-Turcotte-Pugh score ($p = 0.312$).

Conclusion: Patients with ACLF have a higher mortality than those with CLD. High serum creatinine, high CRP and higher MELD scores predict poor outcome in patients with ACLF.

Disclosure of Interest: None declared

P0027 ROLE OF ACOUSTIC RADIATION FORCE IMPULSE ELASTOGRAPHY AND 13C-METHACETIN BREATH TEST IN PREDICTING THE SEVERITY OF CHRONIC LIVER DISEASE

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Introduction: Noninvasive investigations, such as various imaging techniques and breath tests offer considerable promise in their ability to stage liver disease and avoid an invasive liver biopsy.

Aims & Methods

Aim: To evaluate the role of Acoustic Radiation Force Impulse (ARFI) elastography and ^{13}C-methacetin breath test (MBT) in predicting the severity of chronic liver disease.

Methods: We performed ARFI elastography and ^{13}C-methacetin breath test (MBT) in 179 patients with chronic liver disease of different etiologies (alcoholic, chronic hepatitis C, chronic hepatitis B and nonalcoholic fatty liver disease – NAFLD) who underwent liver biopsy for diagnosis and treatment. The METAVIR scoring system (chronic hepatitis C and chronic hepatitis B) and the Brunt scoring system (alcoholic hepatopathy and NAFLD) served as references for the histological staging of liver fibrosis. The accuracy of non-invasive tests to predict the severity of liver disease (Fibrosis ≥ 2 and cirrhosis) was assessed using the area under receiver operating characteristic curve (AUROC) with 95% CI.

Results: The Spearman's correlation coefficient between ARFI (0.795) and MBT (0.678) and the histological diagnosis of NASH was highly significant ($p < 0.001$). The AUROC of ARFI elastography and MBT was 0.861 (95% CI = 0.808 - 0.914) and respectively 0.804 (95% CI = 0.740 - 0.867) for the diagnosis of significant fibrosis ($F \geq 2$). The diagnostic accuracy of ARFI elastography in predicting cirrhosis ($F = 4$) had a validity of 95.4% (95% CI AUROC = 0.928 - 0.981) while MBT had a validity of 82.7% (95% CI AUROC = 0.765 - 0.890, $p < 0.001$). MBT also enables the evaluation of the microsomal liver function involved in severe chronic liver disease.

Conclusion: ARFI Elastography and MBT are very good methods for assessing the severity of liver disease. Due to the complementary role in evaluating microsomal liver function, ^{13}C-methacetin breath test could be a reliable diagnostic and follow-up test for patients with chronic liver disease.

Disclosure of Interest: None declared

P0028 THE IMPACT OF CARVEDILOL VERSUS NON-SPECIFIC BETABLOCKERS ON THE MORTALITY IN CIRRHOSIS

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Introduction: Carvedilol is a good alternative to propranolol for the prophylaxis of variceal bleeding, some researchers suggesting even a greater impact on portal and systemic hypertension. There is still an open debate about the effect of carvedilol and non-specific betablockers (NSBB) on mortality in patients with cirrhosis.

Aims & Methods: We compared retrospectively the impact on mortality of carvedilol versus NSBB in patients with cirrhosis hospitalized in a tertiary referral center in Romania. We included patients with alcoholic and viral cirrhosis admitted in our center from 01 January 2010 to 31 December 2014. We defined risk time for the bleeding as the time between the first administration of betablockers until death or end of follow-up. We adjusted for age, gender, heart disease, variceal bleeding, Child-Pough score to assess the HR.

Results: We identified 2625 cases: 684 patients receiving carvedilol and 1941 patients who were treated with NSBB, respectively. There were 1147 (43.7%) cases with viral cirrhosis and 1478 (56.3%) cases with non-viral cirrhosis. Regarding the Child-Pough score in each group, we identified in the first group 431 (63%) Child A patients, 205 (30%) Child B patients and 48 (7%) Child C patients, while in the NSBB group we had 1296 (66.7%) Child A patients, 452 (23.3%) Child B patients and 193 (10%) Child C patients. The prevalence of variceal bleeding was 23.7% in the first group vs. 26.2% in the second group without significant difference, while the heart disease was significantly more frequent in the carvedilol group (57% vs. 24%). We recorded significantly fewer deaths in the carvedilol group during follow-up compared with the NSBB group (10.7% vs. 21.3%, Chi-square ($p < 0.05$). We found the un-adjusted HR for carvedilol vs. NSBB to be 0.56 (95% CI 0.3-0.7) and the HR adjusted for covariates was 0.58 (95% CI 0.3-0.7).

Conclusion: The use of carvedilol in patients with cirrhosis was associated with a significant lower mortality compared with the use of NSBB even though the variceal bleeding rate was similar between the two groups.

Disclosure of Interest: None declared

P0029 INCREASING FREQUENCY OF GRAM-POSITIVE COCCI IN SPONTANEOUS BACTERIAL PERITONITIS. A SINGLE CENTRE EXPERIENCE

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Introduction: Sponteneous bacterial peritonitis (SBP) in patients with hepatic cirrhosis is mostly related to gram negative enterobacteriaceae. Recent studies have reported a change in the epidemiology of microbes that are being isolated in SBP and an increased prevalence of gram positive and multiresistant bacteria.

Aims & Methods: Record the bacteria that have been isolated in the ascitic fluid of patients with hepatic cirrhosis and their resistance in commonly used antibiotics. Positive ascitic fluid cultures of cirrhotic patients that have been admitted in our hospital and the respective antibiograms have been retrospectively recorded.

Results: 62 patients (49 male) with hepatic cirrhosis with a median age of 66 years (32-68) had positive ascıtic fluid culture. In 36/62 cultures Gram + positive bacteria have been isolated. In detail the isolated bacteria were: enterococcus spp. (19), Escherichia coli (13), streptococcus spp (12), Klebsiella (6), staphylococcus (5), Proteasspp (2), Enterobacter (2) Acinetobacter (1), Cronobacter (1), Pseudomonas aurigonosa (1).
Resistance to 3rd generation cephalosporines has been found in 20 out 47 strains, in ciprofloxacine in 20 out of 40 and in ampicilline in 29 out of 46.

Conclusion: Gram + bacteria have been isolatedin the majority of positive ascitic fluid cultures. Resistance to 3rdgeneration cephalosporines and ciprofloxacine is common. Therapy should be individualized according to culture results and patients' characteristics.

Disclosure of Interest: None declared

P0030 EARLY IN-PATIENT MANAGEMENT OF ALCOHOL-RELATED LIVER DISEASE: RESULTS OF A LIVER CARE BUNDLE TO IMPROVE QUALITY OF CARE

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Introduction: The incidence of Alcohol Related Liver Disease (ARLD) is rising in the UK, as is its associated mortality. A recent National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report highlighted recurring deficiencies in the management of ARLD in UK hospitals and the British Society of Gastroenterology provided guidance in the treatment of these patients during acute hospital admissions.
Aims & Methods: Between 1 August 2013 and 31 October 2013, consecutive admissions of patients with ARLD to a district general hospital were identified from discharge and mortality data. A liver care bundle (LCB) using NCEPOD recommendations was generated. Case notes were analysed prior to institution of this LCB and re-audited following its inception from 1 April 2014 to 31 July 2014. Electronic referrals to specialist gastroenterology and dieticians formed part of the LCB, as well as a checklist of actions for the admitting physician.
Results: 20 patients (median age 51 (28-67) years) were identified initially with ARLD, of which 13 (65%) were male. Median Model for End-stage Liver Disease (MELD) score was 14 (range 6-35). Post LCB institution a further cohort of 25 patients studied was matched for age (59 (32-79) years), sex (13/25 (52%) male) and MELD score (13 (6-40)). Inpatient mortality was 7/20 (35%) prior to and 2/23 (9%) post LCB ($p = 0.065$). All patients were screened for ongoing alcohol use and in 65% a withdrawal regime was prescribed. Only 1/20 (5%) had dietician input in the first 48 hours rising to 11/25 (44%) post LCB institution ($p < 0.001$). In all patients with ascites in the presence of acute kidney injury, diuretics were discontinued in both cohorts. In 92% of cases of ascites, diagnostic parascentesis was performed, however blood cultures were performed on admission in only 6/20 (30%) initially rising to 40% post LCB. 13/20 of patients (65%) had consultant review within 12 hours pre LCB with 18/25 (72%) post LCB. The proportion of patients receiving specialist review by a gastroenterologist within 72 hours rose from 45% to 54% following LCB use.
Conclusion: Instituting a liver care bundle for the management of alcohol-related liver disease at our centre improved both the quality of care and outcome from patients admitted during acute decompensation, particularly related to early specialist review. Initiation of bundles of care in liver disease requires close collaboration between specialist medical services and allied health professionals such as dieticians to optimise patient care.

Reference

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Disclosure of Interest: None declared

P0031 SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH CIRRHOSIS AND ASCITES – ITS PREVALENCE, CLINICAL AND PARACLINICAL FEATURES

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Introduction: Spontaneous bacterial peritonitis (SBP) is a severe complication occurring in patients with liver cirrhosis and ascites and it is associated with a high mortality rate.
Aims & Methods: The aim of this study is to evaluate the prevalence of the SBP in hospitalised patients with cirrhosis and ascites and also their clinical and paraclinical characteristics.
Materials and methods. This cross-sectional study enrolled all patients diagnosed with liver cirrhosis and ascites , who were hospitalised in a tertiary medical center over a period of 18 months (January 2012- June 2013).
The diagnosis for SBP consists of polymorphonuclear (PMN) counts ≥ 250 cells/mm^3 and/or a positive ascitic fluid culture, without any evidence of external or intra-abdominal infectious source.
To evaluate our patients, who were divided in two groups (SBP and non-SBP), we compared the following data: age, gender, etiology of cirrhosis, volume of ascitic fluid, hypotension, tachycardia, hepatic encephalopathy, upper gastrointestinal bleeding, hepatorenal syndrome, hepatocellular carcinoma, hepatic hydrothorax, leukocytosis and MELD Score (Model of End-stage Liver Disease).
Results: 763 patients with cirrhosis and ascites were included in our study. The mean age was 60.41 years (min 17 years, max 91 years) and there was a male predominance (63.3%). 11.1% of the patients had SBP.
By comparing the SBP and the non-SBP patients, the following significant differences were discovered: male gender 75.3% vs 61.8% ($p = 0.02$); voluminous ascites 83.5% vs 31.6% ($p < 0.001$); hepatic encephalopathy 82.4% vs 54% ($p < 0.001$); hepatorenal syndrome 15.3% vs 2.5% ($p < 0.001$); hepatic hydrothorax 24.7% vs 11.7% ($p = 0.001$); leukocytosis 32.9% vs 18% ($p = 0.002$) and the MELD Score ≥ 17 points 68.2% vs 39.7% ($p < 0.001$).
Using multivariate analysis, four out of these factors were identified as being independent factors significantly associated with SBP: voluminous ascites (OR = 8.33, 95%CI:4.50-15.42, $p < 0.001$), hepatic encephalopathy (OR = 2.25, 95%CI:1.21-4.20, $p = 0.010$), hepatorenal syndrome (HR = 4.21, 95%CI:1.71-10.38, $p = 0.002$) and the MELD Score ≥ 17 points (HR = 1.77, 95%CI:1.03-3.02, $p = 0.037$).
Conclusion: Spontaneous bacterial peritonitis was found in 11.1% patients with liver cirrhosis and ascites and was significantly associated with voluminous ascites, hepatic encephalopathy, hepatorenal syndrome and a MELD Score ≥ 17 points.
Disclosure of Interest: None declared

P0032 PANTOPRAZOLE VERSUS RABEPRAZOLE EFFECTS ON CYTOCHROME P450 ACTIVITY ASSESSED BY 13C-AMINOPYRINE BREATH TEST IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Proton pump inhibitors (PPIs) are one of the most widely used drugs worldwide. Almost all PPIs, undergo extensive hepatic metabolism via cytochrome (CYP)-P450 system and their clearance significantly depend on CYP-2C19 activity. Otherwise, the primary pathway of rabeprazole metabolism is non-enzymatic. In patients with advanced liver disease, the activity of CYP-P450 system is impaired, thus leading to a drug clearance reduction and an increased risk of drug-drug interaction. 13C-aminopyrine breath test (13C-ABT) is a non-invasive, liver function test that explores CYP enzyme activity.
Aims & Methods: Aim of the study was to evaluate the effects of different PPIs on the activity of CYPs by 13C-ABT in patients with Hepatitis C virus (HCV)-related liver cirrhosis. We compared two PPIs with different metabolic pathway: pantoprazole, which employs the CYP-P450 pathway, and rabeprazole, which undergoes non-enzymatic metabolism.
Thirty consecutive patients with HCV-related liver cirrhosis, Child-Pugh A, needing PPI therapy, were randomly assigned to pantoprazole (40mg/day) or rabeprazole (20mg/day) treatment. Exclusion criteria were: other causes of liver cirrhosis, severe cardiovascular or respiratory disorders, use of PPI in the 30 days before the study. 13C-ABT was performed before and 15 days after starting therapy according to the following protocol: breath samples were collected baseline and at 30-minute intervals for 2 hours after oral administration of 13C-aminopyrine (2mg/Kg body weight). 13C-enrichment of CO2 was determined by purification-isotope ratio mass spectrometer. Results were expressed as maximum percentage of 13CO2-recovery per hour (max 13C% dose/h) at any time (“excretion peak”) and percentage of 13CO2-cumulative dose recovered in 2 h (%13C cum dose at 120 min).
Results: Overall, we enrolled 13 males and 17 females with a mean age of 60.9 ± 7.5 yrs. Age, gender distribution, BMI and laboratory findings did not significantly differ among pantoprazole and rabeprazole group. Baseline, 13C-ABT results were altered in 13/30 (43%) patients (6 in pantoprazole and 7 in rabeprazole group). Fifteen day after starting therapy, the pantoprazole group had a mean 13C-ABT %dose/h at 30 min of 6.20 ± 4 versus 6.35 ± 4.5 at baseline and a mean %dose/cumulative at 120 min of 11.52 ± 6.9 versus 11.27 ± 7 at baseline. Similarly, during rabeprazole treatment, the mean %dose/h at 30 min was 5.81 ± 3.9 versus 6.13 ± 4.3 at baseline and the mean %dose/cumulative at 120 min was 10.9 ± 6.5 versus 10.7 ± 7.5 at baseline.
Conclusion: No differences is detectable between pantoprazole and rabeprazole use in patients with HCV-related liver cirrhosis. Pantoprazole do not significantly impair the CYP-450 pathway activity in these patients. Both PPIs are safe for treatment of patients with advanced liver disease.

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Disclosure of Interest: None declared

P0033 MANAGEMENT OF GASTRIC VARICES: A FRENCH NATIONAL SURVEY

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Introduction: Gastric variceal bleeding accounts for 10% of upper gastrointestinal bleeding related to portal hypertension. Level of evidence in managing gastric varices is low.

Aims & Methods: We aimed to determine the modalities of management of non-GOV1 gastric varices in France. Hepato-gastroenterologists (HGE) working in general hospitals (GH) or in university hospitals (UH) received a self-administered questionnaire.

Results: One hundred and fifty four HGE from 109 centers (37UH, 72GH) among the 336 (32.4%) contacted responded. Regarding primary prophylaxis, beta-blockers were used by 96% of HGE. Only 17.2% of HGE used glue obliteration (UH: 27.7% vs GH: 9.3%; $p=0.004$), 8% used TIPS and 5.3% proposed no treatment. Most HGE (77.6%) estimated that they had local access to glue obliteration but 64.2% declared that TIPS placement required transfer to another center. Obliteration was performed under general anesthesia by 86% of HGE. N-butyl-2-cyanoacrylate plus methacryloxysulfolane (Glubran®) and N-butyl-2-cyano-acrylate (Histoacryl®) were used respectively in 48.2% and 55.9% of cases (3.5% of HGE used both). Dilution with lipiodol was performed in 78% of cases. The technique of obliteration was variable between centers and within the same center: maximal dilution was 1/10; injected volume varied from 0.5 to 20mL per varix and from 1 to 30mL per procedure. To control active bleeding, 77.6% of HGE used obliteration (UH: 85.7% vs GH: 70.9%, $p=0.04$) and 34% used band ligation (UH: 28.6% vs GH: 38.8%; $p=0.02$). Early-TIPS was proposed by 56.3% of HGE (UH: 71.7% vs GH: 39.2%, $p<0.001$). Regarding secondary prophylaxis, 74.4% used betablockers, 66% used obliteration (UH: 76.6% vs GH: 56.6%; $p=0.014$) and 14% used TIPS. Endoscopic control was performed by 62.6% of HGE, 70% evaluated the varix stiffness with a closed biopsy forceps. Side effects of obliteration were reported by 59.5% of HGE (UH: 70.4% vs GH: 41.2%; $p=0.08$) and concerned mainly glue migration (UH: 66.7% vs GH: 33.3%; $p<0.001$), an event systematically searched by 22.9%.

Conclusion: The management of gastric varices in France is very heterogeneous between centers and even within the same center. University hospitals have a better access to obliteration and especially to TIPS. Obliteration as a primary prophylaxis procedure was rarely performed. Glue migration was frequently observed although probably underreported. Specific guidelines on the management of gastric varices should be established by expert groups to standardize clinical practices.

Disclosure of Interest: None declared

P0034 EXTERNAL VALIDATION OF THE CLIF-SOFA IN CIRRHOTIC PATIENTS ADMITTED TO INTENSIVE CARE UNITS (ICUS): A META-ANALYSIS

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Introduction: The prognostic performance of the Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) score in cirrhotic patients admitted to Intensive Care Units deserves large external validations.

Aims & Methods: The aim of this meta-analysis was to assess the ability of the CLIF-SOFA to predict in-ICU, in-hospital, and 6-month mortality in ICU survivors.

The CLIF-SOFA was computed retrospectively in 6 studies including 1221 cirrhotic patients admitted between 1995 and 2012. Studies have been selected by the participation of the corresponding authors who responded to a standardized questionnaire. The prognostic performance of different cutoffs of the CLIF-SOFA to predict mortality at different timepoints was assessed by the weight-adjusted odds ratios and positive predictive values and compared to that of the SOFA, the modified SOFA (mSOFA) and the MELD.

Results: On admission, 72.1% of patients ($n=880$) had a CLIF SOFA ≤ 14 and only 1.1% ($n=13$) had a CLIF-SOFA > 22. Among all the available prognostic scores, the best predictor of in-ICU mortality was a CLIF-SOFA ≥ 22 (OR = 5.94; CI95%: 1.71-20.64; $p=0.005$; PPV = 1.00), followed by a SOFA > 19 (OR = 10.37; 95%CI: 5.65-19.01; $p<0.001$; PPV = 0.94). Predictive value of in-ICU mortality was better for a CLIF-SOFA ≥ 15 (OR = 7.44; CI95%: 3.43-16.12; $p<0.01$; PPV = 0.81) than for an increased SOFA on day 3 (OR = 4.75; 95%CI: 2.33-8.97; $p<0.001$; PPV = 0.71) or a MELD score ≥ 26 (OR = 5.37; 95%CI: 4.01-7.21; $p<0.001$; PPV = 0.66). Prognostic value of in-hospital mortality was good for a CLIF-SOFA ≥ 15 (OR = 3.93; 95CI%: 2.13-7.26; $p<0.001$; PPV = 0.88), for a mSOFA > 13 (OR = 11.92; 95%CI: 4.59-30.94; $p<0.001$; PPV = 0.94) and a SOFA > 19 (OR = 11.56; 95%CI: 3.23-41.32; $p<0.001$; PPV = 0.94). Among ICU survivors, 6-month mortality was still predicted by a CLIF-SOFA ≥ 22 (OR = 7.43; 95%CI: 1.18-46.62; $p=0.032$; PPV = 1.00), and a MELD ≥ 26 (OR = 3.97; 95%CI: 1.92-8.22; $p<0.001$; PPV = 0.75), whereas high values of SOFA and mSOFA did not provide any significant prediction.

Conclusion: In critically ill cirrhotic patients, the CLIF-SOFA is able to predict both in-ICU mortality and 6-month mortality in ICU survivors, conversely to the SOFA and mSOFA. High values of CLIF-SOFA better predict in-ICU mortality than high values of SOFA or increase in SOFA on day three, and better predict 6-month mortality in ICU survivors than the MELD score. The CLIF-SOFA thus appears as the prognostic score of choice for the critically ill cirrhotic patients.

Disclosure of Interest: None declared

P0035 SIX-MONTH MORTALITY OF CIRRHOTIC PATIENTS WHO SURVIVED INTENSIVE CARE: A META-ANALYSIS

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Introduction: The medium-term survival of cirrhotic patients who survived intensive care and its determinants have never been evaluated, due to the small number of ICU survivors in the published studies.

Aims & Methods: This meta-analysis evaluated the predictors of 6-month mortality in ICU survivors.

13 studies (2695 cirrhotics) were analyzed after selection of original articles and response to a standardized questionnaire by the corresponding authors. The endpoint was 6-month mortality of 412 ICU survivors (reported in 5 studies). 95 pooled analyses concerned patient characteristics, reason for admission, organ replacement therapy, and composite scores.

Results: Only 48 patients (3.4%) were transplanted during follow-up. Six-month mortality was lower in high volume centers (OR = 0.45; 95%CI: 0.30-0.67; $p<0.001$), in general ICUs (OR = 0.31; 95%CI: 0.21-0.47; $p<0.001$) in centers with TIPS (OR = 0.42; 95%CI: 0.25-0.46; $p=0.002$), but not with liver transplantation available (OR = 2.21; 95%CI: 1.21-4.04; $p=0.008$). Age, sex and alcohol-related cirrhosis had no significant impact on 6-month mortality. Unlike for in-ICU mortality, high values of SOFA did not predict 6-month mortality in ICU survivors. Eight parameters of liver and renal function were associated with 6-month mortality, including Child-Pugh C stage (OR = 2.43; 95%CI: 1.44-4.10; $p<0.001$), MELD ≥ 26 on ICU admission (OR = 3.97; 95%CI: 1.92-8.22; $p<0.0001$; PPV = 0.75), hepatorenal syndrome (OR = 4.67; 95%CI: 1.24-17.64; $p=0.022$; PPV = 0.88) and admission for acute renal failure (OR = 3.29; 95%CI: 1.70-6.40; $p<0.001$; PPV = 0.73). Septic shock (OR = 3.95; 95%CI: 1.38-11.30; $p=0.010$; PPV = 0.62) and nosocomial infection on admission (OR = 2.72; 95%CI: 1.09-6.76; $p=0.031$; PPV = 0.76) were also associated with higher 6-month mortality. Among medical interventions, only the use of norepinephrine (OR = 2.07; 95%CI: 1.07-4.00; $p=0.029$; PPV = 0.61), given for hepatorenal syndrome, was predictive of 6-month mortality.

Conclusion: Only a minority of ICU survivors undergo liver transplantation. Liver and renal failures in ICU have a sustained impact on long-term mortality. The prognostic performance of general ICU scores decreases over time, unlike Child-Pugh and MELD scores, even measured in the context of organ failure. Eligible patients could thus be listed for transplantation in ICUs or shortly after ICU discharge.

Disclosure of Interest: None declared

P0036 IMPACT OF INFLAMMATION AND INFECTION ON SHORT- AND MEDIUM-TERM MORTALITY IN CIRRHOTIC PATIENTS ADMITTED IN INTENSIVE CARE UNITS: RESULTS FROM A META-ANALYSIS

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Introduction: The impact of inflammation and infection on the outcome of cirrhotic patients admitted to Intensive Care Units (ICU) has been little studied.
Aims & Methods: This meta-analysis aimed to assess the ability of events related to inflammation or infection present on admission, to predict in-ICU mortality and to investigate whether inflammation or infection present on ICU admission was associated with 6-month mortality in ICU survivors. 13 studies (2695 cirrhotics) were analyzed after selection of original articles and response to a standardized questionnaire by the corresponding authors. The endpoint was the prognostic performance of 25 variables (including SIRS and its compounds, biochemical makers of inflammation, overt bacterial infection, germ involved, infection site) to predict short- and medium-term mortality.
Results: On admission, 57.5% of patients had ≥ 2 criteria for SIRS. Lung was the most common infected site (14.2%), followed by spontaneous bacterial peritonitis (11.4%). 12.8% of patients had positive blood culture(s). The most common bacteria were GN bacillus (GNB) (13.7%), followed by GP cocci (10.1%). Fungal infection was diagnosed in 3.9% of patients. Higher in-ICU mortality was predicted by 14 variables related to inflammation/infection, including fungal infection (OR = 3.98; 95%CI: 1.28-12.36; $p < 0.001$; PPV = 0.86), pneumonia-induced acute respiratory failure (OR = 4.48; 95%CI: 4.60-18.15; $p < 0.001$; PPV = 0.81), sepsis-related refractory oliguria (OR = 9.14; 95%CI: 4.60-18.15; $p < 0.001$; PPV = 0.79), sepsis-induced hypotension (OR = 5.74; 95% CI: 3.41-9.71; $p < 0.001$; PPV = 0.77), GNB infection (OR = 2.24; 95%CI: 1.49-3.37; $p < 0.00$; PPV = 0.70), community acquired infection (OR = 2.37; 95%CI: 1.29-4.34; $p < 0.001$;PPV = 0.68), the presence of ≥ 2 criteria for SIRS (OR = 2.44; 95%CI: 1.64-3.65; $p < 0.001$; PPV = 0.57), CRP > 29mg/dL (OR = 1.82; 95%CI: 126-2.62; $p < 0.001$; PPV = 0.57) and leucocytes < 4000/mm3 (OR = 10.29; 95%CI: 6.63-16.00; $p < 0.001$; PPV = 0.45). Most of these parameters better predicted in-ICU mortality than a MELD score ≥ 13 (OR = 4.95; 95%CI: 2.47-9.89; $p < 0.001$; PPV = 0.51), a Child Pugh stage C(OR = 3.87; 95%CI: 2.47-6.07; $p < 0.001$; PPV = 0.52), or a SOFA ≥ 7 (OR = 7.70; 95%CI: 3.01-15.17; $p < 0.001$; PPV = 0.53). Among ICU survivors, only nosocomial infection on admission (OR = 2.72; 95%CI: 1.09-6.76; $p = 0.03$; PPV = 0.76) and admission for septic shock (OR = 3.95; 95%CI: 1.38-11.29; $p = 0.01$; PPV = 0.62) were associated with higher 6-month mortality.
Conclusion: In critically ill cirrhotics, some parameters related to SIRS and infection are able to better predict short-term mortality than prognostic scores. A history of septic shock is a strong predictor of 6 month mortality, even after the control of organ failures allowing ICU discharge, and may become an indication for secondary antibioprophylaxis and/or liver transplantation. Nosocomial infection also have sustained impact on mortality.
Disclosure of Interest: None declared

P0037 ESOPHAGEAL VARICES BAND LIGATION IN THE PROPHYLAXIS OF VARICEAL HEMORRHAGE – EFFICACY AND SAFETY CONCERNS

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Introduction: Variceal hemorrhage is a severe complication of chronic liver disease with a well-known tendency to recur. Following the first episode, recurrence risk is over 60% in the following years. As such, safe and effective primary and secondary prophylactic strategies must be adopted.
Aims & Methods: All patients that underwent elective esophageal varices band ligation in 2012 and 2013 were followed for a year. Immediate, 24-hour and long term complications of these procedures were recorded. The success of this strategy was evaluated through its capacity to prevent new episodes of variceal bleeding.
Results: A total of 82 patients were submitted to 104 procedures with a 2-4 or 6-8 week interval until eradication of varices was achieved (male patients – 78%, average age – 63.8 ± 10.6 years-old; Primary prophylaxis – 73.2%, Secondary prophylaxis – 26.8%). Concomitant treatment with beta-blockers was prescribed to 43.9% of patients. Most patients were sedated by the Gastroenterologist (70.7%), while anesthetic support was adopted in 17% of the procedures. Immediate complications occurred in 10 patients (9.6%): self-limited bleeding in 6, while sclerotherapy was performed in 3 of them. In one patient, a Sengstaken-Blackmore balloon was placed to stop the hemorrhage. In the 24 hours after the procedure, no further complications occurred. In the following year, 14 patients had episodes of variceal hemorrhage (13.7%), on average about 7 months after the elective procedure. Six of them eventually died (5.8%). Variceal bleeding recurrence was less common in patients that underwent less frequent procedures (6-8 weeks).
Conclusion: Esophageal varices band ligation is an effective method to prevent both inaugural and recurrent episodes of bleeding. A larger time span between procedures is probably a safer option to prevent bleeding from scars. Its safety profile is good and the 24-hour admission for surveillance is not necessary as no further complications usually occur in that period.
Disclosure of Interest: None declared

P0038 CIRRHOTIC PATIENTS IN ICU WITH GASTRO-INTESTINAL BLEEDING MANAGED ACCORDING TO RECENT GUIDELINES DISPLAY ALTERED BRAIN HEMOGLOBIN OXYGEN'S SATURATION ASSESSED BY NEAR INFRARED SPECTROSCOPY

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Introduction: Near Infrared Spectroscopy (NIRS) is a non-invasive optical technique allowing a continuous measurement of brain's hemoglobin saturation in oxygen (rSO2). It is considered as a surrogate marker of cerebral insult, and recognized as a useful tool in in cardiovascular surgery and neuromonitoring. A rSO2 < 50% is associated with increased neurological impairment and post-operative mortality. In cirrhotic patients with gastrointestinal bleeding (GIB), hemoglobin (Hb) threshold for transfusion has been recently lowered to 7g/dL. Some patients develop hepatic encephalopathy (HE) after GIB. In subarachnoid hemorrhage, a threshold of 7g/dL of Hb could worsen neurological outcome.
Aims & Methods: The aim of this study was to assess brain oxygenation using NIRS in cirrhotic patients with acute GIB admitted to ICU and managed according to recent guidelines, and to determine if brain injury was associated with Hb levels.
Cirrhotic patients admitted in ICU for acute GIB were prospectively included. Bilateral continuous recording of rSO2 was started upon admission using a NIRS monitor (INVOS 5100c Cerebral Oxymeter (Covidien©) with two sensors placed on the patient's forehead. Minimal rSO2 (mini rSO2), average rSO2 (avr rSO2) and AUC of rSO2 50% (AUC50% rSO2), an integrated parameter depending on the depth/duration of desaturation under 50%, were extracted.
Results: 26 patients were included (median age: 60 years; 69%men). Etiology of cirrhosis was alcoholic 54%/ viral 19%/ NASH 23%/other 4%; Child Pugh A 15%/ B 20%/ C 65% and median MELD score 18. Median initial Hb was 7.9g/dL and nadir within 24 first hours was 7.8g/dL. 14 patients (54%) had a nadir of Hb below 8 g/dL within the 24 first hours, and 15 (58%) patients were transfused. Median mini rSO2 was 37% right/37% left, avr rSO2 46% right/48% left and AUC50% rSO2 1138 right/698 left. 22 patients (85%) had mini rSO2 < 50%. Mini rSO2 was significantly lower in patients having a nadir of Hb below 8g/dL. Mini rSO2, avr rSO2 and AUC50% rSO2 were independently correlated to initial Hb ($p < 0.01$ for all), nadir of Hb within the 24 first hours ($p < 0.005$ for all), and MELD score ($p < 0.05$ for all).
Conclusion: 85% of cirrhotic patients admitted to ICU for acute GIB and managed according to recent guidelines displayed mini rSO2 below 50% within 24 hours after admission. Low Hb levels within the 24 first hours were associated with brain desaturation. Further studies are mandatory to assess the influence of Hb thresholds on the development of HE.
Disclosure of Interest: None declared

P0039 CHANGES OF SERUM LEVELS OF CYTOKERATIN-18 FRAGMENTS IN PATIENTS WITH CHRONIC HEPATITIS C UNDER ANTIVIRAL THERAPY

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Introduction: Studies performed in the recent years have indicated that the cleavage level of serum CK-18 is correlated with hepatic fibrosis and disease severity in chronic hepatitis C and non-alcoholic steatohepatitis. Significant correlation between apoptosis level and responses to chronic viral hepatitis B and C treatments have shown a correlation between decreased CK18 levels during the treatment, and sustained viral response is also defined.
Aims & Methods: Our aim was to reveal the correlation between CK 18 level and treatment response in patients with chronic viral hepatitis C. 60 patients with diagnosis of chronic viral hepatitis C were enrolled to the study. Eligible patients for treatment criteria received PEG-interferon-ribavirin administration for 48 weeks. In Weeks 12-24, HCV RNA amount was measured at the end of treatment. Additionally, CK 18 levels were measured in Weeks 0-24 and at Week 72.
Results: Mean age of 60 patients was 52 ± 10.9 years. Of patients, 31 (51.6%) were in sustained viral response (SVR) group with the CK 18 level with CK 18 level of 116 ± 12.4 at the Week 24 of, whereas 29 (48.4%) were in non-SVR group with CK 18 level of 134 ± 23.5 (U/L). When the change in CK 18 levels between Week 0 (baseline value) and Weeks 24 and 72 in SVR-obtained patients and the level in the Week 24 in patients without SVR were compared, CK 18 levels in SVR-obtained patients were 243 ± 214 (U/L) in the Week 0, and 115 ± 12 (U/L) in the Week 24, thus the change was defined as 127 ± 209 (U/L), and the change was statistically significant ($P = 0.014$). While CK 18 level in the Week 0 was

270 ± 143 (U/L) in patients without SVR, it was 133 ± 19 (U/L) in the Week 24; the change was defined as 136 ± 156 (U/L). This change was statistically insignificant ($P > 0.5$).

Conclusion: There are many studies proving clinically that disease progression and fibrosis, which are related to significant decreases in cytokeratin 18 levels in the circulation in hepatocellular apoptosis, are decreased in patients who had successful HCV clearance. Similarly, significant decrease was detected in CK 18 levels in SVR-obtained patients our study. However, no significant correlation was defined in recurrent and nonresponsive patients. In conclusion, it has been shown that hepatocellular apoptosis is significantly decreased in chronic viral hepatitis C patients by successful antiviral therapy; and CK 18 is a reliable marker to indicate apoptosis of hepatocyte. When the obtained data are evaluated, CK-18 can be used in the follow up of treatment efficacy and improvement in apoptosis level as well as it can be used as a non-invasive marker instead of liver biopsy.

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P0040 NEWS TOOLS OF SCREENING VIRAL HEPATITIS IN REAL LIFE: NEW FRENCH MODEL OF CARE

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Introduction: Hepatitis B and C screening was usually done by serology in laboratories or medical centers. If serology was positive, viral load and genotype was determined and after that patient saw hepatologist if viral load was also positive. Liver fibrosis was usually measured after first medical consultation. All steps took 3 to 6 months. Drug injection was main contamination route of hepatitis C virus (HCV) in France and western Europe since 1990. Although highest European screening rate in France, 44% of patients didn't take care of hepatitis C. French guidelines were to treat all inmates and drug users, even fibrosis level.

Aims & Methods: Hepatitis Mobile team was created in July 2013. We proposed 10 services to patients and to our partners: 1/ Point of Care Testing POCT (HIV HBV HCV) 2/ Mobile liver stiffness Fibroscan* (indirect measurement of liver fibrosis) in site 3/Social screening and diagnosis 4/ Advanced on-site specialist consultation 5/ Easy access to pre-treatment commissions (''RCP'') with hepatologists, nurse, pharmacist, social worker, GP, psychiatric and/or addictologist 6/ Individual psycho-educative intervention sessions 7/ Collective educative workshops 8/ Staff training 9/ Drug users information and prevention 10/ Green thread: outside POCT and FIBROSCAN* with specific converted truck. So our French mobile mobile team proposed a new model of triple screening high risk patients for hepatitis C or B. All team members (nurses and social worker) came together in outreach centers, jailhouses, drug services centers and all structures which care for drugs users, homeless or other vulnerable patients. They offer triple screening at the same time: social screening with specific score of 11 questions called EPICES, POCT for HCV HBV (and also HIV if necessary) and liver fibrosis screening by FIBROSCAN*. With the results of triple screening, patient could do his/her biology quickly and see a hepatologist in 2 or 3 weeks only.

Results: 711 POCT were done in first 12 months; 19 were positive for new patients and 69 were positive for already known patients who returned to medical care by this pathway. One POCT was positive for HIV and 7 for HBV (but only done for 6 months); 393 FIBROSCAN* were done with medium rate of 7.8 KPa (fibrosis level F2): 68% for HCV, 3% for HBV and 29% for alcoholic liver disease. Social screening showed that 91% of our patients were vulnerable. 134 patients were addressed by on site hepatologist consultations and 112 came almost at one time. 45% of patients were treated and only 3% were lost to sight. All these patients had access to new direct antiviral agents. Follow up of treated patients showed only one relapser for 41 finished treatments.

Conclusion: In our model of care, triple screening by mobile services and follow up was necessary and successful to increase number of patients diagnosed, treated and cured.

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P0041 MEASURING QUALITY OF LIFE IN HCV-INFECTED PATIENTS TODAY: THE BURDEN OF A "LIMITED" ACCESS TO THE NEW ANTI-VIRAL DRUGS

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Introduction: The Health Related Quality of Life (HRQoL) in patients with chronic HCV infection is significantly impaired in respect to uninfected people and directly correlates with severity of hepatic dysfunction. The achievement of a sustained virological response (SVR) is associated with a significant and long-lasting improvement in the HRQoL. The recent introduction of new potent direct antiviral agents seems to promise the definitive cure for HCV infection in almost the totality of infected individuals. However, the economic burden of the therapeutic schedules significantly limits the access to therapy particularly for patients with early stage liver disease.

Aims & Methods: To evaluate the impact of the awareness of new therapy availability on HRQoL, anxiety, depression and stress in patients with early-stage of HCV-related liver disease.

A set of questionnaires was administered to consecutive patients with chronic active HCV-related diseases to evaluate the HRQoL (Short Form Health Survey, SF-36), the depression, anxiety and stress levels (Depression Anxiety Stress Scale, DASS-42) and the perception of discrimination for such a difficult therapy access (Visual Analog Scale, VAS).

Exclusion criteria were: clinical, laboratory or histological signs of liver cirrhosis, concomitant liver diseases (HBV infection, autoimmunity or alcohol abuse) or hepatocellular carcinoma, HIV coinfection, < 3 years of education, diagnosis of major depression or other psychiatric disorders, current use of antidepressant medications or other pharmaceuticals known to affect cognitive function, cerebrovascular disease.

Results: Sixty patients with active chronic HCV infection (HCV-RNA +) and 36 patients with SVR to prior treatment were enrolled. There were… male, mean age was 60.6 years (range 32-74 years).

Patients with chronic active HCV infection showed significantly lower scores than the SVR group, in the following SF-36 domains: ''Physical Functioning'' (70 ± 26.2 vs 81.6 ± 22.2; p = 0.001), ''General Health'' (45.9 ± 22 vs 63.3 ± 17.7; p < 0.0001), ''Vitality'' (55.8 ± 23.6 vs 65.8 ± 24.6; p = 0.001) and ''Role-Physical'' (69.8 ± 25.1 vs 87.4 ± 18.7; p < 0.0001).

In addition, patents with showed higher scores, compared to the SVR group, in all the three DASS-42's scales: ''Depression'' (10.5 ± 8.4 vs 6.9 ± 6.5; p = 0.03), ''Anxiety'' (10.6 ± 7.2 vs 7.2 ± 6.1; p = 0.02) and ''Stress'' (13.4 ± 7.5 vs 9.3 ± 7.5; p = 0.012).

Finally, the mean VAS score for the perception of discrimination was 7.27 ± 2.62.

Conclusion: The awareness of new effective antiviral drugs and, at the same time, the limited access to therapies significantly reduce the HRQoL and increase depression, anxiety and stress in patients with chronic active HCV infection.

Disclosure of Interest: None declared

P0042 HIGH RISK OF INFECTION DURING TRIPLE THERAPY WITH FIRST-GENERATION PROTEASE INHIBITORS: A NATIONWIDE RETROSPECTIVE COHORT STUDY

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Introduction: Peginterferon (PegIFN) remains the backbone of therapy for chronic hepatitis C (CHC) in many economically constrained regions, as all oral regimens are not globally available. However, PegIFN has a high rate of (serious) adverse events, frequently reported is neutropenia due to bone marrow suppression. Addition of a first-generation protease inhibitor (telaprevir or boceprevir) to PegIFN and ribavirin (RBV) can lead to a higher risk of neutropenia. Guidelines recommend dose reduction or treatment discontinuation in case of moderate or severe neutropenia out of concern for infections.

Aims & Methods: The aim of this study is to assess the risk of infections during first-generation protease inhibitor-based therapy in clinical practice and its relation to treatment-induced neutropenia. This nationwide multicenter retrospective cohort study included CHC patients treated with PegIFN, RBV and telaprevir or boceprevir in 37 centers in the Netherlands. Absolute neutrophil counts (ANC) were divided in 3 categories: severe (< 500/μL), moderate (500-750/μL) and mild (750-1500/μL). Likewise, infections were classified as severe (i.v. treatment with antibiotics or hospitalization), moderate (oral or topical antibiotics or antimycotics) or mild (no treatment). We assessed associations between risk factors and infectious events adjusting for multiple measurements with multivariable logistic regression analysis.

Results: We included 409 CHC patients: 233 telaprevir and 176 boceprevir treated patients. In our cohort 277 (68%) patients were male, mean age was 50.4 (range 19-77) years and 236 (58%) patients were treatment naive. Based on liver biopsy, fibroscan, ultrasound or FIB-4 index, 127 (31%) patients were classified as cirrhosis.

A total of 238 infections occurred in 156 patients (38%) and 35 (15%) were severe occurring in 29 (7.1%) patients. Mean baseline ANC was 3.421/μL and 4.4% of patients had a baseline ANC < 1500/μL. During treatment 274 patients developed neutropenia (severe, n = 28). In 40 patients ANC was

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Table: SVR and SAE in WQ vs. WNQ patients.

	Phase 3 trial	n	n WQ (%) / n WNQ (%)	SVR % WQ / WNQ	p	SAE % WQ / WNQ	p
Boceprevir	SPRINT2/RESPOND2[a]	134	68(51)/66(49)	76.5/60.6	**0.048**	7.4/18.2	0.06
	RESPOND 2[b]	42	20(48)/22(52)	45.0/40.9	0.789	10.0/27.3	0.155
Telaprevir	ILLUMINATE/ADVANCE[a]	173	107(62)/66(38)	72.9/65.2	0.28	16.8/30.3	**0.037**
	REALIZE[a]	173	112(65)/61(35)	72.3/65.6	0.355	16.1/32.8	**0.011**
	REALIZE[b]	60	31(52)/29(48)	48.4/41.4	0.586	19.4/13.8	0.563

[a]treatment naive and relapse group; [b] NR-group (nonresponders, viral breakthrough and early discontinuation)SVR = Sustained Virological Response; SAE = Serious Adverse Event; WQ = would qualify for trial; WNQ = would not qualify for trial

missing. Multivariable analysis showed that female sex (OR 1.81, 95 CI 1.30-2.51, $p < 0.001$), diabetes mellitus (OR 1.50, 95 CI 1.04-2.16, $p = 0.030$), COPD (OR 2.77, 95 CI 1.72-4.46, $p < 0.001$) and history of decompensated liver cirrhosis (OR 1.69, 95 CI 1.04-2.75, $p = 0.033$) were associated with the infection incidence. Neutropenia at the previous visit was not associated with infection (univariable analysis: OR 0.83, 95 CI 0.59-1.15, $p = 0.263$).
Conclusion: This nationwide multicenter retrospective cohort study showed that triple therapy with first generation protease inhibitors was complicated by an infection in 38% of patients. The majority of infections were mild or moderate. Female gender, diabetes mellitus, COPD and a history of decompensated liver cirrhosis were associated with an increased risk of infections during treatment, suggesting that these patients should be monitored carefully.
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P0043 COMPROMISED SAFETY OF FIRST-GENERATION PROTEASE INHIBITORS IN CHRONIC HEPATITIS C PATIENTS WHO DO NOT MEET INCLUSION CRITERIA FOR REGISTRATION TRIALS. NATIONWIDE REAL-WORLD EXPERIENCE

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Introduction: Registration of drugs in chronic hepatitis C (CHC) is supported by phase 3 trials. These randomized controlled trials preserve internal validity using strict eligibility criteria which may limit the generalizability of findings.
Aims & Methods: This study aims to compare effectiveness and safety of boceprevir and telaprevir based treatment in CHC clinical practice patients who would qualify (WQ) and would not qualify (WNQ) for phase 3 trials. We performed a nationwide multicenter retrospective cohort study of CHC genotype 1 patients treated with boceprevir or telaprevir in 37 centers in the Netherlands. We compared sustained virological response (SVR) and serious adverse events (SAE) in WQ vs. WNQ patients. Phase 3 clinical trials were identified through systematic review [1-5], eligibility criteria of original protocols were applied to clinical practice population to determine WQ and WNQ. Given comparable SVR in treatment naive (TN) and relapse patients, we combined these groups in the analysis.
Results: This study includes 409 CHC patients, 236 TN and 173 treatment experienced: 71 relapse and 102 prior nonresponders (NR), viral breakthrough or early discontinuation patients (NR-group). In total, 35% to 49% of TN and relapse patients would not qualify for one of the phase 3 trials (Table). WNQ patients treated with boceprevir have lower SVR rates ($p = 0.048$) and a trend for higher SAE rates ($p = 0.06$) than WQ patients. WNQ patients on telaprevir had similar SVR rates, but higher SAE rates than WQ patients ($p = 0.037$ and $p = 0.011$). Between 48% and 52% of NR-group patients would not qualify for trials, but there SVR and SAE rates were comparable between WQ and WNQ.
Conclusion: Patients in clinical practice are likely to not qualify for phase 3 trials and these patients are at higher risk for developing serious adverse events. Phase 3 trials should extend eligibility criteria to increase generalizability to clinical practice. Physicians should be aware that first generation protease inhibitors have worse safety profile and decreased effectiveness (boceprevir) in patients that would not qualify vs. patients that would qualify for clinical trials.

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P0044 DOES NORMAL ALT MEAN HEALTHY LIVER IN HCV INFECTION ?

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Introduction: HCV carriers with persistently normal ALT (PNALT) have usually mild and stable liver disease with favourable prognosis than patients with elevated ALT. However, several studies reported worsening of liver injury in 20-30% of subjects with PNALT and development of cirrhosis and even HCC. Aim of our study was to compare liver fibrosis stage and fibrosis progression in chronic hepatitis C (CHC) patients with ALT levels within normal limits and CHC patients with elevated ALT.
Aims & Methods: Aim of our study was to compare liver fibrosis stage and fibrosis progression in chronic hepatitis C (CHC) patients with ALT levels within normal limits and CHC patients with elevated ALT. Patients: Eighty-eight CHC patients were followed up in a five-year period. Fifty-three patients (60%) had ALT levels above our laboratory normal limit (ULN: > 50 Iu/ml), 35 patients (40%) had normal ALT. Liver fibrosis (F0-F4 stages) were assessed by measuring liver stiffness (LS) using transient elastography (Fibroscan).
Results: Female CHC patients had normal ALT more often than males (44% vs. 34%). Out of 35 CHC patients with normal ALT fifteen (49%) had no or only mild liver fibrosis (LS < 6 kPa). In the group of patients with elevated ALT, 17% had F0 or F1 liver fibrosis stage. Advanced liver fibrosis (LS > 12 kPa) was more frequent in patients with elevated ALT compared to normal ALT group (56% vs 23%). Although moderate or more severe liver fibrosis occured more frequently in patients with elevated ALT compared to normal ALT group (83% vs 51%), high proprotion of patients with normal ALT had LS suggesting moderate (> F1) fibrosis stage. In a five-year follow-up period most of the CHC patients with normal ALT had stable liver disease with no fibrosis progression.
Conclusion: Our results prove that normal ALT in CHC does not always mean "healthy liver" since a great proportion of these patients had minimal or moderate liver fibrosis and the possibility of progression to more severe condition. We do suggest that patients with normal ALT should not be excluded a priori from antiviral treatment. Decision on antiviral treatment should depend on multiple factors (e.g. histology, LS, symptoms, co-morbidities) as well as the motivation and the age of the patient, rather than on ALT level alone.
Disclosure of Interest: None declared

P0045 IS OLDER AGE A RISK FACTOR FOR HEPATOCELLULAR CARCINOMA DEVELOPMENT IN PATIENTS WITH CHRONIC HEPATITIS C EVEN IF SUSTAINED VIRUS ERADICATION IS REACHED?

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Introduction: Hepatitis C virus (HCV) is one of the major leading causes of hepatocellular carcinoma (HCC) in Turkey. We aimed to clarify the clinical features of patients with chronic hepatitis C who develop HCC after gaining sustained viral response (SVR) to interferon (IFN)-based treatment.
Aims & Methods: Clinical parameters of 212 patients (mean age: 54 years old, E/K: 132/80) who achieved a SVR from 2002 to 2014 in two reference center hospital were evaluated.
Results: Eighteen patients (8.49%) developed HCC within a median follow-up period of 74 months (range 18–132 months). Cox regression analysis showed that the strongest predictive factor of HCC occurrence was lower platelet ($< 10x10^4$ cells/microL) count (hazard ratio [HR] 5.42, $P = 0.032$) followed by prolonged (< 80%) prothrombin time (HR 3.68, $P = 0.041$) and higher AST (> 50 IU/L) level, (HR 3.18, $P = 0.048$), before IFN therapy. At the time of SVR24, the predictive factors of HCC occurrence were higher AFP (> 10 ng/ml) level (HR 4.33, $P = 0.028$) and older (> 65 years) age (HR 4.40, $P = 0.032$). In multivariate analysis showed that higher AFP (> 10 ng/ml) level and older (> 65 years) age at SVR24 were independent variables of the development of HCC, too.

Conclusion: Patients of older (>65 years old) age at SVR24 should be considered very carefully to detect early HCC development after IFN therapy, especially who have higher AFP level, even if SVR is reached. In patients with chronic HCV, viral eradication of HCV infection should be achieved at a young age as possible to prevent HCC development after IFN based therapy.
Disclosure of Interest: None declared

P0046 FEASIBILITY AND REPRODUCIBILITY OF LIVER STIFFNESS (LSM) BY ELASTPQ POINT SHEAR-WAVE ELASTOGRAPHY

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Introduction: Liver stiffness measurement (LSM) by transient elastography (TE) accurately predicts severity of chronic liver disease (CLD). (1-2) Point quantification shear-wave elastography (pSWE-ElastPQ) is a newly developed technique incorporated into a conventional US system which allows evaluation of LSM.
Aims & Methods: Aim of this study was to assess the feasibility and reproducibility of PSWE-ElastPQ in a consecutive series of patients with CLD who concomitantly underwent TE and liver biopsy. Over a sixteen-months period, 164 patients (103 males, 61 females) (mean age 54 yrs) were consecutively enrolled. CLD was related to HCV (n = 113) and miscellaneous causes (n = 51). pSWE- ElatPQ was blindly performed by two raters whereas TE was performed by one single operator. pSWE-ElastPQ examinations were considered reliable if >10 validated measurements were obtained from each patient with SD <30% of the mean value. TE examinations were considered reliable if >10 validated measurements were obtained from each patient with a success rate >60% and if the interquatile range (IQR) was <30% of the median value. Interobserver agreement for pSWE-ElastPQ was analyzed using the intraclass correlation coefficient (ICC), that was interpreted according to Fleiss classification: agreement was considered poor (ICC = 0.00-0.40), fair to good (ICC = 0.40-0.75) or excellent (ICC < 0.75). Stage of liver fibrosis was classified according to METAVIR score classification.
Results: Reliable LSM (n = 328)determinations were obtained in 100% of the cases by pSWE-ElastPQ and in 97% by TE (n = 5 with SR <60%, IQR > 30%). pSWE-ElastPQ and TE values correlated significantly (r = 0.68, p = 0.0001). LSM values (mean ± SD, median) measured by pSWE-ElastPQ resulted 7.9 ± 4.4, 6.6 kPa for the first rater and 7.7 ± 4.0, 6.6 kPa for the second one. ICC concordance was not influenced by age, BMI, ALT, alkaline phosfatase and GGT levels. ICC in the first 5-months study period was significantly lower (0.69, 95% CI 0.50-0.81) as compared to the second period (0.78, 95% CI 0.64-0.87) and the third one (0.89, 95% CI 0.80-0.95).
Conclusion: pSWE-ElastPQ is a reliable and reproducible technique, whose interobserver agreement significantly improves by experience. Moreover it is not affected by BMI or presence of liver necroinflammation.

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Disclosure of Interest: None declared

P0047 POINT SHEAR WAVE ELASTOGRAPHY (ELAST-PQ) FOR SPLEEN STIFFNESS (SSM) DETERMINATION IS FEASIBLE AND REPRODUCIBLE IN MOST OF THE PATIENTS WITH CHRONIC LIVER DISEASE

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Introduction: Spleen stiffness measurement (SSM) using transient elastography (TE) has widely been demonstrated to predict liver disease severity and progression of chronic liver disease (CLD) [1 - 3]. Its reliability and accurately predicts portal hypertension, oesophageal varices and such clinically relevant outcomes as decompensation [4]. Point quantification shear-wave elastography (pSWE-ElastPQ) is a newly developed technique to measure SSM incorporated into a conventional US system.
Aims & Methods: To assess feasibility and reproducibility of SSM by pSWE-ElastPQ in a consecutive series of patients with CLD who concomitantly underwent spleen TE and liver biopsy.
Over a 16-month period 160 patients were consecutively enrolled. Three were excluded due to previously splenectomy, thus 157 patients (99 males and 58 females; median age 55 years) were analysed.
CLD was HCV related in 109 and miscellaneous in 51. pSWE-ElastPQ was blindly performed by two different raters whereas TE was performed by a single operator. Both pSWE-ElastPQ and TE examinations were considered reliable if >10 validated measurements were obtained from each patient. SD of all measurement was < 30% of the mean value for pSWE-ElastPQ, whereas a success rate >60% and an interquartile range (IQR) of all validated measurements <30% of the median value were considered for TE.
Interobserver agreement for pSWE-ElastPQ was analyzed using the intraclass correlation coefficient (ICC), according to Fleiss classification: was considered poor (ICC = 0.00-0.40), fair to good (ICC = 0.40-0.75) or excellent (ICC > 0.75).
Results: Reliable SSM determinations were more frequently obtained by pSWE-ElastPQ (155 cases; 96%) than by TE (141, 87%) (p = 0.007) . pSWE-ElastPQ and TE SSM values correlated significantly (r = 0.54 , p = 0.0001). SSM values (mean ± SD, median) measured by pSWE-ElastPQ resulted 17.8 ± 8.6, 15.7 kPa for the first rater and 17.6 ± 8.3, 15.6 kPa for the second one. Overall, interobserver ICC for pSWE-ElastPQ was 0.72, 95% (CI 0.64-0.79). Concordance was not influenced by patient's age, sex and BMI. The ICC in the first 10-months study period was significantly lower (0.69, 95% CI 0.58-0.79) as compared to the second 6 months (0.86, 95%CI 0.75-0.93)
Conclusion: pSWE-ElastPQ is a reliable and reproducible technique to assess spleen stiffness in CLD, whose interobserver agreement significantly improves by experience. Noteworthy, pSWE-ElastPQ is feasible in more patients than TE.

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Disclosure of Interest: None declared

P0048 ULTRASOUND DIAGNOSTICS SIMULATORS FOR GASTROENTEROLOGISTS: IMPLEMENTATION EXPERIENCE

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Introduction: Nowadays various types of hospitals and clinics require professional specialists in ultrasound diagnostic not only among radiologists, but also among clinicians to ensure fast and correct diagnosis for adequate treatment prescribing. Unfortunately there is no opportunity for all specialists to have education by the standard scheme ''mentor-specialist in training-patient'' because of limited time, so there is a necessarity to put inexpensive and available for clinicians ultrasound simulators into training-practice.
Aims & Methods: The aim was to create the experimental model of Doppler ultrasound simulation system which will be able to imitate arterial and venous blood flow and focal lesions of parenchymal organs with various type of vascularization for the gastroenterologists ultrasound education.
Material and methods: Vascular phantom was created in our Problem scientific research Laboratory ''Diagnostic researches and miniinvasive technologies'' in 2014. It represents tube system and consists of two parts. The 1st part is vascular - with imitative characteristics of arterial and venous blood flow (with the opportunity of laminar and turbulent flow recreation, using semi-automatic dispenser). The 2nd part is ''pathological foci'', it represents hemodynamics of capillary and cavernous hemangioma, focal nodular hyperplasia and hyper-vascular liver metastases. There were 2 groups of 6-year medical students of Smolensk State Medical University with 20 in each group for the Phantom's efficiency testing. Educational process in the 1st group was by the standard scheme ''mentor-student-patient'' (3 times). Educational process in the 2nd group consisted of 2 stages: at the 1st stage all of the students had practice with the ultrasound simulator and at the 2nd stage there was standard scheme ''mentor-student-patient'' (3 times).
Results: After 3-weeks of training all of the students were tested in real work with patients with arterial blood flow pathology (aneurysm, n = 4), venous blood flow pathology (cavernous portal vein transformation at cirrhosis n = 8, capillary and cavernous hemangioma, n = 13, focal nodular liver hyperplasia n = 2, colorectal liver metastases, n = 4). In the 1st group true-positive results amounted 58.1%, false-positive results - 24.4%, false-negative results - 17.5%. In the 2nd group true-positive results amounted 79.3%, false-positive results - 13.9%, false-negative results - 6.8%.
Conclusion: Phantom's use at the 1st stage of gastroenterologists education in ultrasound technique qualitatively improved the efficiency of medical specialists' work, so it requires overall introduction of simulator-training in courses of postgraduate professional education.
Disclosure of Interest: None declared

P0049 GASTROINTESTINAL NEUROENDOCRINE TUMORS OF UNKNOWN PRIMARY SITE: REPORT FROM A SERIES AT A SINGLE INSTITUTE

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Introduction: Neuroendocrine neoplasms (NENs), a heterogeneous group of neoplasms, differ in biologic behavior, histologic appearance and response to treatment. NENs with unknown primary site (NENs-UP) account for 10 to 13 percent of all NENs.
Aims & Methods: We here describe clinical findings, histologic and anatomic characteristics and the diagnostic work-up of patients with histologically proven metastatic NENs of unknown primary.
Between January 2005 to January 2015, of the 93 patients with metastatic gastrointestinal NENs seen at our Institution, 17 (18%) (M:F = 11:6; median age at the diagnosis 64 years, range 33-74) presented with immunohistochemically proven neuroendocrine metastases without evidence of primary site despite an exhaustive work-up based on computed tomography (CT), magnetic resonance (MRI) and somatostatin receptor scintigraphy (SRS).
Results: Of the 17 patients with NENs-UP, 14 (82%) showed hepatic metastases, whereas an abdominal nodal involvement was detected in the other three patients. Sixteen of the 17 tumors (88%) were well differentiated (G1 in five cases and G2 in 11), with a poorly differentiated carcinoma in the last patient. Carcinoid, Zollinger-Ellison and Verner-Morrison syndromes were diagnosed in eight, two and one case, respectively, accounting for a total number of 11 functioning tumors (65%). In 14 of the 17 cases (82%), liver or nodal metastases were firstly diagnosed by abdominal ultrasound, performed during surveillance of chronic diseases in six patients and for gastrointestinal symptoms in the other eight. In the course of a strict work-up, the primary tumor was eventually diagnosed after a median of 8.5 months (range 3-120) in 12 cases (71%), eight of whom (67%) had a functioning form. In detail, the primary site was identified as pancreas by a repeated abdominal CT (#3); terminal ileum (#2) and colon (#1) by colonoscopy; central ileum by double balloon enteroscopy (#1) and pancreas by endoscopic ultrasound (EUS) (#1). Again, laparoscopy identified a jejunal, ileal, Meckel's diverticulum and pancreatic primary tumor in further four patients, whereas the remaining five were still classified as NENs-UP.
Conclusion: NENs-UP represent a clinical challenge, involving multidisciplinary expertise. Despite the continuous advances in diagnostic techniques, including radiologic, endoscopic and immunohistochemical methods, metastatic NENs remain of unknown primary origin in a notable proportion of cases (5/93, 5.3% in present series), even after an in-depth work-up. Noteworthy, however, the presence of hormone-related symptoms may help to better localize the primary site.

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P0050 COMPARATIVE STUDY BETWEEN FOUR ULTRASOUND SHEAR WAVE ELASTOGRAPHIC METHODS FOR LIVER STIFFNESS ASSESSMENT

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Introduction: Many different types of ultrasound based elastographic methods have been developed for the non-invasive liver stiffness assessment.
Aims & Methods: The aim of this study was to compare the performances of the latest elastographic methods used for liver fibrosis evaluation (Point Shear Wave Elastography-PSWE using ARFI technique-VTIQ and ElastPQ, respectively; and SuperSonic Shear Imaging-2D-SWE) considering Transient Elastography (TE) the reference method, since TE is a validated method for liver fibrosis evaluation.
The study included 151 consecutive subjects with or without chronic hepatopathies (excluding patients with ascites), in which liver stiffness (LS) was evaluated in the same session by means of 4 elastographic methods: TE (FibroScan, Echosens), VTIQ (Siemens Acuson S2000™), ElastPq (Philips, Affinity) and 2D-SWE (Aixplorer™SuperSonic Imagine S.A). Reliable LS measurements were defined as follows: for TE and VTIQ–the median value of 10 LS measurements with a success rate $\geq$ 60% and an interquartile range $<$ 30%, for 2D-SWE–the median value of 3 LS measurements acquired in an homogenous area and for ElastPQ-the median value of 10 LS measurements.
LS was expressed in kPa for TE, 2D-SWE, ElastPQ and m/s for VTIQ . For differentiating between stages of liver fibrosis we used the following cut-off values: for TE-significant fibrosis (F $\geq$ 2)–7.2 kPa and for liver cirrhosis (F4)-14.5kPa (Tsochatzis, 2011); for VTIQ: F $\geq$ 2–1.35m/s, F4 = 1.84m/s (Nierhoff, 2013); for 2D-SWE F $\geq$ 2–7.1 kPa, and F4 = 13.5 kPa (HCV,NAFLD) and 11.5 kPa in HBV (Herrmann, 2015); and for ElastPQ F $\geq$ 2-5.9 kPa, F4 = 12kPa (Ferraioli, 2013).
Results: Considering TE as the reference method, the diagnostic accuracy of VTIQ, 2D-SWE and ElastPQ for the diagnose of absence or mild fibrosis (F $<$ 2) was similar: VTIQ vs. 2D-SWE (86.2% vs. 82.5% p = 0.57); VTIQ vs. ElastPQ (86.2% vs. 84.4% p = 0.85), 2D-SWE vs. ElastPQ (82.5% vs. 84.4% p = 0.84).
For significant fibrosis (F $\geq$ 2) the values obtained were: VTIQ vs. 2D-SWE (84% vs. 76.1% p = 0.19); VTIQ vs. ElastPq (84% vs. 80.7% p = 0.64), 2D-SWE vs. ElastPq (76.1% vs. 80.7% p = 0.50).
For diagnosing cirrhosis we obtained similar diagnostic accuracies: VTIQ vs. 2D-SWE (96.3% vs. 93.6% p = 0.54); VTIQ vs. ElastPQ (96.3% vs. 94.5% p = 0.75), 2D-SWE vs. ElastPQ (93.6% vs. 94.5% p = 0.99).
Conclusion: Considering TE as the reference method for liver fibrosis evaluation, VTIQ, ElastPQ and 2D-SWE had similar accuracies for diagnosing at least significant fibrosis (F $\geq$ 2) and liver cirrhosis.

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Disclosure of Interest: None declared

P0051 FEASIBILITY OF FOUR ULTRASOUND SHEAR WAVE ELASTOGRAPHIC METHODS FOR LIVER STIFFNESS ASSESSMENT

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Introduction: In the last decade , different types of ultrasound-based elastographic methods that non-invasively quantify liver fibrosis, have been developed. Even though Transient Elastography is a validated method for liver fibrosis assessment in chronic B and C hepatitis, being included in EASL Guidelines, reliable elasticity measurements are difficult to obtain in obese (BMI $>$ 30kg/m^2) patients.
Aims & Methods: The aim of this study was to compare the feasibility of four elastographic methods used for liver fibrosis evaluation (Transient Elastography-TE, Point Shear Wave Elastography (PSWE) using ARFI technique -VTIQ and ElastPQ and SuperSonic Shear Imaging-2D-SWE).
The study included 151 consecutive subjects with or without chronic hepatopathies (excluding patients with ascites), in which liver stiffness (LS) was evaluated in the same session by means of 4 elastographic methods: TE (Fibroscan, Echosens), VTIQ (Siemens Acuson S2000™), ElastPQ (Philips, Affinity) and 2D-SWE (Aixplorer, SuperSonic Imagine S.A). Reliable LS measurements were defined as follows: for TE and VTIQ[1] – the median value of 10 LS measurements with a success rate $\geq$ 60% and an interquartile range $<$ 30%, for 2D-SWE[2] – the median value of 3 LS measurements acquired in an homogenous area and for ElastPQ- the median value of 10 LS measurements. For TE M and XL probes are used. LS was expressed in kPa for TE, 2D-SWE, ElastPQ and m/s for VTIQ. All elastographic measurements were performed by experienced operators.
Results: Reliable LS measurements were obtained in a significantly higher proportion of patients by means of ElastPQ as compared with TE, 2D-SWE and VTIQ: 99.3% vs. 87.4% (p $<$ 0.0001), 99.3% vs. 87.4% (p $<$ 0.0001) and 99.3% vs. 92.7% (p = 0.08). TE and 2D-SWE had similar rates of reliable LS measurements 87.4% vs. 87.4% (p = 0.86).
Reliable LS measurements by all four shear waves ultrasound elastographic methods were obtained in 72.2% (109/151 subjects).
Comment: No study concerning the usefulness of technical quality criteria for ElastPQ was published.
Conclusion: ElastPq elastography was the most feasible shear-waves elastographic method for liver fibrosis assessment, followed by VTIQ, while TE and SSI had similar rates of reliable LS measurements.

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Disclosure of Interest: None declared

P0052 INTERSTITIAL CAJAL-LIKE CELLS/TELOCYTES AND GALLBLADDER AUTONOMIC NERVOUS SYSTEM INTERPLAY IN THE PATHOGENESIS OF CHOLELITHIASIS

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Introduction: The major mechanisms of gallstone formation include biliary cholesterol hypersecretion, supersaturation and crystallization, mucus hypersecretion, gel formation and bile stasis. Gallbladder hypomotility seems to be a key event that triggers the precipitation of cholesterol microcrystals from supersaturated lithogenic bile. Recently, we reported a significant decrease in interstitial Cajal-like cell (ICLC) density in gallbladders of patients with cholelithiasis. Such cells in the gallbladder were strongly influenced by lithogenic bile. ICLCs, as well as the autonomic neurons located within gallbladder muscularis propria are considered as predominant regulatory cells of gallbladder motility.

Aims & Methods: The purpose of the current study was to determine the influence of lithogenic bile on the gallbladder autonomic neurons, in relationship to ICLCs. Gallbladder specimens were collected from 20 patients (8 males and 12 females) who underwent elective laparoscopic cholecystectomy for symptomatic gallstone disease. The control gallstone-free group consisted of 20 consecutive patients (9 males and 11 females) who received elective treatment for pancreatic head tumors. ICLCs were visualized in paraffin sections of gallbladders with double immunofluorescence using primary antibodies against c-Kit (anti-CD117) and anti-mast cell tryptase. The telocytes were stained with anti-CD34 antibody and assessed simultaneously. Autonomic neurons within the gallbladder wall were visualized by immunohistochemistry using anti-PGP9.5, anti-ChAT and anti-NOS antibodies and assessed semi-quantitatively. Cholesterol, phospholipid and bile acid concentrations were measured in bile samples obtained by needle aspiration from the gallbladder during surgery.

Results: The number of ICLCs in the gallbladder wall was significantly lower in the study group than in the control group (3.2 ± 1.5 vs. 6.6 ± 1.8 cell/area of view in the muscularis propria, $P < 0.001$) and correlated with a significant increase in the cholesterol saturation index, so did the telocytes count. The glycocholic and taurocholic acid levels were significantly elevated in the control subjects compared with the study group. Numerous PGP9.5-positive neural fibers were present, including some neuron bodies. Only sparse cholinergic (ChAT-positive) as well as nitrergic (NOS-positive) neurons were found. The cumulative neurons count was slightly decreased in patients with gallstones.

Conclusion: These results suggest that bile composition plays an important role in the reduction of ICLC and autonomic neurons density in the gallbladder, and this might lead to the gallbladder dysmotility in patients with cholelithiasis.

Disclosure of Interest: None declared

P0053 SCORING SYSTEM IN ALGORITHM FOR DIAGNOSIS AND TREATMENT OF PATIENTS WITH A SPHINCTER OF ODDI DYSFUNCTION

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Introduction: It is difficult to exclude organic pathology, to choose a proper sequence for examination and treatment of patients with a suspected sphincter of Oddi dysfunction (SOD).

Aims & Methods: To develop diagnostic and medical algorithm for patients with a suspected SOD on the basis of integral estimation of clinical, laboratory and instrumental studies. Multifactor analysis performed in 164 patients after cholecystectomy permitted to single out and express in scores the most significant estimation signs. Typical hepatic colic scored 3; arrested colic – 2 scores, uncertain pains in the right hypochondrium – 1 score; jaundice – 2 scores, jaundice in anamnesis – 1 score; moderate rise in transferases – 1 score; 2-4 fold rise – 2 scores, more than four-fold rise – 3 scores; increase in total bilirubin: up to 40 mcmol/l – 1 score, 40-100 mcmol/l – 2 scores, more than 100 mcmol/l – 3 scores; elevation in serum α-amilase by 1.5-2 times – 1 score; increase in alkaline phosphatase – 1 score; increase in total blood leukocyte number: 9-12 thousand – 1 score, more than 12 thousand – 2 scores; the common bile duct dilatation by TUS data: from 7-12 mm – 1 score, from 13-22 mm – 2 scores, more than 22 mm – 3 scores. Peculiarities of bile outflow were estimated by the results of hepatobiliary scintigraphy (HBSG). In case of doubtful diagnosis, computed tomography, magnetic resonance cholangiopancreatography and/or retrograde cholangiopancreatography were used.

Results: By the developed scoring system, patients were divided into 4 groups. Accordance of this gradation to III Roman classification for patients with SOD was established. In group 1, 60 patients had 4 and more scores (5.1 ± 1.8). HBSG was performed only in 5 (8.3%) patients and bile outflow was delayed in all cases. Later on, choledocholithiasis (CL) was detected in 32 patients, Oddi's sphincter stenosis – 28. All patients underwent surgery. In group 2, in 31 patients the sum of scores varied from 3 to 4 (3.1 ± 0.3) and was lower than in group 1 ($p < 0.05$). 21 patients experienced HBSG, in most cases bile outflow was normal and only in 2 patients bile flow was delayed. Further, CL was diagnosed in 3 patients, Oddi's sphincter stenosis – 2. They underwent papillotomy (PT) with lithoextraction (LE). Group 3 enclosed 63 patients with the sum of scores varying from 1 to 2 (1.5 ± 0.5). In all the cases with HBSG accelerated bile outflow, considered by us as Oddi's sphincter insufficiency, was stated. However, 2 patients were diagnosed CL that became an indication for PT and LE. Group 4 included 10 patients with increase in serum α-amilase. The sum of scores varied from 1 to 3 (2.5 ± 0.5). In all cases with HBSG accelerated bile outflow, as in group 3, was noted. No operative interventions were required in this group.

Conclusion: The developed algorithm for patients with suspected SOD facilitates determination of the sequence of studies and the choice of management. A four-score excess by the estimation sign scale can serve as a reason for invasive studies and surgery. Use of HBSG permits to assess noninvasively the status of bile outflow that is not impaired in most cases but even accelerated. Oddi's sphincter insufficiency can be an independent type of functional disorders which should be taken into consideration when choosing management tactic.

Disclosure of Interest: None declared

P0054 RIP3 KINASE CONTRIBUTES TO NECROINFLAMMATION IN THE CHOLESTATIC LIVER

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Introduction: Cholestasis is associated with liver inflammation and hepatocyte damage, through incompletely understood pathophysiological processes. The kinase activity of receptor interacting protein 3 (RIP3) plays an important role in necroptosis, a novel immunogenic cell death type that may contribute to inflammation-driven liver diseases.

Aims & Methods: Here we aimed to evaluate the role of necroptosis after common bile duct ligation (BDL) in mice, a classic experimental model for acute cholestasis and secondary biliary fibrosis, and in patients with primary biliary cirrhosis (PBC), a cholestatic chronic liver disease.

BDL or sham surgery was performed in C57BL/6 wild-type (WT) or RIP3 knockout (KO) mice. Serum and livers were collected 3 and 14 days after BDL. Histology, serum liver enzymes and bilirubin were evaluated. Liver RIP3, proinflammatory cytokines and fibrosis markers were determined by qRT-PCR. Total and soluble/insoluble liver proteins were analysed by Western blot. RIP3 kinase activity was determined *in vitro*. The functional crosstalk between RIP3 and antioxidant responses was investigated. Finally, RIP3 and phosphorylated mixed lineage kinase domain-like protein (p-MLKL) were evaluated by immunohistochemistry in liver specimens of patients with PBC and healthy controls.

Results: In WT mouse livers, BDL resulted in bile duct hyperplasia, multifocal necrosis, fibrosis and inflammatory cell infiltration. Concomitantly, necroptosis was activated as assessed by: 1) sequestration of RIP3 and its target MLKL in the insoluble protein fraction of the liver; 2) increased RIP3 kinase activity; and 3) increased RIP3 mRNA and protein expression (at least, $p < 0.05$). Remarkably, histological analysis revealed that RIP3 deficiency significantly decreased liver necrosis and inflammation induced by BDL at both 3 and 14 days ($p < 0.05$). At day 3, but not at day 14, BDL RIP3 KO mice showed lower circulating levels of hepatic enzymes, decreased inflammatory and fibrogenic liver gene expression, and enhanced antioxidant responses (at least, $p < 0.05$). Finally, RIP3 and p-MLKL expression was induced in PBC patients ($p < 0.05$).

Conclusion: In conclusion, RIP3-dependent signaling is triggered in human PBC and mediates hepatic necroinflammation in BDL-induced acute cholestasis. As such, targeting RIP3-dependent pathways may provide an unprecedented opportunity to develop novel therapeutic strategies to ameliorate cholestatic liver injury, although complementary approaches may be required to control progression to fibrosis.

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P0055 THE SHORT- AND LONG-TERM OUTCOMES OF SUBTOTAL CHOLECYSTECTOMY: A REVIEW OF 190 PROCEDURES

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Introduction: Complicated cholecystolithiasis occurs in about a third of all patients with gallstones and is frequently associated with a difficult cholecystectomy with unclear anatomy. Several techniques to safely remove the gallbladder in these patients exist, including a subtotal cholecystectomy (SC).

SC is reported to be safe and feasible, but an increase in bile leaks and retained gallstones have also been described.

The objective of this study was to assess the short- and long-term outcomes following SC.

Aims & Methods: A retrospective review of all patients who received cholecystectomy in 3 hospitals (from January 2003 to October 2013) in the Netherlands was performed. Patients who underwent SC were identified based on operative reports. Patient characteristics, operative details and the short and long term outcomes were recorded from patients files.

Short-term outcome was defined as the occurrence of bile duct injuries, intra-abdominal abcesses, biloma's, woundinfections and the rate of readmittance and reinterventions. The completion of the cholecystectomy and the occurrence of bile duct strictures were considered long-term outcomes.

Results: A total of 5155 operative records were screened, of which 190 were SC (3.7%). A third of patients (n = 56, 30%) had SC for symptomatic uncomplicated cholelithiasis. The remaining patients were diagnosed with complicated cholelithiasis, of whom 72 patients (38%) had acute cholecystitis. Short-term total morbidity was 34.2% (n = 65). A total of 25 patients (13.2%) were diagnosed with a bile duct injury, of which 24 patients solely had a leakage of the cystic duct. In only one patient an injury to the common bile duct (0.5%) was seen. An ERC was necessary in 41 patients, mostly due to persistent bile leakage (9.5%) or common bile duct stones (11.1%). In the long-term a bile structure was seen in only 1 patient (0.5%) and 20 patients (10.5%) underwent a completion of the cholecystectomy with an associated morbidity of 30%.
Conclusion: Subtotal cholecystectomy is an effective strategy to circumvent severe bile duct injury and bile strictures, but the risk is transferred to cystic duct leakage in 1 out of 10 patient and associated postoperative morbidity.
Disclosure of Interest: None declared

P0056 THE COMPARISONS BETWEEN GENERAL ENDOTRACHEAL ANESTHESIA, AND NON-ANESTHESIA IN RETROGRADE EDOSCOPIC COMMON BILE DUCT STONE REMOVAL IN THE REAL WORLD

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Introduction: In Asia, as well as in some European countries , South America, and the Middle East , conscious sedation is not used routinely for therapeutic endoscopic retrograde cholangiopancreatography (ERCP). However, conscious sedation may easily progress to anesthesia once verbal contact has been lost. Therefore, general anesthesia sedation is conducted for ERCP in our institution, but not moderate conscious sedation anesthesia.
Aims & Methods: We carried out a retrospective evaluation to analyze common bile duct stone extraction in ERCPs under non-sedation and general anesthesia, to determine the safety, successful rate, and complications in these two groups. In retrospectively reviewed study, all ERCPs with stone extraction under general anesthesia or non sedation from Jan, 2010 to Sep. 2013. The participants were aged 18 years and above. Criteria for exclusion: procedure failed due to anatomy change after operation, pyloric ring stenosis, and tumor related obstruction. Non sedation (NS) group: pethidine 40-50mg for pain control 10 minutes before papilloplastic balloon dilatation. General anesthesia (GET) group: general endotracheal anesthesia before ERCP. The definition of primary outcomes: success of stone removal (complete bile duct stone clearance), major complications (post ERCP pancreatitis (PEP) (amylase > 3times of upper limit level), perforation, bleeding, pneumonia in 30 days and mortality in 30 days). The operation time in ERCP was defined as cannulation starting time to complete stone removal.
Results: There are consecutive 166 patients enrolled. Eleven cases are excluded, 2 cases post whipple procedure, 2 case post Billroth II subtotal gastrectomy, 4 cases with stenting to stone obstruction, no attempt to remove. 2 cases with pyloric ring stenosis, one case failed to find papilla. There are 77 patients with NS method and 78 with GET for attempt to bile duct stone removal. Age, sex, personal habitats (alcohol, smoking), American Society of Anesthesiologists (ASA) score, previous ERCP experience, and comorbidities were similar in these two groups. Nine patients (11.5%) in NS group could not complete the procedure due to intolerance. Successful rate of complete stone extraction was higher in the GET (93.6%) versus in the NS (77.9%) group; p = 0.005. The rate of post-ERCP pancreatitis (PEP) was higher in NS group versus the GET group (20.8% versus 10.3%; p = 0.004). The operation time was shorter in NS group versus GET group(23.1 ± 10.1 versus 28.3 ± 13.7, p = 0.023). The complication rate was similar between NS and GET groups (no bleeding case; perforation: 1.3% versus 0%, p = 0.313; pneumonia: 2.6% versus 3.8%, p = 0.660; mortality: 1.3% versus 1.3%, p = 0.993). In multivariate analysis for the clinical factors influencing PEP, sedation group is a negative facotr for PEP (*coefficient of variation:* -1.23 ± 0.55, 95% C.I. 0.29(0.10~0.86), p = 0.026), and operation time (≥*30mins*) (*coefficient of variation:* 1.43 ± 0.57, 95% C.I. 4.20(1.36~12.97), p = 0.013)is a positive predisposing factor.
Conclusion: We conclude that ERCP under GET is safe and effective for common bile stone removal, with lower PEP rate than non-sedation patients.

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P0057 RECURRENCE OF CHOLEDOCHOLITHIASIS FOLLOWING ENDOSCOPIC BILE DUCT CLEARANCE: LONG-TERM RESULTS AND FACTORS ASSOCIATED WITH RECURRENT BILE DUCT STONES

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Introduction: Recurrence of bile duct stones is a possibility following endoscopic extraction.
Aims & Methods: The aim of our study was to evaluate the rate of recurrence of symptomatic choledocholithiasis and to identify factors associated with the recurrence of bile duct stones in patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) for bile duct stone disease.
Patients who underwent ERCP and ES for bile duct stone disease and had their bile duct cleared from 1/1/2005 until 31/12/2008 were enrolled. All symptomatic recurrences during the study period (until 31/12/2014) were recorded. Clinical and laboratory data potentially associated with common bile duct (CBD) stone recurrence were retrospectively retrieved from patients' files.
Results: A total of 495 patients were included. Sixty seven (67) out of 495 patients (13.5%) presented with recurrent symptomatic choledocholithiasis after 39.2 ± 25.6 months (13-168 months) while twenty one (21) of these patients (31%) experienced a second recurrence after 9 – 78 months.
Factors associated with recurrence were the size (diameter) of the largest CBD stone found at first presentation (10.2± 6.9 mm vs 7.2± 4.1 mm p = 0.024) and the diameter of the CBD at the first examination (15.5 ± 6.3 mm vs 12.0 ± 4.6 mm p = 0.005). Number of stones at first presentation (3.9 ±4.3 vs 3.5 ±2.3), age or sex of the patient did not influence recurrence. Moreover oblique CBD angulation (calculated by measuring the angle enclosed between the horizontal portion of the CBD and the horizontal plane) was significantly associated with stone recurrence (43.4 ± 10 vs 50.5 ± 15 p = 0.016).
Conclusion: Bile duct stone recurrence is a likely late complication following endoscopic stone extraction and CBD clearance. It appears to be associated with anatomical parameters (CBD diameter, angulation) and stone characteristics (stone size) at first presentation.

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P0058 LIMITED PRECUT SPHINCTEROTOMY COMBINE ENDOSCOPIC PAPILLARY BALLOON DILATION TO TREAT DIFFICULT BILIARY CANNULATION WITH COMMON BILE DUCT STONES

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Introduction: Difficult biliary cannulation in endoscopic retrograde cholangiopancreatography (ERCP) causes the failure of common bile duct stones removal. Difficult biliary cannulation can also cause more post-ERCP complications (acute pancreatitis, biliary tract infection (BTI) and bleeding).
Aims & Methods: To evaluate the outcome and complications of limited precut sphincterotomy combined with endoscopic papillary balloon dilation (EPBD) to treat difficult biliary cannulation with common bile duct stones retrospectively. From Oct 2009 to Sep 2014 in CGMH, total 3305 patients received ERCP examination and treatment. Of all, 258 (7.8%) patients belonged to difficult biliary cannulation and 145 patients were difficult biliary cannulation with common bile duct stones. We performed limited precut sphincterotomy combined EPBD in 58 patients (M:28, F:30; age 64.02 ± 16.37 yr (26-96). The definition of difficult biliary cannulation in our study was: (1)10 min time limits for cannulation or (2) 5 passage or injection into pancreatic duct or (3) 10 attempts on the papilla without time limit. Limited sphincterotomy means the extent of needle knife cutting < 1/2 length of the papillary mound, then combined CRE balloon dilation (8-20 mm) with dilation time 2 minutes.
Results: Overall successful common bile duct (CBD) stones removal was 94.8% (55/58) and 1st session success was 87.9% (51/58). Mean procedure time was 41 ± 11.48 (20-72) min. Mean CBD size was 1.47 ± 0.44 (0.7-2.6) cm and mean stone size was 1.11 ± 0.40 (0.4-2.0) cm. CBD stone number with 1:2: ≥3 was 28:14:16. Need of mechanical lithotripsy (ML) was 10.3% (6/58). Post-treated complications were bleeding 3.4% (2/58), pancreatitis 8.6% (5/58) and BTI 2.7% (1/58). We analyzed and investigated the relationship of risk factors in published studies in post-treated bleeding and pancreatitis. Coronary artery disease (CAD), stroke, end-stage renal disease (ESRD), liver cirrhosis (LC), age > 70 yrs, distal CBD narrowing, and BTI were not statistically significant factors for post-treated bleeding. Sex, age < 60 yrs, jaundice, previous pancreatitis, lithotripsy, > 3 CBD stones, and CBD < 0.8 cm were not statistically significant factors for post-treated pancreatitis.
Conclusion: There was no significant post-treated duodenal bleeding (3.4%) compared to published studies in patients with post-endoscopic sphincterotomy (EST) (1-3%) or post-precut spincterotomy (2-2.7%) or post-EST + endoscopic papillary large balloon dilation (EPLBD) (5.2-10.3%). There was no significant

post-treated pancreatitis (8.6%) compared to published studies in patients with difficult biliary cannulation (4.3-11.3%) or post-EPBD (5-15%) or post-EST + EPLBD (0-6%). Overall successful stone removal (94.8%) and reduced need for ML (10.3%) is similar to patients with EST + EPLBD (80-100% and 1-11%). Limited precut sphincterotomy combined with EPBD to treat difficult biliary cannulation with common bile duct stones is safe and effective.
Disclosure of Interest: None declared

P0059 ENDOSCOPIC ULTRASOUND VS MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY FOR COMMON BILE DUCT STONES. A SYSTEMATIC REVIEW

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Introduction: Endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography (MRCP) are tests used in the diagnosis of common bile duct stones in patients suspected of having common bile duct stones prior to undergoing invasive treatment.
Aims & Methods
Aims: To determine and compare the accuracy of EUS and MRCP for the diagnosis of common bile duct stones.
Methods: We searched MEDLINE, EMBASE, Science Citation Index Expanded, BIOSIS, and Clinicaltrials.gov until September 2012. We did not restrict studies based on language or publication status, or whether data were collected prospectively or retrospectively.
We included studies that provided the number of true positives, false positives, false negatives, and true negatives for EUS or MRCP. We only accepted studies that confirmed the presence of common bile duct stones by extraction of the stones (irrespective of whether this was done by surgical or endoscopic methods) for a positive test, and absence of common bile duct stones by surgical or endoscopic negative exploration of the common bile duct or symptom-free follow-up for at least six months for a negative test, as the reference standard in people suspected of having common bile duct stones. At least two authors independently screened abstracts and selected studies for inclusion.
Two authors independently collected the data from each study. We used the bivariate model to obtain pooled estimates of sensitivity and specificity.
Results: We included a total of 18 studies involving 2366 participants (976 participants with common bile duct stones and 1390 participants without common bile duct stones). Eleven studies evaluated EUS alone, and five studies evaluated MRCP alone. Two studies evaluated both tests. For EUS, the sensitivities ranged between 0.75 and 1.00 and the specificities ranged between 0.85 and 1.00. The summary sensitivity (95% confidence interval (CI)) and specificity (95% CI) of the 13 studies that evaluated EUS (1537 participants; 686 cases and 851 participants without common bile duct stones) were 0.95 (95% CI 0.91 to 0.97) and 0.97 (95% CI 0.94 to 0.99). For MRCP, the sensitivities ranged between 0.77 and 1.00 and the specificities ranged between 0.73 and 0.99. The summary sensitivity and specificity of the seven studies that evaluated MRCP (996 participants; 361 cases and 635 participants without common bile duct stones) were 0.93 (95% CI 0.87 to 0.96) and 0.96 (95% CI 0.90 to 0.98). There was no evidence of a difference in sensitivity or specificity between EUS and MRCP (P value = 0.5). From the included studies, at the median pre-test probability of common bile duct stones of 41% the post-test probabilities (with 95% CI) associated with positive and negative EUS test results were 0.96 (95% CI 0.92 to 0.98) and 0.03 (95% CI 0.02 to 0.06). At the same pre-test probability, the post-test probabilities associated with positive and negative MRCP test results were 0.94 (95% CI 0.87 to 0.97) and 0.05 (95% CI 0.03 to 0.09).
Conclusion: Both EUS and MRCP have high diagnostic accuracy for detection of common bile duct stones. The two tests are similar in terms of diagnostic accuracy and the choice of which test to use will be informed by availability and contra-indications to each test.Further studies that are of high methodological quality are necessary to determine the diagnostic accuracy of EUS and MRCP for the diagnosis of common bile duct stones.
Disclosure of Interest: None declared

P0060 CLINICAL APPLICABILITY OF TOKYO GUIDELINES 2013 IN DIAGNOSIS APPROACH AND SEVERITY EVALUATION OF ACUTE CHOLANGITIS

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Introduction: Acute cholangitis may be associated with high morbidity and mortality. The Tokyo guidelines (TG) allowed diagnosis improvement and severity assessment of acute cholangitis and cholecystitis. However the accuracy/applicability of the updated TG 2013 remains unclear.
Objective: Diagnostic accuracy of TG13, predictors of poor prognosis in acute cholangitis and relationship with TG.
Aims & Methods: Retrospective case-control study of all episodes of obstructive jaundice, admitted to the gastroenterology service in a year, divided into two groups: those with acute cholangitis (G1: 183cases) and without acute cholangitis (G2), randomly selected in a ratio of 1:1. Variables evaluated were the clinic, analytical parameters, presence of Charcot's triad, TG07 and TG13. The prognosis was defined in terms of mortality, need of hospitalization in the intensive care unit or early ERCP (<48hours).
Results: Patients with acute cholangitis were predominantly women (58.5% vs 41.5%), with mean age 76.1 ± 11.3 years. Charcot's triad was present in 35.5%. The sensitivity/specificity for the diagnosis of acute cholangitis based on Charcot's triad, TG07 and TG13 were respectively 35.5%/100.0%, 96.2%/77.6% and 100.0%/84.7%; giving a diagnostic accuracy ($p < 0.001$) of 67.8%, 86.9% and 92.3%, respectively.
In relation to severity based on the TG, 30.6% of cases were severe. A worse prognosis was found in 26.8% of patients. After multivariate analysis, systolic blood pressure <90mmHg (OR 11.010[1.473;9.899]; p = 0.006), serum albumin <3g/dL (OR 1.355[1.098;1.613]; p = 0.006), active oncologic disease (OR 3.818[1.473;9.899]; p = 0.006) and malignant etiology of obstructive jaundice (OR 3.224[1.197;8.685]; p = 0.021) represented independent predictors of poor prognosis. The discriminative ability of the model with these 4 variables was high (AUROC 0.799; $p < 0.001$). The severity defined by the TG showed sensitivity/specificity of 65.3%/82.1%, with an accuracy of 77.6%, being explained by the 4 factors model in 80.0% ($p < 0.001$).
Conclusion: The TG13 showed high diagnostic accuracy in acute cholangitis, being higher than the Charcot's triad and TG07. Comparing to the TG, the simplified model allows select the patients that will benefit of admission in the intensive care unit and early ERCP.
Disclosure of Interest: None declared

P0061 CLINICAL IMPACT OF PERIAMPULLARY DIVERTICULUM AS RISK FACTOR OF THE POST-ERCP PANCREATITIS

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is now the therapeutic modality for biliary as well as pancreatic diseases. The correlation between Post-ERCP pancreatitis (PEP) and periampullary diverticulum (PAD) was evaluated in several studies. However, the risk of Post-ERCP pancreatitis, according to the types of PAD was not elucidated. The aim of this study was to investigate risk factors for post-ERCP pancreatitis, including three types of PAD.
Aims & Methods: We evaluated risk factors for post-ERCP pancreatitis, according to types of periampullary diverticulum. This is a retrospective case-control study, which included a total of 306 ERCPs, performed by four endoscopists in a single center. 142 (50.2%) patients with PEP, and 141 (49.8%) patients without PEP were enrolled. The correlation between PEP and risk factors, including PD, angle of common bile duct (CBD), endoscopic sphincterotomy (EST), canulation time, procedure time, and three types of PAD were investigated by univariate and multivariate analyses. PAD were classified into three types by the location of ampulla of Vater: type 1 (n = 6), inside the diverticulum; type 2 (n = 79), on the margin of diverticulum; type 3 (n = 44), outside the diverticulum.
Results: In univariate analysis, all types of PAD, type 1 PAD, type 2 PAD, type 3 PAD had variable results for PEP (Odd ratio = 1.654, 0.709, 2.815, 0.359; p = 0.036, 0.732, 0.005, 0.007, respectively). Cannulation time and total procedure time were significantly related with PEP (p = 0.004, and 0.009, respectively). However, the angle of CBD, and EST were not meaning risk factors in this study (p = 0.373, and 0.405, respectively). Age-sex adjusted multivariate analysis showed only cannulation time as independent risk factors for (OR = 1.043, p = 0.01)
Conclusion: PAD, especially Type 2 PAD, cannulation time and procedure time were risk factor for PEP in univariate analysis. However, only cannulation time was significant related to PEP in multivariate analysis. Although, this study had limitations of retrospective case-control study, prospective randomized control study in multi-center was required.

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Disclosure of Interest: None declared

P0062 RECURRENCE OF BILE DUCT STONES AFTER ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION COMBINED WITH SPHINCTEROTOMY: LONG-TERM FOLLOW-UP. A PROSPECTIVE STUDY

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Introduction: Endoscopic papillary large balloon dilation (EPLBD) with endoscopic sphicterotomy (ES) is safe and effective in patients with large bile duct stones. Data regarding the recurrence rate of common bile duct (CBD) stones after EPLBD with ES are limited and the existing studies are retrospective.
Aims & Methods: The aim of this study was to prospectively estimate the recurrence rate and the risk factors for CBD stones after EPLBD + ES. To the best of our knowledge this is the first prospective study on this issue. In total, 106 patients who underwent EPLBD + ES from 2009 to 2011 and had successful clearance of the CBD were prospectively monitored for a minimum of three years for recurrence of CBD stones. These patients belong to a group enrolled in a randomized controlled trial and their data regarding the EPLBD + ES procedure have previously been published [1]. The follow-up was performed with regular appointments in the outpatient clinics. In those patients who became symptomatic during the follow-up period and the presence of a CBD stone was radiologically confirmed, an ERCP was performed.
Results: Of the 106 patients, the duration of follow-up was 30.5 ± 5.5 months. The recurrence rate of CBD stones was 7.5% (8/106). The mean diameter of CBD was higher for the patients with stone recurrence than for those without (2.0 ± 4.9 vs 1.65 ± 0.9, $p = 0.008$). A multivariate stepwise logistic regression analysis revealed that the size of CBD diameter was significantly associated with the recurrence of CBD stones (odds ratio:1.2, $p = 0.01$). Among the others evaluated parameters (sex, stone diameter, CBD tapering, cholocystectomy) no significant differences were detected as far as the stone recurrence is concerned.
Conclusion: These data show that the recurrence rate of CBD stones after EPLBD + ES is low, and a dilated CBD appears to increase the risk of bile duct stone recurrence.

Reference

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Disclosure of Interest: None declared

P0063 SAFETY OF LONG-TERM BILIARY STENTING FOR COMMON BILE DUCT STONES

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Introduction: Though long-term biliary stenting is a useful alternative to endoscopic extraction for common bile duct stone (CBDS) in the elderly and/or frail patients with poor tolerance for prolonged endoscopic and/or surgical procedures, the safety of long-term stenting has remained uncertain. Few reports with sufficient observation period and sample size are available on this method so far.
Aims & Methods: The immediate and long-term outcome of endoscopic biliary stenting as sole treatment of CBDS was therefore compared with the result of biliary sphincterotomy (EST) and endoscopic extraction, along with a survey on complications by cholangitis. In the past 12 years, 1195 patients with CBDS in our hospital were referred to endoscopic treatment. Among these, 401 with high risk were subjected to permanent biliary stent insertion for common duct stones and stent exchange only on complications. In 105 of 401 patients, EST had been used prior to stenting. The remaining 794 patients were subjected to endoscopic stone removal after EST. Kaplan-Meier estimates of survival and time to recurrence of cholangitis were conducted on clinical variables using the Cox model for multivariate analysis.
Results: Successful biliary drainage was achieved in all patients regardless of stone removal. The mean treatment time was significantly shorter in stent patients (21.2 min) than EST patients (41.0 min) ($p < 0.01$). Early complications occurred in 2.7% of stent patients and 6.1% of EST patients. Most of them were trivial except for a few with serious pancreatitis and duodenal perforation requiring surgery in EST patients. The mean hospital stay after treatment was significantly shorter in stent patients (5.3 days) than EST patients (9.3 days) ($p < 0.01$), and than EST patients with stone removal at once (7.9 days) ($p < 0.01$). Late complication of cholangitis occurred more frequently in stent patients (59.7%) than in EST patients (18.8%) within five-year observation ($p < 0.01$, log-rank test). The mean duration to clinical presentation of cholangitis after treatment was 3.4 years (Median: 2.7 years) in stent patients and 8.1 years in EST patients. All patient in need tolerated re-treatment adequately, without biliary tract-related mortality. In stent patients, only the size of stones was significantly correlated with occurrence of cholangitis ($p < 0.05$), but addition of EST was ineffective to prevent recurrence.
Conclusion: This study confirmed the usefulness and safety of long-term biliary stenting as an alternative to endoscopic common duct stone removal and in shortening the hospital stay in CBDS patients. Although recurrence of cholangitis is frequent, this method can be repeated safely, providing a feasible option for selected patients, such as the elderly and or debilitated patients with short life expectancy. Additional EST to biliary stenting failed to prevent late occurrence of cholangitis.
Disclosure of Interest: None declared

P0064 COULD IT BE POSSIBLE TO PREDICT THE RISK OF RECURRENT RESIDUAL SYMPTOMATIC CHOLEDOCHOLITHIASIS AFTER CHOLECYSTECTOMY?

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Introduction: Usually, lithiasis of common biliary duct (CBD) results of the migration of sludge/gallstones from the gallbladder. Cholecystectomy would be useful in relapse prevention. However, the recurrence after cholecystectomy is observed in a considerable number of patients.
Objective: Prevalence and risk factors of recurrent residual symptomatic choledocholithiasis after cholecystectomy (RRSCC).
Aims & Methods: Of total of 1084 inpatient episodes for biliary pathology between 2011-2014, we selected 160 patients with choledocholithiasis after cholecystectomy, after exclusion of episodes with earlier recurrence, before 6 months after cholecistectomy. They were divided into 2 groups: >1 RRSCC episode (cases) versus patients with only one RRSCC (controls). All the cases had done biliary endoscopic drainage. We evaluated clinical variables, comorbidities, biochemical analysis, ultrasound and endoscopic retrograde cholangiopancreatography (ERCP) abnormalities and surgical specimens. The presence of duodenal diverticulum was based on Boix et al. classification.
Results: RRSCC occurred in 26.9% of patients (n = 43). The efficacy of ERCP was 76.3% with a mean number of 1.4 ± 0.7(vs 1.2 ± 0.5; $p = 0.109$) exams. It was technically impossible in 4.4% of cases and the complications peri/post- procedure, mainly pancreatitis, was 13.1%, without any case of mortality. Of cases, the mean time of cholecistectomy-recurrence was 8.5 ± 11.2 years, the mean number of relapses was 3.6 ± 2.2 with mean inter-relapses of 11.5 ± 14.1 months, mean number of choledocholithiasis episodes before cholecistectomy of 1.6 ± 1.2(vs 1.3 ± 0.7; $p = 0.017$) and necessity of surgical treatment in 7.0%. The duodenal diverticulum was presented in 32.6% (vs 9.4%; $p = 0.001$), periampullary(<2cm of papilla) in 27.9%(vs 12.0%; $p = 0.005$) and intradiverticular papilla in 16.3%(vs 4.3%; $p = 0.017$). After multivariate analysis, independent risk factors for relapse of RRSCC were American Society of Gastrointestinal Endoscopy (ASGE) criteria at admission ≥2 (2.8 ± 0.5 vs 2.4 ± 0.6; OR1.554 ,$p = 0.030$; AUROC0.624, $p = 0.017$), CBD ultrasound dilatation ≥12mm at admission (16.5 ± 5.2 vs 13.1 ± 4.5; OR1.145, $p = 0.002$; AUROC0.702, $p < 0.001$) and the presence of periampullary diverticulum (27.9% vs 12.0%; OR3.115, $p = 0.003$).
Conclusion: After a first episode of RRSCC, approximately ¼ of patients will relapse after about 9 years. Patients with ASGE criteria ≥2 at admission, biliary ultrasound dilatation ≥12mm at admission or periampullary diverticulum, will require a careful follow-up and eventually surgical treatment.
Disclosure of Interest: None declared

P0065 THE ECTOPIC OPENING OF COMMON BILE DUCT INTO THE DUODENAL BULB AND GASTRIC ANTRUM AND ITS CLINICAL IMPORTANCE

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Introduction: Ectopic of the common bile duct (CBD) into the duodenal bulb and gastric antrum is an extremely rare congenital anomaly, but its clinical significance has not been adequately determined.
Aims & Methods: The aim of this study was to comprehensively describe the features of this rare anomaly. Clinical, laboratory, endoscopic and cholangiographic findings, therapeutic interventions, and clinical course of consecutive patients that underwent endoscopic retrograde cholangiopancreatography (ERCP) and were diagnosed as ectopic opening of CBD into the duodena bulb and gastric antrum.
Results: Ectopic opening of the CBD was observed in 10 (1.5%) (7 males and 3 females; median age: 56.3 years) of 637 patients that underwent ERCP. All but 1 of the patients with ectopic opening of the CBD had a history of recurrent episodes of cholangitis, and 1 had compensated cirrhosis. The ectopic opening was into the antrum in 2 patients and into the duodenal bulb in 8 patients. In all, 6 of the patients had an ulcer (duodenal: n = 4; gastric: n = 2) and 7 had duodenal deformity associated with apical stenosis. Cholangiography showed dilatation of both the extrahepatic and intrahepatic bile ducts, and tapered narrowing and a hook-shaped configuration of the distal end of the CBD in all 10 patients, bile stones in 7 patients, and bile sludge in 3 patients. Complete clearance of the bile ducts was achieved in all patients with bile sludge and in 1 of the 7 patients with bile stones following balloon dilation of the orifice.
Conclusion: Ectopic opening of the CBD into the duodenal bulb and gastric antrum is usually associated with gastroduodenal and biliary disease. ERCPists should be aware of this anomaly. Abnormal configuration of the biliary tree prevents complete extraction of bile stones in most patients.
Disclosure of Interest: None declared

Abstract Number: P0068

		Day0	Day3	Day7
Platelet count(10^4/μL)	rTM	9.9 ± 5.7	11.9 ± 5.6	18.6 ± 9.1**
	control	12.1 ± 6.9	10.2 ± 5.6	18.2 ± 7.8**
PT-INR	rTM	1.47 ±0.35	1.24 ± 0.20*	1.27 ± 0.26*
	control	1.41 ± 0.27	1.15 ± 0.25*	1.17 ± 0.18*
FDP (μg/ml)	rTM	25.1 ± 17.1	20.1 ± 25.6	18.0 ± 14.9
	control	39.7 ±36 .4	21.5 ± 11.0	18.2 ± 9.5
CRP (mg/dL)	rTM	13.5 ± 7.1	9.9 ± 5.8*	5.7 ± 4.8**
	control	16.2 ± 7.9	12.2 ± 6.3*	7.3 ± 4.6**
DIC score	rTM	5.2 ± 1.2	2.8 ± 1.6**	1.8 ± 1.4**
	control	5.7 ± 1.1	3.8 ± 1.7**$	2.1 ± 1.5**$
DIC resolution rate (%)	rTM		65$32	8078
	control			

Data are shown with Mean ± SD *p < 0.05 vs. Day0, **p < 0.01 vs. Day0 $p < 0.05 rTM vs control

P0066 PREVALENCE AND RISK FACTORS OF GALLBLADDER STONE IN KOREAN HEALTH EXAMINEE

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Introduction: Female gender, age, diabetes mellitus, rapid weight loss, use of oral contraceptives, pregnancy, menopause, chronic hepatitis C, chronic kidney disease and metabolic syndrome have been known as the risk factors of gallbladder (GB) stones. In western countries, females showed higher prevalence of gallbladder (GB) stone than males. However, prevalence of GB stone was higher in males than females in some studies.

Aims & Methods: The aims of this study were to evaluate the prevalence and risk factors of GB stone. Patients who underwent examination through health promotion center in Yeungnam university hospital from Jan 2010 to Dec 2013 were analyzed retrospectively. All subjects checked height, weight, abdominal circumference, and blood pressure and underwent laboratory tests and abdominal ultrasonography. Diagnosis of GB stone was made by abdominal ultrasonography. Subjects with history of cholecystectomy or without visible GB were excluded from this study.

Results: Of the total 23,899 subjects (mean age, 50.0 ± 11.4 years, male to female ratio, 1.3:1), GB stone was diagnosed in 1,259 subjects with overall prevalence of 5.2%. Mean age of the patients with GB stone was 55.4 ± 11.3 years and male to female ratio was 1.6:1. Prevalence of GB stone was significantly higher in male than female (5.7% vs 4.4%, p < 0.001). Males had higher prevalence of GB stone than females in all age groups. Metabolic syndrome (MS) was more frequent in male subjects than females (18.6% vs 13.9%, p < 0.01). Subjects with MS had higher incidence of GB stone compared to subjects without MS (23.3% vs 16.2%, p < 0.001). Males had higher prevalence of MS than females in the age below 60 (22.4% vs 15.5%, p = 0.016). However, the prevalence of MS was higher in females than in males in age above 60 (41.6% vs 23.0%, p = <0.001). On multivariate analysis, older age (95% CI, 1.035-1.046; p < 0.001), male gender (95% CI, 1.171-1.496; p < 0.001), high blood pressure (95% CI, 1.491-1.876; p < 0.001), low HDL cholesterol level (95% CI, 1.106-1.436; p = 0.001), abdominal obesity (95% CI, 1.082-1.408, p = 0.003) and chronic hepatitis B (95% CI, 1.008-1.684; p = 0.036) were found as risk factors of GB stone.

Conclusion: The prevalence of GB stone was 5.7% in males and 4.4% in females with overall prevalence of 5.2%. Age, male gender, high blood pressure, low HDL cholesterol, abdominal obesity and chronic hepatitis B were found as risk factors of GB stone.

Disclosure of Interest: None declared

P0067 THE MANAGEMENT OF BILE DUCT STONES IN VERY ELDERLY PEOPLE

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Introduction: Life expectancy has been prolonged all over the world, particularly in Japan. The increasing population of very elderly people raises the prevalence of bile duct stones. Very elderly patients often have concomitant heart or cerebrovascular diseases. We evaluated the safety of the endoscopic treatment for bile duct stones.

Aims & Methods: From April 2010 to March 2015, 289 consecutive patients (58.5% men; mean age, 75 years) with bile duct stones who underwent endoscopic retrograde cholangiopancreatography (ERCP) were included in the present study. Patients were divided into two age groups: group A (≧85 years old) (n = 76) and group B (<85 years old) (n = 213). We performed endoscopic papillary balloon dilation (n = 242), endoscopic papillary large balloon dilation (n = 25), endoscopic sphincterotomy (n = 22) to remove bile duct stones.

Results: Patients in group A had larger (8.3mm vs 6.8mm, p = 0.031) and more (3.4 vs 2.3, p = 0.004) stones than in group B with significant differences. Overall, bile duct clearance rates were similar in the two groups (96.1% vs 98.6%, p = 0.188), and the mean number of sessions required for complete stone removal was similar in the two groups (1.3 vs 1.2, p = 0.395). The incidence of post-ERCP pancreatitis was lower in group A than in group B (3.9% vs 11.3%, p = 0.067) but was not statistically different. The incidence of pneumonia was higher in group A than in group B (2.6% vs 0%, p = 0.069) but was not statistically different. Duration of hospitalization was significantly longer in group A than in group B (20.0 vs 12.9, p < 0.001).

Conclusion: Although very elderly patients had larger and more stones, bile duct clearance rate was similar. ERCP is safe technique for the treatment of bile duct stones in very elderly patients as well, without increased occurrence of pancreatitis.

Disclosure of Interest: None declared

P0068 THE EFFICACY OF RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN IN PATIENTS WITH BILIARY TRACT INFECTION-INDUCED DISSEMINATED INTRAVASCULAR COAGULATION

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Introduction: The biliary tract infectious disease is sometimes serious, sometimes resulting in disseminated intravascular coagulation (DIC). Recently, recombinant human soluble thrombomodulin (rTM) was approved and has been used in clinical practice for DIC treatment in Japan. However, there are few studies to evaluate the efficacy of rTM for DIC with the biliary tract infection. The purpose of this study is to make a comparison between rTM-treated patients and patients treated other agents, and to evaluate the efficacy of rTM.

Aims & Methods: Thirty-nine inpatients at our department with biliary tract infection-induced DIC between January 2009 and March 2015 were retrospectively analyzed. The patients were classified into the rTM treatment group (n = 20), and conventional treatment group (rTM was not used) as the control group (n = 19). Diagnosis of DIC was made according to the criteria of acute DIC of the Japan Association of Acute Medicine (JAAM). Platelet count, prothrombin time-international normalized ratio (PT-INR), levels of fibrin/fibrinogen degradation products (FDP), C-reactive protein (CRP), DIC scores based on JAAM criteria were measured on days 0.3, and 7 to evaluate therapeutic results. Furthermore, DIC resolution rate were assessed 3 and 7 days after the start of DIC treatment.

Results: There were no significant differences between two groups regarding patient characteristics. All patients underwent biliary drainage. The duration of rTM administration was 3.6 ± 1.7 days (range 1 to 8 days). As shown in the table, significant intra-group improvement was observed in all parameters except for FDP in both groups. However, there were no significant inter-group differences in comparison of all parameters except DIC scores. Significant improvements were seen in the DIC scores in the rTM-treated group (p < 0.05). DIC resolution rate on day3 were higher in the rTM group than in the control group (65% vs 32% on day3, p < 0.05).

Conclusion: These results suggest that rTM would be the useful medicine for early improvement of biliary tract infection-induced DIC.

Disclosure of Interest: None declared

P0069 LASER LITHOTRIPSY FOR GIANT STONES OF BILE DUCT UNDER PERORAL DIRECT CHOLANGIOSCOPY THROUGH TRACTION OF THE BENDING PART OF ULTRASLIM GASTROSCOPE

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Introduction: To evaluate the feasibility and usefulness of a new peroral direct cholangioscopy(PDSC) technique through traction of the bending part of ultraslim gastroscope for the laser lithotripsy of giant stones of bile duct.

Aims & Methods: This study involved 9 patients with giant stones of bile duct whose endoscopic treatment failed by a conventional method involving mechanical lithotripsy. Firstly, endoscopic retrograde cholangiography (ERC)

and small sphincterotomy was performed using a conventional duodenoscope. Endoscopic papillary balloon dilation was performed up to 12-15mm before the introduction of an ultraslim upper endoscope(Fijinon 530NW). Before inserting the ultraslim gastroscope, a snare was tightened around the end of the bending section of the scope(about 6cm from the tip). Then the ultraslim gastroscope was advanced into the duodenum with the snare. A J turn was made in the second portion of the duodenum, and the tip of the endoscope was positioned facing the papilla. Then the snare was pulled slightly as a fulcrum to prevent the endoscope be pushed too far downward in the duodenum and to make insertion of the endoscope easier. Using this method, the ultraslim gastroscope was advanced into the CBD, and laser lithotripsy (U100plus, Germany) was performed. The stone fragments were extracted by basket and balloon through PDSC or ERC finally.

Results: The procedures of PDSC and laser lithotripsy were succeeded in all 9 patients (5 men and 4 women; mean age 79.7 years, range 52-93 years). The mean diameter of giant CBD stones was 23.2mm (range, 14-40mm). The overall success rate of bile duct clearance by laser lithotripsy and extraction was 100%. The mean intubation time was 8.8 minutes (range, 4-16 minutes). No procedure-related complications were observed.

patient	sex	age	Stone size (mm)	Intubation time (min)	No. of times entering CBD
1	M	70	14	10	1
2	F	93	20	8	1
3	M	52	25	14	4
4	M	77	40	4	6
5	M	93	20	4	2
6	F	85	20	7	2
7	F	86	22	9	2
8	F	86	30	8	3
9	M	75	18	16	1

Conclusion: Snare-assisted PDSC through traction of the bending part of ultra-slim gastroscope and laser lithotripsy were safe, simple and practical techniques for the treatment of giant stones of bile duct. The new PDSC method sometimes facilitated the entrance into bile duct repeatedly for further procedures including direct removal of stone fragments.

Disclosure of Interest: None declared

P0070 FEASIBILITY OF ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION IN PATIENTS WITH DIFFICULT BILE DUCT STONES AND WITHOUT DILATATION OF THE LOWER PART OF THE EXTRA-HEPATIC BILE DUCT

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Introduction: Endoscopic sphincterotomy (EST) combined with mechanical lithotripsy (ML) is an established method for the removal of difficult biliary stones. Some bile duct stones were difficult to remove because of their large size, the rectangular shape of the CBD, or anatomical difficulties interfering with endoscopic procedures. Ersoz et al. first reported on the usefulness of large balloon (10–20 mm in diameter) dilation after EST (EPLBD) for the removal of large bile duct stones in 2003[1]. However, difficult cases have been encountered with large stones and without dilatation of the lower part of the CBD (WDLBD). The usage of the combination of EST and ML in such cases often requires multiple treatment procedures, whereas EPLBD has been avoided so far because of the high risk of procedure-associated complications.

Aims & Methods

Aims: To evaluate the technical feasibility and safety of EPLBD for the removal of large bile duct stones in WDLBD patients.

Methods: Between October 2009 and July 2014, 212 patients underwent EPLBD for the removal of bile duct stones at Yokohama City University Hospital, NTT Tokyo Medical Center, and Tokyo Metropolitan Hiroo Hospital. We retrospectively reviewed them. There were 60 patients (28.3%) in the WDLBD group and 152 patients (71.7%) in the non-WDLBD group. The state WDLBD was defined as a state with the diameter of the lower part of the extra-hepatic bile duct <10 mm and its length >10 mm as measured by cholangiography.

Results: There were no significant differences between the two groups in the total success rates (100% vs. 98.7%), frequencies of the use of mechanical lithotripter (31.7% vs. 23.0%, $P = 0.193$), and recurrence rates (3.3% vs. 4.6%). The success rate in the first session was significantly lower (63.3% vs. 75.7%, $P = 0.040$) and the procedure time was significantly higher (58.1 ± 31.5 vs. 48.1 ± 22.9, $P = 0.032$) in the non-WDLBD group. There were no significant differences in the rates of post-ERCP pancreatitis, perforation, and bleeding (6.7% vs. 3.3%, $P = 0.471$, 0% vs. 1.3%, $P = 0.917$, and 1.7% vs. 0.7%, $P = 0.917$, respectively).

Conclusion: EPLBD appears to be a safe and effective method for the common bile duct stone removal in WDLBD patients.

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Disclosure of Interest: None declared

P0071 COST-EFFECTIVENESS TRIAL OF SELF-EXPANDABLE METAL STENTS AND PLASTIC BILIARY STENTS IN MALIGNANT BILIARY OBSTRUCTION

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Introduction: Self-expandable metal (SEMS) and plastic stents can be applied in the palliative endoscopic treatment for patients with unresectable malignant biliary obstruction. SEMS is substantially expensive, but the stent patency is significantly longer. Current guidelines recommend the use of SEMS if the patient's life expectancy is more than four months.

Aims & Methods: The aims of this study were to compare the therapeutic efficacy and cost-effectiveness of SEMS and plastic stents in the treatment of malignant biliary obstruction. 74 patients with unresectable malignant biliary obstruction were retrospectively enrolled who received a SEMS (34 patients) or a plastic stent (34 patients). We evaluated the technical and functional success, the complication rate, the stent patency and the cumulative cost of treatment.

Results: The complication rate of SEMS was lower compared with plastic stents (40.54% vs. 56.76). The stent occlusion was the most frequent complication. The mean time of stent patency were significantly higher in the SEMS group (19.11 vs. 8.29 weeks; $p = 0.0041$). In these cases the length (10.89 vs. 13.7 days; $p = 0.19$) and frequency (1.18 vs. 2.32; $p = 0.05$) of hospitalization of patients in context with stent complications were substantially lower, but the necessity of reintervention for stent dysfunction was higher (17 vs. 27; $p = 0.033$). In the plastic stent group the multiple stent implantation increased the stent patency: the second stent raised it from 7.68 to 10.75 weeks. In the three quarter of cases the stent complications were manageable endoscopically in both groups: re-ERCP, re-stent implantation or stent replacement were performed. There was no difference in the total cost of treatment of malignant biliary obstruction between the two groups ($p = 0.848$). If the patients' survival time was more than two months, the cost-effectiveness of SEMS was better than plastic stents.

Conclusion: Considering the cost of treatment, the burden of patients and health care system we recommend the SEMS implantation if the life expectancy of patients is more than two months. In short survival cases or if the SEMS not available the multiple plastic stent implantation is recommended.

Disclosure of Interest: None declared

P0072 GALLBLADDER CARCINOMA: THE 6 YEARS EXPERIENCE OF A TERTIARY REFERRAL CENTER

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Introduction: The gallbladder carcinoma is an uncommon neoplasm but often fatal, with a high geographical variability in relation to its incidence.

Aims & Methods: The authors propose to evaluate the clinical and pathological aspects of this neoplasm and its relation with cholelithiasis, as well as its prognosis. Retrospective analysis of patients with diagnosis of gallbladder cancer between 2008-2013, in a referral tertiary center.

Results: We included 44 patients (68% women), with a median age of 70 years. The median time of follow-up was 6 months, with a mortality rate of 71% ($n = 31$). The majority of patients (61%) had history of cholelithiasis and 46% were diagnosed after cholecystectomy (35% of these in the context of acute cholecystitis). The most common symptoms reported at admission were abdominal pain (59%), jaundice (41%), and nausea/vomiting (34%). The majority of the patients had slight cholestasis in laboratorial analysis. The neoplasms involved the gallbladder body or were panvesicular in 77% of cases. A non-specific adenocarcinoma was the most common diagnosis (86%), with a median size of 33mm. At diagnosis, 84% were in an advanced stage (III/IV). A surgery of curative intent was performed in 59% of patients. The palliative approaches more frequently used were percutaneous drainage (39%) and chemorradiotherapy (27%). An endoscopic drainage was performed only in 6 patients (14%). The mortality rate at 3, 6, 12 and 24 months was 23%, 39%, 55% and 66%, respectively. The presence of cholestasis ($p = 0.036$) and renal dysfunction ($p = 0.012$) at diagnosis correlated independently with early mortality.

Conclusion: The gallbladder carcinoma was more prevalent in women with advanced age, in many cases with prior cholelithiasis and in an advanced stage at diagnosis. Adenocarcinoma was the most common histological type. Despite the high rate of surgical approaches for curative intent, 66% did not survive beyond 2 years after the diagnosis.

Disclosure of Interest: None declared

Abstract number P0074
Table 1.

	Hepato-gastrostomy jejunostomy[HG(J)S]	Choledocho or cystoduodenostomy [CD(Cy)S]	Choledochal-Rendezvous (C-RV)	Cholecysto-gastrostomy-jejunostomy[CG(J)S]	Total
Number of the pts (A/B)	7/24	8/6	2/10	2/0	19/40
Male-Female	22-9	8-6	8-4	1-1	39-20
Mean age (range) years	67 (34-87)	61 (45-81)	65 (48-80)	60 (52-68)	65 (34-87)
Malignities	7/2	7/4	0/4	2/0	16/30
Benign pathologies	20/2	1/2	2/6	0/0	3/10
Indications (A/B)					
Technical success rate A/B (Number of the patients)#	[100% (7/7)/87.5% (21/24)]	[100% (8/8)/50% (3/6)]	[100% (2/2)/60% (6/10)]	[100% (2/2)/0/0	[100% (19/19)/77.5% (31/40)]]
Serious Complications:A/B¥	0/5 (Bleeding in two cases-one died, one surgery; cholangitis and sepsis in one case; perforation in two cases (surgery needed)	0/2 (Bile leak and biloma formation (10 cm) requiring surgery in one-cardiopulmonary arrest and death in one)	0/1 (Surgery due to guide-wire knotting in duodenum)		0/8 (2 death, 5 surgery, 1 extended intensive care stay)

P0073 DIRECT RETROGRADE CHOLANGIOSCOPY-DIRECTED BIOPSY IS SUPERIOR TO FLUOROSCOPY-GUIDED BIOPSY TO DIFFERENTIATE INDETERMINATE BILIARY STRICTURE IN THE DISTAL COMMON BILE DUCT, BUT NOT IN THE PORTA HEPATIS

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Introduction: Differentiation of indeterminate biliary stricture (IBS) by imaging modalities is limited. Definite diagnosis is based on histopathology, but high rates of false negative biopsies constrain the clinical management.

Aims & Methods

Aims: To investigate reason of high false negative results of intraductal biopsies obtained under fluoroscopic guidance in comparison to direct retrograde cholangioscopy (DRC).

Methods: All patients were retrospectively included who presented for diagnostic workup of IBS at our University hospital and who underwent an intraductal biopsy between 2009 and 2015. Histopathological results of fluoroscopic vs DRC-directed intraductal biopsies were compared with the golden standard of either postoperative histology or follow-up of at least one year and underlying disease of false negative biopsies in proximal and distal biopsies was compared.

Results: 106 patients were included in this study. IBS was evaluated by fluoroscopy-guided biopsy in 68 patients and by DRC-directed biopsy in 38 patients. A malignant stenosis was diagnosed in 47/106 cases (44.3%). Sensitivity and specificity for fluoroscopy guided and DRC directed biopsies were 46% and 100% vs. 58% and 100%, respectively. Underlying disease in the 24 false negative histological diagnoses was cholangiocarcinoma (CCA, 14/24, 58%), adenocarcinoma of the pancreatic head (PC, 7/24, 29%) and others (3/24, 13%). Majority of false negative samples was in distal biopsies (19/24, 79%), where etiology was mainly CCA (9/20, 45%) and PC (7/20, 37%). Etiology in false negative biopsies in the hilar region was only CCA (n = 5, 100%). DRC directed biopsy correctly detected all PC (2/2, 100%) compared to 2/9 PC (22%) found by fluoroscopy guided biopsy and 4/8 CCA (50%) compared to 6/16 CCA (37.5%), respectively.

Conclusion: DRC is superior to fluoroscopy in distinguishing ductal infiltration from external common bile duct compression, e.g. in PC, and might be preferred to direct intraductal biopsies.

Disclosure of Interest: None declared

P0074 ENDOSONOGRAPHY-GUIDED BILIARY DRAINAGE: EXPERIENCE COUNTS

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Introduction: ERCP is unsuccessful in 10% of the cases of biliary obstruction. Previously, percutaneous transhepatic drainage was the only alternative. Recently, endosonography (EUS) –guided drainage was suggested as an alternative. However, the technique is still in evolution

Aims & Methods

Aim: To assess the efficacy and safety of different techniques in EUS-guided biliary drainage.

Patients and Methods: We collected the data of 59 patients treated over 46 months. The data included baseline characteristics, indications, techniques, success rates and complications. Patients were classified according to the different types of approaches shown in Table. In the first 41 months, we used tapered ERCP catheter, and in case it fails, needle-knife sphincterotomy for inital tract dilation and plastic or metal stents eventually. For the last five months, we revised our technique so that we used exclusively 6F cystotome. We preferred CDS over HGS in distal obstructions in long-scope position.

Results: The overall results and the results after it was broken down to previous 41 months (group B) vs. the last 5 months (group A) are shown in Table 1. Work volume was 0.97 patient per month in group B vs. 3.8 in group A ($p < 0.05$). There was no significant difference between the groups for any indication (NS). Technical success rate in group A was significantly higher in group A (p: 0.046) and complication rate was lower ($p = 0.045$).

Conclusion: Experience, volume of the centre and the initial tract dilation technique and use of metallic stent are the most important determinants of success and complications in EUS-guided biliary drainage.

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Disclosure of Interest: None declared

P0075 SIMVASTATIN USE AND ITS IMPACT ON SURVIVAL IN PANCREATIC CANCER PATIENTS

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Introduction: Statins are cholesterol-lowering medications and are associated with a number of signaling pathways involved in carcinogenesis. Recent observational studies raised the possibility that the use of statins may reduce the overall mortality in various types of cancer. We investigated whether statins used after pancreatic cancer diagnosis reduce the pancreatic cancer mortality in patients with pancreatic cancer.

Aims & Methods: We analyzed data on 2981 patients newly diagnosed with pancreatic cancer between January 1, 2006 and December 31, 2014. We used the Cox proportional hazards regression model to estimate mortality among pancreatic cancer patients according to statin use.

Results: Among the 2981 patients, 428 pancreatic cancer patients had used statins. During the study period, 1616 patients (54.2%) died. After adjustment for age, sex, tumor characteristics, DM, dyslipidemia, BMI, and tumor marker, statin use was associated with lower risk of pancreatic cancer death (HR, 0.821; 95% Confidence interval, 0.716 – 0.941), especially among simvastatin users (HR, 0.620; 95% Confidence interval, 0.448 – 0.858). Subgroup analysis showed that patients who used simvastatin in non-resectable pancreatic cancer had more favorable outcomes than patients with resectable pancreatic cancer.

Conclusion: We found that the use of statins after cancer diagnosis is associated with longer survival in patients with pancreatic cancer. This effect was stronger in patients who used simvastatin in advanced pancreatic cancer.

Disclosure of Interest: None declared

P0076 THE POSSIBILITY OF LIQUID BIOPSY WITH BILE JUICE IN PATIENTS WITH GALLBLADDER CANCER

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Introduction: Gallbladder cancer (GBCa) is one of the most difficult to treat cancers in the field of gastroenterology. To achieve good treatment effect in future, so called "custom-made" therapy based on the character of the each tumor is mandatory. However, GBCa tissue cannot be obtained easily. In this study, we try to elucidate the possibility of "liquid biopsy" with bile juice on the concept of non- invasive diagnostic method as circulating tumor DNA in blood.
Aims & Methods: Eleven patients with GBCa enrolled in this study. Surgically removed tumors and their surrounding normal tissue were analyzed for mutations of 48 oncogenes (Cancer panel; Haloplex, Agilent Technology) by next generation sequencing (NGS; Illumina, San Diego, CA, USA) in all patients. Bile juice obtained from 6 of 11 patients prior to the treatment was examined simultaneously. As negative controls, additional 2 healthy gallbladder tissue samples were analyzed.
Results: We set cut-off value at 3% for rare mutation rate. TP53 mutation was detected in 2/11 (18.2%) of the tumor tissue. Mutations of CTNNB1, MET, AR were detected in 1/11 (9%), 1/11 (9%), 1/11 (9%) samples, respectively. In these mutation-positive samples, more than 10% of the DNA was mutated in 23.8% of TP53 (E153K), 15.9% of TP53 (R148K) and 29.7% of CTNNB1 (T41I). None of the corresponding normal tissues and controls had any mutations. Interestingly, we could detect the same TP53 mutation even in bile juice as liquid biopsy in patients who had TP53 mutation in tumor tissue (2/2; 100%).
Conclusion: Tumor DNA in bile juice could be detected by NGS. It may allow us to make a new genetic diagnosis of GBCa.
Disclosure of Interest: None declared

P0077 RANDOMIZED TRIAL COMPARING THE EFFICACY OF BILATERAL METALLIC STENT DEPLOYMENT WITH THAT OF UNILATERAL DEPLOYMENT IN PATIENTS WITH MALIGNANT HILAR BILIARY STRICTURES DUE TO BILIARY TRACT CARCINOMA

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Introduction: Several single-arm studies demonstrated the feasibility of metallic stent (MS) in the management of the malignant hilar biliary strictures (HBS). However, the efficacy of the bilateral MS deployment to the malignant HBS has not been compared and discussed with those of unilateral MS deployment yet.
Aims & Methods: We conducted the multi-center prospective randomized study to investigate the clinical significance of the bilateral MS deployment to the patients with malignant HBS caused by unresectable biliary tract carcinoma (BTC) (UMIN000005182). To exclude the possibility to include the patients who absolutely needed bilateral stenting, the patients with HBS due to pathologically confirmed unresectable BTC were subjected to the unilateral biliary decompression before MS deployment. The patients whose unilateral portal blood flow was lost due to tumor invasion were also excluded. The biliary branch to be drained first was that which drained the most part of the liver under the CT or MR imaging. After confirming the improvement of the liver function, the patients gave informed consent and were randomly allocated to the endoscopic unilateral or bilateral MS deployment. The MS which was employed in this study is Zeostent (Zeon Medical, Tokyo, Japan). The patients who were allocated to the bilateral stenting (BS) had two MS deployed in the initially inserted branch and the branch of the contralateral lobe using the endoscopic partial stent-in-stent procedure. The patients who were allocated to the unilateral stenting (US) had one MS deployed in the initially selected branch. The primary endpoint is the stent-functioning (SF) time, the definition of which is the time from the MS deployment to the stent dysfunction which necessitates the biliary interventions. The data was analyzed based on the intention-to-treat.
Results: Between April 2011 and March 2014, 86 patients with BTC were enrolled in this study. After excluding 7 patients due to patients' refusal, death before stenting, breach of protocol or misdiagnosis, 40 patients were randomly allocated to the BS group and 39 patients to the US group. The procedure success rate was 93% (37/40) in BS group and 100% (39/39) in US group (ns). The early pancreatobiliary complication rate was 25% (10/40) in BS group and 23% (9/39) in US group (ns). The mean survival time was 237 days in BS group and 236 days in US group (ns). The mean SF time was 295 days in BS group and 187 days in US group (ns, $p = 0.075$). The biliary re-intervention was successfully performed on both groups. Other late complications were noted in US group only.
Conclusion: Judging from these data, it is suggested that the bilateral MS deployment is the procedure to try first for the patients with HBS due to unresectable BTC.
Disclosure of Interest: None declared

P0078 PREDICTIVE FACTORS FOR POSITIVE DIAGNOSIS OF MALIGNANT BILIARY STRICTURES BY TRANSPAPILLARY BRUSH CYTOLOGY AND FORCEPS BIOPSY

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Introduction: Endoscopic transpapillary brush cytology and forceps biopsy are used widely for the pathological diagnosis of malignant biliary strictures (MBS). However, the diagnostic yield remains unclear because of the wide variation in reported values, and predictive factors for a positive diagnosis using these methods have not been established.
Aims & Methods: We aimed to clarify the diagnostic yields of the two methods and predictive factors for a positive diagnosis.
We reviewed 241 patients with biliary strictures who underwent transpapillary brush cytology ($n = 202$) and/or forceps biopsy ($n = 208$) between 2004 and 2014 at a single academic center.
Results: The sensitivity of forceps biopsy for MBS was significantly higher than that of brush cytology (60.6% [97/160] vs. 36.1% [57/158]; $P < 0.001$). The sensitivity of forceps biopsy was significantly higher in bile duct cancer than pancreatic cancer (82.0% [50/61] vs. 42.4% [28/66]; $P < 0.001$). Multivariate analysis revealed that a serum total bilirubin level (T-Bil) ≥ 4 mg/dL (OR: 2.51, 95% CI: 1.14-5.50; $p = 0.022$) was a significant independent predictive factor for a positive diagnosis by brush cytology, and bile duct cancer (OR: 4.93, 95% CI: 2.18-11.11; $p < 0.001$), length of stricture ≥ 30 mm (OR: 2.94, 95% CI: 1.12-7.75; $p = 0.029$), and T-Bil ≥ 4 mg/dL (OR: 2.25, 95% CI: 1.05-4.83; $p = 0.037$) were significant indicators of a positive diagnosis by forceps biopsy.
Conclusion: Endoscopic transpapillary forceps biopsy showed higher sensitivity than that of brush cytology for MBS. Bile duct cancer, length of stricture ≥ 30 mm and T-Bil ≥ 4 mg/dL are good indicators of a forceps biopsy.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 09:00–17:00
PANCREAS I – HALL 7

P0079 COPPER DEFICIENCY RESULTS IN PANCREATIC STELLATE CELLS ACTIVATION WITHOUT THEIR TRANSDIFFERENTIATION INTO MYOFIBROBLASTS

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Introduction: Pancreatic stellate cells (PSCs) are supposed to play an important role in pancreatic fibrogenesis. However as they are quite common with hepatic stellate cells their role in pancreatic regeneration couldn't be excluded.
Aims & Methods: The aim of our work was to study the role of PSCs in pancreatic tissue regeneration in rat copper-deficient diet model.
24 white Wistar male rats (80-100 g weight) were maintained on copper-deficient diet (MP Biomedicals, USA) containing a relatively non-toxic copper-chelating agent, triethylenetetramine tetrahydrochloride (Tokyo Chemical Industry Co., Ltd, Japan) in final concentration of 0.6% w/w for 8 weeks, and then returned to normal rat chow for another 8 weeks (recovery phase). Animals of control group were maintained on normal rat chow for the whole duration of experiment.
Groups of 3 animals each were killed after 2, 4, 6, and 8 weeks of copper-deficient diet and 2, 4, 6, and 8 weeks of recovery phase. Paraffin sections of pancreas were stained immunohistochemically using antibodies to desmin, a marker of PSCs, and alpha smooth muscular actin (a-SMA), a marker of myofibroblasts, which are supposed to be involved in pancreatic fibrogenesis.
Results: Signs of pancreatic acinar tissue injury were observed in rats after 4 weeks of copper-deficient diet. After 6 and 8 weeks of copper deficiency tissue was almost totally destroyed, however, few ducts and islets were still present; the similar pattern was observed 2 and 4 weeks after animals were returned to normal rat chow. Partial restoration of acinar tissue was observed by the 6 and 8 weeks of recovery phase.
Staining with antibodies to desmin revealed single desmin-positive cells located mainly around the blood vessels in control group animals. Similar results were found after 2 and 4 weeks of copper-deficient diet.
After 6 weeks of a diet intensive colouring of desmin-positive cells on periphery of islets was noted, the number of desmin-positive cells in acinar tissue increased. After 8 weeks of copper-deficient diet some desmin-positive cells located around blood vessels and ducts were observed along with the more intensive colouring of islet cells.

After rats were transferred to normal rat chow the number of desmin-positive cells slightly decreased. Along with the pale colouring of islets few desmin-positive stellate-shaped cells were found in islets and on the border of the existing islets and newly formed acinar tissue.
Staining with antibodies to a-SMA revealed only smooth muscle cells of blood vessels for the whole duration of the experiment.
Conclusion: The increased number of PSCs in areas of the newly formed acinar tissue probably reflects their participation in pancreas regeneration. However PSCs activation doesn't result in their transdifferentiation into myofibroblasts thus not increasing the risk of pancreatic fibrosis.
Disclosure of Interest: None declared

P0080 PANCREATIC ISLET CELLS COULD BE THE SOURCE OF PANCREAS RESTORATION IN COPPER-DEFICIENT MODEL OF PANCREAS INJURY

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Introduction: Few possible sources of pancreas regeneration including islet cells are discussed in literature.
Aims & Methods: The aim of our work was to study the phenotype of rat pancreatic islets cell in copper-deficient model of pancreas injury.
24 white Wistar male rats (80-100 g weight) were maintained on copper-deficient diet containing a copper-chelating agent, triethylene tetraminetetrahydrochloride, in final concentration of 0.6% w/w for 8 weeks, and then returned to normal rat chow for another 8 weeks. Control group animals were maintained on normal rat chow for the whole duration of experiment.
Groups of 3 animals each were killed after 2, 4, 6, and 8 weeks of copper-deficient diet and 2, 4, 6, and 8 weeks after return to normal rat chow. Paraffin sections of pancreas were stained immunohistochemically with antibodies to cytokeratin 19 (CK19), marker of pancreatic ducts cells, and alpha-fetoprotein (AFP), which is considered to be the marker of hepatoblasts as well as hepatocellular carcinoma cells.
Results: Both large ducts and small ductules between the acini stained with antibodies to CK19 were observed in pancreas sections in control group rats. No positive staining was found in pancreatic islets. Similar results were observed after 2 weeks of copper-deficient diet.
After 4 weeks of diet CK19-positve ducts as well as positive staining in central part of pancreatic islets was noted. After 6 and 8 weeks the number of CK19-positive cells and duct-like structures increased substantially, central part of islets was still CK19-positive.
After rats were transferred to normal rat chow the number of CK19-positive cells and ducts decreased, however, the central part of islets was positive until the end of the experiment.
The presence of CK19-positive cells in pancreatic islets was found recently in pancreas embryogenesis. So we suppose CK19-positive cells could be one of the steps of pancreatic stem cells differentiation in case of tissue recovery after injury.
Staining with antibodies to AFP was negative in normal pancreas as well as after 2 weeks of copper-deficient diet. After 4 weeks of diet solitary AFP-positive cells in acinar tissue were noted. After 6 and 8 weeks both single positive cells and duct-like structures as well as staining of central parts of pancreatic islets were observed.
After rats were transferred to normal rat chow the number of AFP-positive ducts decreased and disappeared by 8th week, the cells of central part of islets remained positive until the end of the experiment.
Our results allow us to suppose that in the case of copper deficiency progenitor cells which could be common for liver and pancreas timely change their phenotype to hepatoblast-like cells, as described by Rao et al. (1989). However there is no possibility of oncogenic transformation as the number of AFP-positive cells decreased by the end of the experiment.
Conclusion: The abovementioned changes of CK19- and AFP-positive cells number allows us to suppose that pancreatic islet cells could be the source of pancreas regeneration. These progenitor cells are probably common for pancreas and liver and under certain conditions can express markers of hepatoblasts.
Disclosure of Interest: None declared

P0081 ADIPOSE TISSUE IS TOXIC FOR PANCREATIC PARENCHYMA: CO-CULTURE MODEL OF PANCREATIC TISSUE AND VISCERAL ADIPOSE TISSUE FROM OBESE PATIENTS

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Introduction: Recently, obesity and metabolic syndrome have been identified as independent risk factors for chronic pancreatitis and pancreatic cancer. Visceral adipose tissue (VAT) of obese patients induces pro-inflammatory cytokines synthesis (TNF-α, IL- 6, adiponectin, leptin) known to be involved in pancreatic fibrogenesis by the activation of pancreatic stellate cells (PSC).
Aims & Methods
Aim: To study interactions between VAT from obese patients and ex-vivo pancreatic parenchyma by developing a co-culture model
Methods: We developed a 3D co-culture model. A slice of normal pancreas (300 µm) was cultured with 0.4g of VAT from obese patients embedded in a collagen gel layer. Culture was realized under normoxemic conditions (21% O2) and incubation time ranged from 24h to 48h. Morphological analysis of pancreas and VAT were performed at baseline, 24h and 48h. Cell differentiation (CK7, insulin), apoptosis (caspase 3), proliferation (Ki-67) and PSC activation (smooth muscle actin (SMA)) were assessed using immunostaining. Adiponectin and leptin were measured by ELISA method in the culture media. Control experiments were pancreas slice culture and VAT culture alone.
Results: 11 co-cultures were performed: 3 for 24h, 8 for 48h. Pancreatic necrosis at 24h and 48H were 30% [0- 70] and 37% [5-100] for pancreas culture versus 44% [0-80] and 62% [10- 100] for co-cultures, respectively. Necrosis was higher at 48h in co-cultures ($p = 0.024$). In co-cultures, we observed an increase of 1/ SMA expression in PSC, 2/ number of duct cells in apoptosis or proliferation, 3/ insulin expression in the Langerhans islets. Leptin and adiponectin concentrations were high in VAT culture and very low in pancreas culture. After 24h of co-culture, adiponectin concentration decreased in co-cultures compared to VAT culture ($p = 0.016$). At 24h and 48h of co-culture, leptin concentration compared to VAT culture decreased ($p < 0.05$).
Conclusion: This model is the first co-culture model between VAT and human pancreas tissue. It validated the lipotoxic role of VAT from obese patients on pancreatic tissue by altering pancreatic cells population (duct cells, Langerhans islet, PSC). It obtained reproducible results and was able to underline the interactions between these two tissues through the cytokines secretions. This new method could permit to clarify the physiopathology of obesity and metabolic syndrome in pancreatic diseases.
Disclosure of Interest: None declared

P0082 PANCREATIC EXOCRINE FUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Introduction: An exocrine pancreatic insufficiency has been demonstrated to be present in about 50% of type 1 and 30- 50% of type 2 diabetes mellitus (T2DM) cases. However, the significance of an exocrine pancreatic dysfunction in DM has recently been questioned.
Aims & Methods: The aim of our study was to assess the prevalence of exocrine pancreatic dysfunction in T2DM.
Methods: Consecutive patients with type 2 DM treated in our clinic were prospectively recruited into the study. Exocrine pancreatic insufficiency was diagnosed by fecal elastase-1 (FE1) determination. All patients underwent abdominal ultrasound and pancreatic diabetes cases were excluded.
Results: One hundred eighty four patients (91 male, 93 female, mean age 61.74 ± 17 years) were recruited in the study. FE1 was abnormal in 37 patients, 12 patients had non-insulin treated T2DM and 25 patients insulin-treated T2DM. The severity of exocrine insufficiency was mild in 29 and severe in 8 patients. The FE1 level was not correlated with HbA1c ($p = 0.487$), the duration of DM ($p = 0.88$), age ($p = 0.907$), BMI ($p = 0.157$), pancreatic steatosis ($p = 0.528$) or the presence of microvascular complications of DM ($p = 0.465$).
Conclusion: Exocrine pancreatic insufficiency is less frequent in type 2 DM, than in previous study, probably because pancreatic diabetes cases were excluded. Exocrine pancreatic insufficiency was not associated with the duration of DM, BMI, HbA1c level, pancreatic steatosis or the presence of microvascular complications of DM.
Disclosure of Interest: None declared

P0083 BETAINE ATTENUATES ALCOHOLIC PANCREATIC STEATOSIS THROUGH DOWN-REGULATION OF STEROL REGULATORY ELEMENT BINDING PROTEIN-1C

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Introduction: Growing studies have shown that chronic alcohol consumption caused pancreatic steatosis. However, medical interventions for alcoholic pancreatic steatosis have not been extensively investigated. Betaine was found to alleviate alcoholic fatty liver disease in multiple studies. In the present study, we investigated the effect of betaine on alcoholic pancreatic steatosis and its mechanism.
Aims & Methods: 45 male Wistar rats were randomized into control, alcohol and alcohol + betaine group with 15 animals in each group. Rats in the three groups were given free access to distilled water, ethanol (25%, v/v) and ethanol (25%, v/v) plus betaine (1%, w/v), respectively, for six months. Morphological changes of the pancreatic acinar cells were identified by hematoxylin-eosin staining, oil red O staining and transmission electron microscope. Pancreatic triglyceride (TG) and total cholesterol (TC) contents were measured by enzymatic colorimetric assay. Serum adiponectin levels were determined by enzyme-linked immunosorbent assay. The protein and mRNA expression of pancreatic adiponectin receptor-1 (AdipoR1), AdipoR2, sterol regulatory element binding proteins-1c (SREBP-1c), and SREBP-2 were determined by immunohistochemistry (IHC), Western blot (WB) and quantitative real-time PCR (qRT-PCR). The effect of betaine (168 mmol/L) and/or adiponectin (0.5 µg/mL) on SREBP-

1c expression in ethanol-treated (100 mmol/L) SW1990 pancreatic adenocarcinoma cells was also assessed by WB and qRT-PCR.
Results: Alcohol-induced morphological changes of the pancreatic acinar cells, including lipid droplets, swelling mitochondria and reduced zymogen granules, were attenuated after betaine treatment. Compared with control group, pancreatic TG level in ethanol group was markedly increased by 90.5% ($P<0.01$). Interestingly, betaine treatment dramatically reduced pancreatic TG level of alcoholic rats by 39.3% ($P<0.05$). However, pancreatic TC content was similar among the three groups ($P>0.05$). Serum adiponectin level in alcohol-fed rats was significantly decreased by 66.5% ($P<0.01$) when compared to that in control group and was greatly increased by 148.6% after treatment with betaine ($P<0.01$). Immunohistochemical staining showed that pancreatic AdipoR1 expression was dramatically down-regulated after ethanol exposure and was up-regulated to control level after betaine treatment. Moreover, pancreatic SREBP-1c expression was elevated in alcohol group but remained at control level after treatment with betaine. Nevertheless, no significant difference was shown in pancreatic AdipoR2 and SREBP-2 expression by IHC among the three groups. The immunohistochemical staining results were further confirmed by qRT-PCR and WB. *In vitro*, betaine or/and adiponectin significantly suppressed up-expression of SREBP-1c induced by ethanol with the maximum inhibitory effect achieved when they were given in combination.
Conclusion: Betaine attenuated alcohol-induced pancreatic steatosis probably by suppressing SREBP-1c activation and this effect of betaine was partly attributed to the restoration of pancreatic adiponectin signaling as well as the direct action of betaine on pancreatic SREBP-1c.
Disclosure of Interest: None declared

P0084 CELL DAMAGE INDUCED BY CHENODEOXYCHOLATE ON PANCREATIC DUCTAL EPITHELIAL CELLS CAN BE AMELIORIATED BY URSODEOXYCHOLATE PRETREATMENT

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Introduction: Our previous results showed that high concentration of chenodeoxycholate (CDC) strongly inhibits ion transporters via destruction of mitochondrial function in guinea pig pancreatic ductal epithelial cells (PDECs). Ursodeoxycholic acid (UDC) has been reported to protect mitochondria against hydrophobic bile acids and have antiapoptotic effect.
Aims & Methods: The aim of this study was to investigate the effect of UDC on CDC-induced cell damage.
Intra-interlobular ducts were isolated from the pancreas of guinea pig. Ducts were then pretreated with UDC (0.1 mM and 0.5mM) for 5 h and 24 h and changes in intracellular Ca^{2+}concentration $[Ca^{2+}]_i$, ATP level $[ATP]_i$, pH $[pH]_i$ and mitochondrial permeability transition pore (MPTP) opening were measured by microfluorometry. Mitochondrial transmembrane potential (MTP) was studied by confocal microscopy. Expressions of bile acid transporters were analysed by reverse transcriptase PCR (RT-PCR). Morphological changes of mitochondria were investigated by transmission electron microscopy. We also developed a CDC induced pancreatitis model in rats. Rats were fed with 250 mg/kg UDCA for 2 weeks then pancreatitis was induced by intraductal administration of 0.1% CDC.
Results: 5 h pretreatment with 0.1 or 0.5 mM UDC and 24 h pretreatment with 0.1 mM UDC did not significantly influence the effect of 1 mM CDC on duct cells. However, 24 h pretreatment with 0.5 mM UDC significantly reduced the rate of ATP depletion, mitochondrial injury, MPTP opening and the decrease of MTP induced by 1 mM CDC. In addition, 0.5 mM UDC prevented the inhibitory effect of CDC on the acid-base transporters, however, had no effect on the CDC-induced calcium signaling. mRNA expression of Slc10A1 and A2 was detected in the ducts by RT-PCR. Animal experiments showed, that UDCA fed group had less severe pancreatitis in CDC induced pancreatitis model.
Conclusion: Our results indicate that UDC administration protects the bile-induced mitochondrial injury which may represent a novel therapeutic option in pancreatitis.
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Disclosure of Interest: None declared

P0085 ANALYSIS OF THE STRUCTURAL AND SENSORY INNERVATION IN THE MOUSE PANCREAS

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Introduction: Human pancreatic cancer/PCa and chronic pancreatitis/CP are characterized by neural hypertrophy, neural sprouting, and reduced sympathetic innervation. However, our knowledge on the innervation of current murine models of PCa and CP and even of normal mouse pancreas is very scarce.
Aims & Methods: In this study, we aimed to systematically analyze the structure, distribution and quality of nerves in the mouse pancreas. Whole pancreata derived from 6-8-week-old C57BL/6J mice (n = 10) were paraffin-embedded and entirely sectioned into 3µm consecutive sections from the anterior to the posterior/retroperitoneal plane. All sections were immunostained with the pan-neural-marker PGP 9.5, with the sensory fibre markers substance-P/SP and calcitonin-gene-related-peptide/CGRP and were subject to systematic morphometric analysis.
Results: Nerves enter the mouse pancreas around pericapsular lymphoid structures and penetrate into the tissue along vessels and interlobular septae. The size and the density of nerves in the pancreatic head and corpus were significantly greater than in the pancreatic tail. The majority of nerves were localized in the anterior and posterior surface of the head and the anterior surface of the corpus. The proportion of sensory fibres was ca. 8% of all nerve fibres in the mouse pancreas and did not vary between the head, corpus and tail. 74% of sensory fibres were localized in the pancreatic head, 19% in the corpus and 7% in the tail.
Conclusion: Murine pancreatic head has the highest density of pancreatic nerves. Overall, due to its intraperitoneal and perilymphoid localization, the mouse pancreas bears a substantially different structural innervation pattern when compared to the human pancreas.
Disclosure of Interest: None declared

P0086 FLUID AND HCO3- SECRETION AND CFTR ACTIVITY ARE INHIBITED BY CIGARETTE SMOKE EXTRACT IN GUINEA PIG PANCREATIC DUCTAL CELLS

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Introduction: Smoking represents an independent risk factor for the development of chronic pancreatitis (CP). It is well documented that secretion of pancreatic ductal alkaline fluid (which is regulated mostly by the anion exchanger and CFTR) is diminished in CP. In this study we would like to understand whether smoking has any effects on pancreatic ductal fluid and HCO_3^- secretion.
Aims & Methods: Intra/interlobular pancreatic ducts were isolated from guinea pig pancreas. Cigarette smoke extract (CSE) was prepared by smoking of 30 cigarettes into 20ml distilled water by a smoking machine. Three different doses (20, 40 and 80µg/ml) were diluted using the stock solution. Basal and forskolin-stimulated fluid secretion was measured by video microscopy. Intracellular pH and Ca^{2+} concentration were evaluated by microfluorometry. Luminal anion exchange activity was determined by the chloride withdrawal technique using microperfusion. CFTR currents were detected by whole-cell configuration of patch clamp technique.
Results: CSE dose dependently decreased forskolin-stimulated fluid secretion in guinea pig pancreatic ducts, bicarbonate secretion (20µg/ml by 17.3%, 40µg/ml by 40.5%) and forskolin-stimulated Cl^- current of CFTR Cl^- channel (20µg/ml by 44.5%, 40µg/ml by 69.3% and 80µg/ml by 81.3%). Moreover, CSE induced dose-dependent intracellular calcium elevation suggesting that some of the inhibitory effects may be regulated by calcium signalling.
Conclusion: CSE inhibits pancreatic ductal fluid and HCO_3^- secretion and the activity of the CFTR which may play role in the smoke-induced pancreatic damage. This study was supported by OTKA, MTA and NFÜ/TÁMOP.
Disclosure of Interest: None declared

P0087 ABSENCE OF SEROTONIN SIGNIFICANTLY ELEVATES PANCREATIC EPITHELIAL FLUID AND BICARBONATE SECRETION IN MICE

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Introduction: Serotonin (5-hydroxytryptamine, 5-HT) is a potent bioactive molecule, which regulates zymogen secretion in pancreatic acinar cells and inhibits pancreatic ductal epithelial secretion. Recently it was demonstrated that tryptophan hydoxylase-1 (TPH-1) knock-out mice, which lack peripheral 5-HT, develop less severe acute pancreatitis (AP) compared to wild type (WT) controls. Decreased pancreatic fluid and bicarbonate secretion can lead to more severe AP, however the pancreatic ductal secretion of TPH-1 knock-out mice has not been evaluated, which might contribute to the protection against AP.
Aims & Methods: Our aim was to evaluate the pancreatic ductal secretion in TPH-1 knock-out and WT mice.
Intra/interlobular pancreatic ducts were isolated from the pancreas of TPH-1 knockout and WT mice. *In vitro* pancreatic ductal fluid secretion has been evaluated using videomicroscopy. Bicarbonate secretion of pancreatic ductal epithelial cells was measured by microfluorimetry.
Results: *In vitro* pancreatic ductal fluid secretion was significantly elevated in TPH-1 knock-out mice compared to WT controls. Basolateral administration of 20mM NH_4Cl revealed that the activities of the apical Cl^-/HCO_3^- exchanger (CBE) and the basolateral Na^+/HCO_3^- cotransporter and Na^+/H^+ exchanger were significantly elevated in TPH-1 knock-out mice. The acidification caused by basolateral administration of dihydro-4,4'-diisothiocyanostilbene-2,2'-disulfonic acid (H_2DIDS) and amiloride was markedly increased in TPH-1 knock-out mice confirming the increased activity of the apical HCO_3^- secretion. The administration of serotonin significantly decreased the activity of the acid/base transporters in TPH-1 knock-out and WT ductal epithelial cells. As a further step we provided evidence that the Cl-/HCO3- exchanger is crucially important in the elevated ductal secretory process important in the elevated ductal secretory processesion, since. T the rate of pHi recovery was significantly elevated in TPH1-/- mice from the intracellular alkalization-caused byafter Cl-withdrawal from the lumeinal space of the microperfused pancreatic ducts
since the rate of pHi recovery significantly elevated in TPH1-/- mice from the intracellular alkalization-caused by Cl- withdrawal from the luminal space of the microperfused pancreatic ducts.
Conclusion: These findings indicate that the fluid and bicarbonate secretion is significantly increased in the absence of serotonin, which might contribute to the decreased severity of AP in TPH-1 knock-out mice.
Disclosure of Interest: None declared

P0088 VITAL IMPORTANCE OF THE DISSEMINATION OF IAP/APA GUIDELINES: DRAMATIC RESULTS DURING THE VALIDATION STUDY ON A NATIONWIDE COHORT

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Introduction: The IAP/APA evidence-based (EBM) guidelines for the management of acute pancreatitis(AP) have been published in 2013. Unfortunately in many countries, especially in Eastern and Central Europe, it has not been translated to national languages and no EBM guidelines are available so far. The Hungarian Pancreatic Study Group (HPSG) has established a national registry in 2011 for prospective data collection of patients suffering from different pancreatic disorders,including AP.
Aims & Methods: Our aim was to summarize the Hungarian cohort and importantly, assess and validate the usefulness of the IAP/APA guidelines. 580 patients with AP have been enrolled from 23 centers.
Results: The diagnosis of AP was made according to the 2/3 rule. 322 males and 258 females with mean age of 58.4 ± 16.5 were enrolled.The most common cause of AP was biliary disease (44%)followed by regular alcohol consumption or dietary mistake (26%). 61.9% of the patients had mild, 29.6% moderate, whereas 8.5% severe pancreatitis. Concerning the intravenous fluid therapy, only 41% of the patients received 2500-4000 ml of fluids during the first 24 hours.The mortality was only 0.51% in this group, however, it was increased by 4 times among those patients who received either more or less fluid. In terms of the enteral feeding, 31% of patients with severe pancreatitis did not receive it. The mortality rate in this group was unacceptably high(42.9%) compared to those patients who received the right treatment(19.3%).
Conclusion: Proper utilization of the IAP/APA EBM guidelines could save thousands of lives. It is vitally important to make the guidelines available in all languages of the countries.
Disclosure of Interest: None declared

P0089 EARLY DIFFERENTIAL DIAGNOSIS OF MILD ACUTE PANCREATITIS FROM MORE SEVERE FORMS

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Introduction: Acute pancreatitis (AP) is characterized by a wide range of clinical courses, varying from interstitial edema to pancreatic necrosis. This determines the relevance of simple and fast criteria for early detection of the disease severity.
Aims & Methods: The aim is to determine the effectiveness of rating scales for early stratification of AP. The severity of patient's condition was estimated in 24 hours with the help of such rating scales as BISAP, HAPS, SOFA, SIRS, US scale [1]. The severity of AP was detected in accordance with the classification of Atlanta 2012 in 48-72 hours. Balthazar-Ranson scale was used at the same time period. ROC-analysis of the scales was performed with the calculation of the area under the operating characteristic curve (AUC).
Results: There were 61 patients with AP (mean age 44.0 ± 1.7, 57.3% male), of which 24.7% were classified as mild, 34.4% as moderate & 40.9% as severe. Determination of mild AP according to the BISAP ≤ 1 и US scale ≤ 3 was characterized by high accuracy (AUC (95% confidence interval) 0.77 (0.66–0.87) & 0.90 (0.82–0.98) respectively), sensitivity (71.1 & 81.0% respectively) and negative predictive value (48.0 & 66.6% respectively). The scales HAPS ≤ 1, SOFA ≤ 3 and SIRS ≤ 1 had smaller AUC ($p < 0.05$) (0.62; 0.62 & 0.66 respectively), lower quality of determining of mild AP (60.0; 68.8 & 51.1% sensitivity respectively). They also had smaller negative predictive value (35.7; 36.6 & 35.2% respectively).
Conclusion: The BISAP scale and US scale are reliable methods for early detection of mild AP (in 24 hours). Their high positive prognostic values (81.6 & 88.8%) allow to identify on early stage the patients that are not needed intensive care. This could save significant costs for the hospital.

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2. This work was supported by a grant from the Russian Science Foundation № 14-15-00809.

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P0090 SEVERITY PATTERN OF RECURRENT ACUTE PANCREATITIS. IS IT STABLE?

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Introduction: Acute pancreatitis (AP) varies from mild, to moderately-severe and severe forms, the last with complications and high mortality rate. Knowledge of its natural course and recurrence is limited.
Aims & Methods: The aim of this study was to evaluate the severity pattern of recurrent AP and compare the clinical outcomes to those with a single episode. We performed a retrospective study on 1079 patients (58.7% male, 41.3% female) with mean age of 55 ± 16 years old admitted in our unit from 2006 to 2014 with acute pancreatitis. We compared patients with recurrent AP to those who had a single episode. We looked to the mortality, the severity of AP, the trend of the recurrences and made an overview analysis.
Results: In the 9-year analysis, 995 patients (92.2%) were admitted with a single episode of AP and 84 (7.8%) patients had a recurrent form. The readmissions varied from 2 episodes in most cases (78.5%) to 3(13.1%), 4 (4.8%), 5(1.2%) and 6 episodes (2.4%). The severity pattern for the majority of AP readmission was mostly unchanged, 70% of them presented at recurrences a similar form with the initial episode, 14% had a worse outcome and 16% had a milder form. The mortality rate in patients experiencing a single episode of AP was 3.7%, as compared to 0% in patients with recurrent AP ($p = 0.0096$). Recurrent episodes of AP seem to be protective against multiple organ failure (odds ratio 0.056, 95% CI 0.0034-0.928, $p = 0.0442$). Regarding the etiology, in patients that had only 2 recurrences the most common cause was biliary (50.7%) followed by alcohol (33.8%) and other etiologies (15.5%) whereas in patients with 3 or more recurrences, the predominant cause was alcohol (66%) as compare to non-alcoholic etiologies (33%).
Conclusion: Patients that have recurrent form of AP seem to have lower risk of clinically severe course. The severity pattern remains stable in most cases of recurrent AP. Furthermore, the mortality of these patients seems to be lower as compared to that of patients with a single episode of AP.
Disclosure of Interest: None declared

P0091 IMIPENEM PROPHYLAXIS FOR PREDICTED SEVERE ACUTE PANCREATITIS - PRELIMINARY RESULTS OF A RANDOMIZED CLINICAL TRIAL

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Introduction: Infected necrosis is a serious complication of acute pancreatitis leading to a mortality rate of about 40%[1]. Although prophylactic antibiotics are not recommended, meta-analytic data show that imipenem significantly reduces the rate of infected necrosis[1].
Aims & Methods: The aim of our study is to evaluate the prophylactic use of imipenem in patients with predicted severe acute pancreatitis. We conducted a prospective randomized trial in a tertiary care setting in Rijeka. Patients with AP and an APACHE II ≥ 8 were randomized to receive either imipenem 500 mg i.v. three times daily for the first ten days or an identical placebo. Exclusion criteria included age < 18 years, any infection present at admission, chronic pancreatitis, active malignancy, immunodeficiency, post-surgical patients, pregnant and breastfeeding women and patients unwilling to participate in the study. All patients received early enteral nutrition administered via a nasojejunal tube. Concomitant treatment was similar in both groups. All patients had an abdominal CT scan performed between days 3 to 7, and in cases of clinically suspected infected pancreatic necrosis.
Results: Forty-seven consecutive patients were randomized. Twenty-three received imipenem and 24 received placebo. Three patients died in the imipenem group, while two patients died in the placebo group ($p = 0.667$). There were no differences in the occurrence of infected necrosis, with 2 vs. 3 cases, respectively. Other local complications were present in 7 and 13 patients ($p = 0.142$), while persistent organ failure was present in 4 and 5 patients ($p = 1.00$) in the imipenem and placebo group, respectively. Other infection were detected in 2 patients receiving imipenem and 5 patients on placebo ($p = 0.416$).
Conclusion: Preliminary data showed no significant beneficial effects of prophylactic imipenem use in patients with predicted severe acute pancreatitis.

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Disclosure of Interest: None declared

P0092 A SYSTEMATIC REVIEW OF ENTERAL NUTRITION FORMULATIONS FOR ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) is a common disease with increasing incidence. Severe cases are characterized with high mortality and despite improvements in intensive care management, there is still no specific treatment that relevantly benefits clinical outcome.
Aims & Methods: To assess effects of different enteral nutrition (EN) formulations in patients with AP. We conducted searches of Medline, Embase, Central, and SCI-E for RCTs assessing use of a specific EN formula compared to control (other EN formula, TPN, placebo, or no intervention). We assessed the following outcomes: mortality, organ failure, and local septic complications (LSC).
Results: Twenty-five RCTs with a total of 1979 patients were included. Immunonutrition significantly decreased mortality ($P = 0.005$), but subgroup analysis comparing immunonutrition to another EN did not confirm this finding. Probiotics did not confirm any significant effect, however sensitivity analysis by exclusion of one trial with inconsistent results showed decrease in mortality ($P = 0.02$) and LSC ($P = 0.002$), but not organ failure. Semi-elemental EN reduced mortality ($P = 0.002$), organ failure ($P < 0.00001$), and LSC ($P < 0.00001$). Few trials evaluated polymeric and fibre-enriched formulas, showing no significant effect. Any EN compared to TPN confirmed reduced mortality ($P < 0.0001$), organ failure ($P < 0.00001$) and LSC ($P < 0.00001$), and any EN compared to no intervention was associated with lower mortality ($P = 0.01$).
Conclusion: Whether supplementation of EN with potential immunomodulatory agents leads to beneficial effects is still debatable. Studies assessing probiotics yielded inconsistent results, therefore we do not support the routine use of these formulations in clinical practice, but further research is required. EN is significantly more efficient than TPN and no nutritional support.
Disclosure of Interest: None declared

P0093 LOW MOLECULAR WEIGHT HEPARIN TREATMENT OF ACUTE SEVERE PANCREATITIS: A RANDOMIZED, CONTROLLED STUDY

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Introduction: Severe acute pancreatitis which constitutes 20-30% of all acute pancreatitis, may cause pancreatic necrosis, persistent organ failure and mortality. Beginning and progression of acute pancreatitis is accompanied with systemic inflammatory cascade activation and pancreatic microcirculation disturbance. Heparin inhibits inflammatory cascade, and improves pancreatic microcirculation. The purpose of this study is to determine the effect of low molecular weight heparin (LMWH) in the prevention of pancreatic necrosis in severe acute pancreatitis.
Aims & Methods: A total of sixty-eight moderately severe and severe acute pancreatitis patients were randomised to receive conventional therapy or conventional therapy plus LMWH therapy. LMWH was administrated 1 mg/kg by subcutaneous injection two times per day between 1th and 7th days. Revised Atlanta criteria are used in the diagnosis. Imrie Score, HAPS (Harmless Acute Pancreatitis Score), Balthazar computed tomography (CT) score are evaluated. Patients with coagulation disorders, severe comorbidities, using clopidogrel or warfarin, under hemodialysis, pregnant and lactating women are excluded.
Results: The mean age $\pm$ SD of the patients (31 male and 37 female) were 52.1 ± 19.7 years (range; 17-100 years). There were 34 (50%) patients in the LMWH group and 34 (50%) patients in the control group. The etiology of these patients included biliary diseases in 43 patients (63.2%), hyperlipidemia in 4 (5.9%), and other in 9 (13.3%). Etiology can not be defined in 12 (17.6%), On admission, all the clinical and laboratory parameters and Balthazar CT score in the two groups were similar. After one week of follow-up, pancreatic necrosis developed in 3 (8.8%) patients in the LMWH group and 9 (26.4%) in the control group (p:0.049). Complications were observed in 6 (17.6%) patients of LMWH group and 11 (32.4%) patients of controls group. No haemorrhagic complications occurred. Three patients died in the control group, while no death occured in LMWH group (p: 0.072).
Conclusion: LMWH treatment is safe and provides a tendency for better prognosis in severe acute pancreatitis.
Disclosure of Interest: None declared

P0094 HEMORRHAGE COMPLICATING THE COURSE OF SEVERE ACUTE PANCREATITIS

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Introduction: Course of severe acute pancreatitis (SAP) can be complicated by hemorrhage, which is associated with poor outcome.
Aims & Methods: 183 patients (mean age 39.6 ± 13 years, M:F 2.6:1) of SAP were evaluated prospectively ($n = 86$) and retrospectively ($n = 97$) for hemorrhagic complications. Hemorrhagic complications were categorised based upon the site (luminal or intra-abdominal), timing (occurring prior to or after an intervention) and severity (minor or major, depending on the need for blood transfusion). Data was analysed using SPSS version 22 and outcome measures studied were predictors of bleed, mortality and final outcome.
Results: 24 (13.1%) patients had hemorrhagic complications; 12 intra-abdominal and 12 intraluminal. 13 had a major and 11 had minor bleed; 16 patients bled before and 8 after intervention (radiological 3, surgical 5). The mean duration of pancreatitis prior to bleed was 27.0 ± 27.2 days. Predictors of bleed on univariate analysis were male sex ($p = 0.014$), organ failure ($p = 0.008$), venous thrombosis ($p = 0.033$), infected necrosis (0.001) and systemic sepsis (0.037). On multivariate analysis, infected necrosis ($p = 0.015$, OR 5.55) was a significant risk factor. Radiological drainage was associated with decreased risk of bleeding (45.8% vs 54.4%; $p = 0.000$). Need for surgery (50% vs 12.6%, $p = 0.003$), intensive care stay (7.4 ± 7.9 vs 5.4 ± 5.2 days; $p = 0.001$) and mortality (41.7% vs 10.7%; $p = 0.000$) were significantly higher in bleeders. 7/13 of major bleeders had pseudoaneurysms. 4/12 with luminal bleed had hollow viscus erosion, all needed surgery. CT severity index and surgical intervention, were significantly associated with intra-abdominal bleed. 7/12 intra-abdominal bleeders required surgical intervention. Organ failure, presence of pseudoaneurysm and surgical intervention were associated with major bleed. No significant factor could be identified for post-intervention bleed.
Conclusion: Infected necrosis predisposes to hemorrhage. Luminal bleed may be indicative of erosion into the adjacent viscera. Pseudoaneurysms were associated with major bleeding.
Disclosure of Interest: None declared

Abstract number: P0095

	AP	Severe AP	Mild AP	Control
Fe	6.44 ± 5.44*	7.33 ± 6.03*	5.74 ± 4.98*	20.81 ± 7.47
Transferrin	1.69 ± 0.45*	1.61 ± 0.43*	1.76 ± 0.46*	2.60 ± 0.42
Ferritin	518.32 ± 277.39*	603.20 ± 281.82*	451.32 ± 261.82*	118.11 ± 94.38
TS	16.74 ± 18.78*	21.51 ± 25.87#	12.97 ± 9.61*	32.56 ± 12.81
ROM	239.91 ± 142.17*	219.77 ± 150.85#	255.82 ± 136.94#	368.97 ± 72.54
TOC	0.05 ± 0.06*	0.06 ± 0.06$^{0\ a}$	0.03 ± 0.05*	0.12 ± 0.08
FRAP	1472.94 ± 513.83*	1637.25 ± 559.25#	1343.23 ± 447.80#	1012.36 ± 187.76
TAC	1.55 ± 0.76	1.77 ± 0.64	1.38 ± 0.81	1.76 ± 0.30

Results are presented as mean ± standard deviation.*$P<0.001$, #$P<0.01$, $^0P<0.05$ compared to controls,[a]$p < 0.05$ compared mild to severe AP.

P0095 IRON METABOLISM AND OXIDATIVE STRESS IN ACUTE PANCREATITIS PATIENTS

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Introduction: It is suggested that oxidative stress (OS) may play a role in the development of pancreatic injury and systemic complications during acute pancreatitis (AP). Iron is one of important payers in the redox state. The data about iron metabolism and its role during AP is limited to some experimental findings. To our knowledge this study is the first evaluating the disturbance of iron metabolism as well as its associations with oxidative stress in the early phase of AP.
Aims & Methods: The study was addressed to find out possible disturbances of iron metabolism and its interactions with oxidative stress during the early phase of acute pancreatitis. Blood samples were collected from patients with mild (n = 22) and severe (n = 17) AP, and a group of healthy individuals (n = 26). Serum oxidative stress markers measured in serum included Reactive Oxygen Metabolites (ROM) and Ferric Reducing Antioxidant Power (FRAP), Total Oxidative Capacity (TOC) and Total Antioxidative Capacity (TAC). Serum ferritin, iron (Fe) and transferrin were measured and the iron saturation of transferrin (TS) was calculated.
Results: A disturbed iron status in all pancreatitis groups was found. Iron, transferrin and the iron saturation of transferrin were significantly lower and ferritin was significantly higher in all AP groups. The serum oxidative stress parameters reflecting the lipid peroxidation process ROM and TOC showed significantly decreased levels in the AP group as well as mild and severe AP groups comparing to controls. TOC decreased more in mild AP patients than in severe AP patients, the difference was significant. One of the measurements of total antioxidant capacity (FRAP) was increased in all AP groups, compared with the control group. TAC showed no significant changes in the groups. There was a significant correlation between ROM with transferrin (Spearman's correlation coefficient 0.44, p = 0.00) and with ferritin (Spearman's correlation coefficient 0.32, p = 0.008), between FRAP and transferrin (Spearman's correlation coefficient 0.38, p = 0.001) and ferritin (Spearman's correlation coefficient 0.52, p = 0.000). There was a significant correlation between TOC and TS (Spearman's correlation coefficient 0.352, p = 0.006) as well as TOC and Fe (Spearman's correlation coefficient 0.346, p = 0.007).
Conclusion: The iron metabolism is disturbed and the oxidative stress markers are altered during the early phase of acute pancreatitis. The disorders of iron metabolism are associated with the changes of oxidative stress markers.
Disclosure of Interest: None declared

P0096 IMAGING OF PANCREATIC CYSTIC LESIONS WITH CONFOCAL LASER ENDOMICROSCOPY: AN EX VIVO PILOT STUDY

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Introduction: The differential diagnosis of pancreatic cystic lesions (PCLs) is an increasingly common clinical challenge. A needle-based confocal laser endomicroscopy probe (nCLE, Cellvisio, Maura Ken Technologies, France) through a 19 G needle has been shown to be helpful for differential diagnosis of PCLs by imaging the cyst wall during endoscopic ultrasound-fine needle aspiration. However, clinical experience is still limited, and better image definition and characterization of the cyst wall from different lesions are needed.
Aims & Methods: The aim of this pilot study was to develop a reference standard in CLE characterization of various types of PCLs. Patients who underwent surgery of a PCL at Mass General Hospital were enrolled to study if they gave their consent. During surgery, intravenous fluorescein (2.5 ml of 10%) was injected just prior to the ligation of blood vessels supplying the pancreas. The injected fluorescein was expected to retain for at least an hour after the injection. The fresh specimens were transected along the long axis to fully expose the luminal surface. A Gastroflex-UHD CLE probe (pCLE) was used manually to acquire images directly from the surface of the cyst wall. The cyst walls were screened longitudinally in 2 millimeter ranges by the tip of the probe and sequences recorded for a total 15 minutes. The entire resected specimen subsequently underwent cross sectional histology. All recorded data were analyzed by two investigators for predefined and original image findings of PCLs.
Results: During the 4-month study period, 10 cases (4 male and 6 female) were recruited into the study. The median age of the patients was 77 (range, 33-88). All patients underwent surgery because of a mucinous cyst with worrisome features or a symptomatic PCL. The median duration between fluorescein injection and confocal imaging was 55 minutes (range, 40-90). Imaging was successful in all patients, and various papillary projections with a vascular core and mucinous epithelial borders were visualized in 8 of the patients. In 2 patients, typical vascular network were visiualized without papillary structures. The conventional pathological examination confirmed 6 cases with Intraductal Papillary Mucinous Neoplasm (IPMN), 2 cases with Mucinous Cystic Neoplasm (MCN) and 2 cases with serous cysts. Pancreatic ductal adenocarcinoma arising in high-grade dysplasia was found in one patient, and high-grade dysplasia in 2 patients. The sensitivity and specificity of ex-vivo confocal imaging to demonstrate papillary structures was 100%.
Conclusion: Pancreatic cyst epithelial wall can be visualized successfully by pCLE in *ex vivo* surgical specimens. Various papillary projections have been seen in all cases of IPMN and MCN in this examination. The variety of images which have been acquired in this model will be helpful for the definition of similar structures during *in vivo* examination of pancreatic cysts. To develop a reference standard for definition of IPMN subtypes and for grade of differentiation would be the ultimate aim of this model.
Disclosure of Interest: None declared

P0097 ADIPOSE TISSUE-DERIVED HORMONS AS PROGNOSTIC INDICATORS IN RESECTABLE PANCREATIC CARCINOMA PATIENTS

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Introduction: Prediagnostic plasma adiponectin levels have been inversely associated with an elevated risk of pancreatic cancer (1). We recently demonstrated that in patients with pancreatic cancer (PC) adiponectin levels are inversely correlated with tumor size and tumor grading, identifying a potential link between adipokines and tumor proliferation (2). To date, however, no data on the possible prognostic significance of adipokines in patients with PC have been shown.
Aims & Methods: The aim of the study was to evaluate plasma concentrations of adiponectin and leptin in PC patients and to analyze their possible prognostic value in predicting relapse-free and overall survival. Baseline levels of adiponectin and leptin were determined in 37 consecutive patients with resectable pancreatic adenocarcinoma followed-up from time of surgery for 28 months or until relapse. 37 control subjects were individually matched to case patients by age, sex and BMI. Survival analysis used the Kaplan-Meier curve and the Cox proportional hazards model.
Results: Adiponectin concentrations were lower in PC patients versus control subjects (8.1 vs 10.8. mg/mL, $p<0.01$) and inversely correlated with tumor size (r = -0.715, $p<0.05$). The mean leptin levels were not significantly decreased in PC patients ($p = 0.465$). However, the levels of leptin were significantly decreased in cachectic PC patients (N = 19) compared with healthy controls (53.9± 25.5 *vs* 87.0 ± 23.9 ng/ml $p < 0.001$). Multivariate analysis showed that, beside tumor size, low adiponectin levels were the only independent predictor of recurrence (beta = 0.563, $p<0.001$). High adiponectin levels were associated with an increased overall survival (Cox F test = 2.213, $p<0.05$) and a reduced recurrence rate (Cox F test = 2.913, $p = 0.01$) compared to patients with low adiponectin levels.
Conclusion: This study suggests, for the first time, that serum adiponectin levels might represent a prognostic indicator in patients with resectable PC. Our results support the hypothesis linking adipokines levels to malignant tumor growth (3) and suggest that adipokines might exert an adjunctive tool in risk prediction and management of pancreatic adenocarcinoma patients.

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P0098 FOLFIRINOX IN PANCREATIC CANCER – EXPERIENCE WITH A NOVEL SCHEME OF INDUCTION, MAINTENANCE, TREATMENT PAUSE AND RE-INDUCTION

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Introduction: Chemotherapy regimens for locally advanced or metastatic pancreatic ductal adenocarcinoma (PDAC) have changed since the introduction of polychemotherapies such as FOLFIRINOX (5-fluoruracil (5FU/LV), oxaliplatin, irinotecan and leucovorin) which confer a significant survival benefit compared to gemcitabine-based monotherapy. Increased toxicity, mainly sensory peripheral neuropathy, limits its use and the number of applied chemotherapy cycles. In analogy to chemotherapy strategies in colon cancer we used a scheme of induction, maintenance, treatment pause and re-induction therapy in locally advanced or metastatic PDAC to alleviate such toxicities and increase the number of applied cycles. In this retrospective study we report our experience with this scheme.

Aims & Methods: We retrospectively identified all patients who received FOLFIRINOX for metastatic or locally advanced PDAC in our center using the induction, maintenance, treatment pause and re-induction scheme until March 2015. Response to therapy and toxicity of the treatment were assessed.

Results: Eleven patients met the inclusion criteria. The median number of cycles of induction therapy including all three active substances or only 5FU/LV combined with oxaliplatin was 6 (range 5-13). All patients had stable disease or partial response and received maintenance therapy consisting of 5FU/LV with a median cycle number of 6 (2-21). Four patients had a treatment pause after maintenance therapy of median 24 weeks (8-42). Re-induction due to progressive disease during treatment pause or maintenance therapy was applied in eight patients using all three active substances or only 5FU/LV combined with oxaliplatin, with a median of 4.5 (2-7) cycles of re-induction therapy. The median time to first progression, death or loss to follow up was 10.8 months (4.1-20.7). The median time to second progression, death or loss to follow up in patients undergoing re-induction chemotherapy was 14.1 months (8.9-29). Peripheral neuropathy was clinically relevant in ten patients after induction therapy. In four of these neuropathy has subsided completely before re-induction therapy.

Conclusion: The maintenance strategy after induction chemotherapy with subsequent re-induction in patients undergoing FOLFIRINOX chemotherapy for advanced PDAC seems to be safe. It might help reduce sensory peripheral neuropathy and potentially leads to a prolonged progression-free survival.

Disclosure of Interest: None declared

P0099 USING A COMBINATION OF MOLECULAR AND CLINICAL FEATURES TO IMPROVE THE CLASSIFICATION OF PANCREATIC CYSTS: A MULTICENTER RETROSPECTIVE STUDY

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Introduction: The clinical management of patients with pancreatic cysts is currently imperfect. The recent identification of a distinct mutational profile in each of the main cyst types (SCAs, SPNs, MCNs and IPMNs) may improve the diagnosis of pancreatic cysts.

Aims & Methods: The aim of this study was to evaluate whether a combination of molecular markers and clinical information could improve the classification and management of pancreatic cysts. A multi-center, retrospective study of patients with resected pancreatic cystic neoplasms was performed. Cyst fluid was analyzed: (i) to identify subtle mutations in genes known to be mutated in pancreatic cysts: BRAF, CDKN2A, CTNNB1, GNAS, KRAS, NRAS, PIK3CA, RNF43, SMAD4, TP53, and VHL; (ii) to identify loss of heterozygozity at the CDKN2A, RNF43, SMAD4, TP53, and VHL tumor suppressor loci; and (iii) to identify aneuploidy. These analyses were performed with highly accurate massively parallel sequencing-based technologies for data acquisition and interpretation. An algorithm was used to select composite molecular markers for classifying cyst type and grade. The accuracy of these composite molecular markers was compared to that of the composite clinical markers, and to a combination of molecular and clinical markers.

Results: We analyzed 12 serous cystadenomas, 10 solid-pseudopapillary neoplasms, 12 mucinous cystic neoplasms, and 96 intraductal papillary mucinous neoplasms. The composite clinical and molecular features classified cyst type with sensitivities of 90% to 100% and specificities of 92% to 98%. The molecular marker panel correctly identified 67 of 74 patients who did not require surgery, thus potentially decreasing the number of unnecessary operations by 91%.

Conclusion: A combination of molecular and clinical markers shows promise for the accurate classification of cystic neoplasms of the pancreas and for the identification of cysts that require surgery.

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P0100 USEFULNESS OF HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) THERAPY FOR PANCREATIC CANCER

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Introduction: High-intensity focused ultrasound (HIFU) is anticipated as a new advanced therapy for unresectable pancreatic cancer (PC). HIFU therapy with chemotherapy is being promoted as new method to control local advance by ablation of the tumor, and mainly to achieve relief of pain caused by PC.

Aims & Methods: We have evaluated the therapeutic effect of HIFU therapy in locally advanced and metastatic PC. We treated PC patients by HIFU as optional local therapy as well as systemic chemo / chemo-radiotherapy, with whom an agreement was obtained in adequate IC, from the end of 2008 in our hospital. This study was approved by the ethics society of our hospital. HIFU device used is FEP-BY02 (Yuande Bio-Medical Engineering Co.LTD., China). The subjects were 90 PC patients, i.e. 54 cases in stage III, 36 cases in stage IV.

Results: All tumors were visualized by HIFU monitor system. Treatment data in Stage III and IV were as follows: mean tumor size was 33.8 vs 35.7 mm, mean treatment sessions: 2.6 vs 2.4 times, mean total treatment time: 2.2 vs 1.8 hours, mean total number of irradiation: 2595 vs 1962 shots, respectively. There was no significant difference in treatment data between two groups. The effects of HIFU therapy in Stage III and IV were the following; the rate of complete tumor ablation was 87.0 vs 75.0%, the rate of symptom relief effect was 80.0 vs 68.2%, the effectiveness of primary lesion was CR:0, PR:7, SD:38, PD:9 vs CR:0, PR:4, SD:18, PD:14, primary disease control rate (DCR) more than SD was 83.3% vs 61.1%. Comparison of mean survival time (MST) after diagnosis in Stage III and IV was 32.6 vs 16.1 months, respectively ($p < 0.01$, $p = 0.002$). MST after diagnosis in HIFU with chemotherapy and chemotherapy alone (38 patients in our hospital) was 26.7 vs 12.2 months, respectively ($p < 0.001$). Combination therapy of HIFU with chemotherapy was better result than common chemotherapy alone in Stage III.

Conclusion: This study suggested that HIFU therapy has the potential of a new method of combination therapy for PC.

Disclosure of Interest: None declared

P0101 SPECTRAL PATTERN OF DIABETES ASSOCIATED WITH PANCREATIC CANCER

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Introduction: Due to the aggressive nature of pancreatic cancer (PC), the diagnosis of an early stage is essential. In more than 80% of cases, PC is connected with paraneoplastic hyperglycemia called diabetes mellitus associated with PC (DMPC), although only 1% of recent onset diabetics (RODM) have PC.[1] The group of RODM in addition with progressive weight loss or unexplained dyspepsia is a potential screening group for sporadic PC.[1,2] Current diagnostic procedures fall short in distinguishing DMPC from the very frequent type 2 diabetes mellitus (DM2), which represents most of RODM.
Aims & Methods: To specify the differences between DMPC and DM2, we tested a new approach based on combination of spectroscopic methods. The main aim is to determine the sensitivity and specificity of these spectroscopic methods. Plasma samples collected from 23 DMPCs and 24 DM2 patients were analysed by chiroptical spectroscopy, specifically electronic circular dichroism (ECD) and Raman optical activity (ROA), which are inherently sensitive to the 3D structure of chiral molecules.[3] To obtain more structural information, the ROA and ECD measurements were supplemented by conventional infrared (IR) and Raman spectroscopies.
Results: The ECD spectra of the DMPCs generally showed not only a lower intensity profile than type 2 diabetics, but also slight changes in the spectral patterns. In the IR spectra, we also observed intensity and spectral pattern variations in the regions corresponding to protein secondary structure. The Raman and ROA spectra showed mainly α-helical peptide/protein conformation with a low content of β-structures. Other observed differences corresponded to aliphatic and saccharide/glycoprotein moieties. The spectra obtained from all four spectral methods were processed by linear discriminant analysis (LDA) showing a clear separation of DMPCs and DM2 patients. The quality of the established statistical model was confirmed by leave-one-out cross-validation where sensitivity and specificity reached 90%.
Conclusion: The results obtained in this pilot study show a high potential of the combination of chiroptical and vibrational spectroscopy as a promising tool in the identification of potential screening group for the diagnosis of early PC.

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Disclosure of Interest: None declared

P0102 OPTIMAL FOLLOW-UP AND LONG-TERM CLINICAL OUTCOME OF PANCREATIC CYSTIC LESIONS

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Introduction: It is generally accepted that cystic lesions in the pancreas (CLPs) 3 cm or less in size and without features suggesting malignancy can be managed conservatively with follow-up. However, the optimal duration and interval of follow-up for CLPs is not yet well established.
Aims & Methods: We have performed the current study to investigate the optimal duration and interval of follow-up for CLPs in clinical practice. Patients with CLPs 3 cm or less in size and without features suggesting malignancy received follow-up with computed tomography at 6, 12, 18, and 24 months and then per 12 months. A retrospective analysis with prospectively collected data was performed.
Results: A total of 205 patients with CLPs detected from 2004 to 2009 (initial mean size, 1.8 ± 0.7 cm) received follow-up during the median period of 56.6 months. Within the first 12 months of follow-up, no patients experienced the growth of cyst and three patients (1.5%) underwent surgery for the presence of symptoms related to CLPs. 11 patients (5.4%) experienced the growth of cyst after 5 years of follow-up. A total of 18 patients underwent surgery during follow-up and four malignant cysts were detected. Overall rate of malignant progression during follow-up was 2.0%. The malignant progression occurred after 48 months and 60 months of follow-up in one and three patients, respectively.
Conclusion: The results of this study provide the evidence of the optimal duration and interval of follow-up for CLPs in clinical practice. Long-term follow-up of more than 5 years should be performed because of the potential for malignant transformation of CLPs. The 12 months interval of follow-up for asymptomatic CLPs might be sufficient in clinical practice.
Disclosure of Interest: None declared

P0103 QUALITY OF LIFE AND CANCER WORRY OF INDIVIDUALS WITH INCREASED RISK FOR FAMILIAL PANCREATIC CANCER

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Introduction: Individuals with a genetic susceptibility for cancer often have a lower quality of life (QoL) than the general population. Little is known about the QoL of individuals with increased risk for familial pancreatic cancer (PC).
Aims & Methods
Aims: 1) To compare the QoL and the cancer worry of asymptomatic adult high-risk individuals (HRI) in a screening program with that of control patients and the general population; 2) To compare the QoL and cancer worry before and after surgical treatment for suspected pancreatic neoplasms detected during screening and surveillance.
Methods: Asymptomatic HRI with a family history of PC or PC genetic syndrome were screened with EUS and MRI within the Cancer of the Pancreas Screening (CAPS) studies from 2000-2011. Participants completed a baseline 36-Item Short-Form Health Survey (SF-36) for QoL analysis and the Cancer Worry Scale (CWS) prior to screening. Cross-sectional comparison of measures was performed with that of concurrently enrolled normal and disease (chronic pancreatitis, pancreatic cyst) controls. Baseline and post-operative scores were compared in surgical patients > 1 year from treatment.
Results: Scores from baseline pre-screening SF-36 and CWS questionnaires of 307 HRI (46% M, mean age 59 years) with 54 controls (42% M, mean age 63 years) were compared. 29 of 32 surgically-treated HRI had follow-up assessments; 13 of these completed both baseline and follow-up questionnaires. Prior to screening, 7 of the 8 QoL domain scores were significantly higher in HRI compared to controls: Physical Functioning (PF; 92 vs 81.9, $p = 0.005$), Role limitation-Physical (RP; 91.2 vs 71.5, $p < 0.001$), Bodily Pain (BP; 85.3 vs 71.8, $p < 0.001$), General Health (GH; 71.9 vs 64.5, $p < 0.001$), Vitality/fatigue (VT; 63.7 vs. 53.4, $p < 0.001$), Social Functioning (SF; 91 vs 77.2, $p < 0.001$), and Role limitation–Emotional (RE; 91.3 vs 82.4,$p = 0.005$). Mental health (MH) was comparable (78.7 vs 76.6, $p = 0.21$). HRI had significantly higher mean CWS scores than controls (6.4 vs 5.2, $p = 0.001$). Qol domain scores for the control group were comparable to published normative data for the average U.S. population. There were no statistically significant changes in the QoL parameters before and after surgery: PF (90.4 vs 91.2, $p = 0.87$), RP (80.8 vs 96.2, $p = 0.09$), BP (81.7 vs 87.9, $p = 0.24$), GH (63.5 vs 66.2, $p = 0.56$), VT (59.6 vs 64.2, $p = 0.54$), SF (89.6 vs 88.5, $p = 0.83$), RE (87.2 vs 84.6, $p = 0.86$), and MH (74 vs 76.3, $p = 0.64$). In patients who had pancreatic resection, QoL was high and PC worry was lower after surgery (11.1 pre-op vs 4.8 post-op, $p = 0.004$).
Conclusion: The baseline QoL of asymptomatic HRI is high, and is generally better than that of the controls, despite greater cancer worry. Pancreatic surgery does not negatively impact the QoL of HRI and results in a reduction in cancer worry
Disclosure of Interest: E. Shin: None declared, M. Goggins Conflict with: Epigenomics, Myriad Genetic Laboratories, Inc, R. Schulick: None declared, G. Petersen: None declared, R. Hruban Conflict with: Myriad Genetic Laboratories, Inc., H. Cosby: None declared, M. Topazian: None declared, S. Syngal: None declared, J. Farrell: None declared, J. Lee Lecture fee(s): Boston Scientific Corporation, M. Khashab Consultancy: Boston Scientific Corporation, A. M. Lennon: None declared, C. Yeo: None declared, M. Canto: None declared

P0104 IN-VIVO IDENTIFICATION OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASIA WITH CONFOCAL ENDOMICROSCOPY

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Introduction: Despite several advances in sensitivity and accuracy of diagnostic techniques in abdominal imaging, in the last decades, pancreatic cancer still remains a high-mortality disease with a poor prognosis after 5 years.
Pancreatic cysts are a heterogeneous group of lesions; serous cystadenoma and pseudocyst shows a benign behavior, intraductal papillary mucinous neoplasia (IPMN), mucinous cyst adenoma are considered to be premalignant lesions.
While the management and work up of cystic pancreatic lesions is quite homogeneous between experts, the accuracy of diagnostic techniques is very low. A needle-based confocal laser endomicroscopy probe (nCLE), introduced through an FNA needle, has been presented as able to visualize epithelial layer of a cyst's wall and recently a specific criteria for identification of serous cystadenoma has been identified with nCLE. However nCLE criteria for IPMN, the most common incidental findings in EUS has note been defined yet.

Aims & Methods: The aim of the study was to identify specific imaging criteria of IPMN. After nCLE procedure, all patients underwent aspiration of cystic fluid for CEA, amylase and cytology analysis.
After EUS and nCLE examinations, all findings were compared to cytology, cystic fluid analysis and EUS findings if a surgical specimen was not available and discussed with pathologist in order to recognize typical findings IPMN.
Results: Sixteen patients consequently underwent nCLE during FNA (11 IPMN, 3 Serous cystadenoma, 1 mucinous cystic neoplasm, 1 pseudocyst). nCLE was able to identify images featured finger-like projection suitable with papillary structures in all IPMN (Sens. 100%, Spec 100%, $p < 0.02$). This finding was not present in serous cystadenoma/pseudocyst/mucinous cystadenoma.
Conclusion: In this pilot study, nCLE was able to identify a criteria common in all IPMN. Multicentric studies on this topic are ongoing.
Disclosure of Interest: None declared

P0105 A COMPARISON OF COVERED AND UNCOVERED METAL STENTS IN PANCREATIC CANCER PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION DURING NEOADJUVANT CHEMORADIOTHERAPY

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Introduction: Increasing numbers of pancreatic cancer patients have been treated with neoadjuvant chemoradiotherapy (NCRT) to improve clinical outcome and survival. Neoadjuvant regimen in our institution would require 5 weeks of chemoradiotherapy, followed by a recovery period of an additional 4 to 6 weeks before surgery. We conducted this study to compare the efficacy and complication rates of covered and uncovered self-expandable metal stents (c-SEMS, u-SEMS) in relieving biliary obstruction in patients undergoing neoadjuvant therapy for pancreatic cancer.
Aims & Methods: We retrospectively analyzed patients who received biliary stent placement between April 2006 and December 2014. Forty-seven patients (34 men/13 women) with locally advanced pancreatic cancer and biliary obstruction had stent placement (24 cases c-SEMS, 23 cases u-SEMS). Endoscopic sphincterotomy (ES) was performed before stent placement.
Results: Stent occlusion occurred in 3 patients (12.5%) in c-SEMS group, 6 patients (26%) in u-SEMS group. Two cases (8.3%) in c-SEMS group and three cases (13%) in u-SEMS group had interruption of NCRT. There was no significant difference between two groups in occlusion rate and interruption of NCRT. There were also no significant differences in stent patency time between two groups ($p = 0.16$). Although tumor ingrowth with recurrent obstruction was more common in the u-SEMS group (21.7%vs 0%), acute cholecystitis (20.8% vs 4.3%) and acute pancreatitis (20.8%vs 8.7%) were more common in the c-SEMS group.
Conclusion: Both c-SEMS and u-SEMS are effective and safe in achieving durable biliary drainage in patients with pancreatic cancer receiving neoadjuvant therapy, despite different patterns of late stent failure.
Disclosure of Interest: None declared

P0106 SURVIVAL PROGNOSTIC FACTORS OF ENTEROPANCREATIC NEUROENDOCRINE TUMORS: A SINGLE-CENTER RETROSPECTIVE ANALYSIS OF 178 CASES

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Introduction: Enteropancreatic neuroendocrine tumors (EP-NET) are rare and heterogeneous diseases. The aim of our study was to identify clinical, histopathological and therapeutic factors impacting the survival of patients with EP-NET.
Aims & Methods: All patients with histopathological diagnosis of EP-NET in our university hospital between October 1994 and October 2013 were included. Data were retrospectively collected. When proliferative index (Ki67 and mitotic index) were not available on our database, a prospective review of tumor tissue was performed. Prognostic factors were determined by univariate analysis, survival rates were assessed by Kaplan-Meier method.
Results: One hundred and seventy-eight patients (Male: 53.9%, median age: 57, range: 5-87) were enrolled. There were 112 (62.9%) pancreatic NET and 66 (37.1%) intestinal NET. Sixty-six (37.1%) patients had secretory syndrome. According to the ENETS classification, NET were grade 1, grade 2 and grade 3 in 67 (37.6%), 95 (53.4%) and 9 (5.1%) cases, respectively. Overall survival was significantly longer for pancreatic NET than intestinal NET (192.9 versus 105.2 months, respectively ($p = 0.0003$)). For EP-NET, the identified negative prognostic factors were: age over 75 at diagnosis (HR = 5.39; 95% CI: 2.01-14.4), WHO performance status > 1 (HR = 9.49; 95% CI: 3.74-24.1), sporadic NET (HR = 2.09; 95% CI: 1.06-4.11), presence of distant metastases (HR = 2.49; 95% CI: 1.5-4.14), ovarian localization of metastases (HR = 6.13; 95% CI: 1.38-27.2) and Ki67 index > 5% (HR = 2.21; 95% CI: 1.3-3.76). For pancreatic NET, insulinomas (HR = 0.35; 95% CI: 0.14-0.87), primary tumor size < 25mm (HR = 0.31; 95% CI: 0.14-0.72) and mitotic index of 0 per 10 fields (HR = 0.38; 95% CI: 0.16-0.91) were positive prognostic factors. For intestinal NET, peritoneal localization of metastases (HR = 2.65; 95% CI: 1.12-6.28) and emergency surgery for acute complication (HR = 2.39; 95% CI: 1.07-5.34) were negative prognostic factors. For patients under 75 years, median survival time was 160 months for grade 2/3 NET while it was superior to 230 months for grade 1 NET ($p < 0.05$).
Conclusion: Negative prognostic factors such as ovarian or peritoneal metastases should be taken into account for the management of EP-NET. In intestinal NET, surgery should be performed as soon as possible, to avoid the occurrence of severe symptoms leading to emergency surgery. As a cut-off of 5% for the Ki67 index seems to better correlate with survival than a cut off of 2%, the ENETS classification should be reviewed.
Disclosure of Interest: None declared

P0108 PLAC8 OVEREXPRESSION REGULATES CELL GROWTH IN PANCREATIC NEUROENDOCRINE TUMOURS (PNET)

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Introduction: Plac8 is a small protein with unknown molecular function which depending on the cellular context shows different subcellular localisation and may be involved in a wide variety of physiological and pathophysiological processes. In normal pancreata, Plac8 is expressed neither in the endocrine nor in the exocrine compartment. Here we demonstrate that the protein is strongly upregulated in human pancreatic neuroendocrine tumours (pNETs) and centrally regulates the growth of cultured cells derived from pNETs.
Aims & Methods: Immunohistochemistry, RNAi, cell proliferation and viability assays, Western blots, apoptosis assays
Results: Plac8 is strongly overexpressed in primary human pNET tissues both on the mRNA level, as determined by quantitative RealTime PCR, as well as on the protein level, as determined by Western blot and immunohistochemistry. Moreover, strong Plac8 expression is also retained in cultured cell lines from human and rat pNETs. siRNA-mediated knockdown of Plac8 expression in these cells uniformly resulted in strong inhibition of cell growth, as determined by BrdU incorporation and MTT assays, while apoptosis levels were not influenced. This growth inhibition was associated with upregulation of the cell cycle inhibito p21/CDKN1A as well as downregulation of cyclin D1.
Conclusion: Overexpression of Plac8 protein in pancreatic neuroendocrine tumours is centrally important for the maintenance of the proliferative phenotype of the tumour cells. Further analyses to identify the involved molecular mechanisms and signalling pathways are ongoing.
Disclosure of Interest: None declared

P0109 CLINICAL MANAGEMENT OF SMALL PANCREATIC NEUROENDOCRINE TUMORS (PNETS): RESULTS FROM A 5-YEAR SINGLE-CENTER PROSPECTIVE STUDY

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Introduction: The most appropriate clinical management for small (≤ 20 mm) non functioning pancreatic neuroendocrine tumors (pNETs) is still a matter of debate and whether all the small and asymptomatic lesions should be routinely resected still has to be defined.
Aims & Methods: Primary endpoints of this prospective study were to evaluate the overall survival (OS) and the progression free survival (PFS) of pNETs, according to their clinical management.
From September 2009 to September 2014, a total of 51 patients had a definite diagnosis of pNETs based on clinical data, imaging (CT, MRI, Ga68-PET), ultrasound endoscopy, histology, and were consecutively enrolled. Among them, 15 patients (M/F = 6/9, median age 65 yrs, range 27-84 yrs) with small pNETs (diameter ≤20 mm) underwent an intensive 3-month follow-up for the first year and biannual thereafter (FU)). TNM stage was I in all but one patient who was at stage IIA. Twenty-one patients (M/F = 7/14, median age 52 yrs, range 27-82 yrs) underwent surgical resection (SR): TNM stage was I, IIA, IIIB and IV in two, nine, one and nine cases, respectively The remaining 15 patients (M/F = 7/8, median age 72 yrs, range 27-87 yrs) received systemic therapy (ST) due to advanced disease or contraindications to surgery; of them five, two and eight were at stage IIA; IIB and IV, respectively.
Results: Median follow up of the entire cohort was 56 months (range 3-70). OS was similar in FU and SR groups, whereas it was significantly worst in ST subset (log-rank test $P = 0.014$, median not reach in each group). Five-year survival rate was 100% in the FU group, 90% in the SR one, and 61% in the ST group ($p < 0.0001$), although these results were largely affected by the different stage at presentation. PFS did not differ in the three groups as disease remained stable in all but one patient in the FU group, whereas six patients (28%) in the SR group showed a pNET recurrence or metastatic spread and finally five (31%) showed disease progression in the ST group.
Conclusion: The "wait and watch"approach appears to be safe in ≤ 20mm, early stage pNETs, although further studies are needed to confirm these results in larger cohorts of patients.

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Disclosure of Interest: None declared

P0110 ENDOSCOPIC ULTRASOUND-BASED SURVEILLANCE OF ASYMPTOMATIC PANCREATIC NEUROENDOCRINE TUMORS IN MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 SYNDROME; A RETROSPECTIVE COHORT STUDY TO ASSESS GROWTH RATE

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Introduction: Endoscopic ultrasound (EUS) is used to identify pancreatic neuroendocrine tumors (PNETs) in multiple endocrine neoplasia type 1 (MEN1) syndrome. The role of surveillance in small (<20 mm), asymptomatic PNETs is unclear, mostly because the natural course of these lesions is largely unknown. Therefore, current advice is to perform EUS at 6-12 months intervals.

Aims & Methods: We assessed the incidence of small, asymptomatic PNETs in MEN1 patients using EUS and calculated the growth rate of PNETs in general, but also of the largest PNET per patient and of incident PNETs identified during follow-up EUS. All linear array EUS procedures in patients with MEN1 syndrome between May 2002 and April 2015 at the UMC Utrecht were identified. Number, size and location of PNETs were recorded. Mean growth rate of PNETs <20 mm identified at initial EUS (prevalent PNETs) and incident PNETs at follow-up was calculated with mixed model linear regression analysis.

Results: Fifty-four patients were identified. After excluding patients that underwent only one EUS-procedure (N = 14) and patients without PNETs (N = 2), 38 patients were included (13 males [34%]) with a mean age at the first procedure of 41 years (SD 14). Follow-up was 129 patient years (mean 3.4 years [SD 2.3]) and 169 EUS procedures were performed. In total, 225 PNETs were identified with a median size of 5 mm (IQR 4-8). Of these, 124 PNETs (55%) were identified during the initial EUS procedure (prevalent PNETs: median size 6 mm, IQR 4-9) and 101 (45%) during surveillance EUS (incident PNETs: median size 4.3 mm, IQR 3.0-6.0 mm) after a median of 2.4 years (IQR 1.1-3.5). Median size of the largest prevalent PNET (N = 33) was 9 mm (IQR 8-13). Mean annual growth rate of all PNETs was 0.10 mm (95% CI 0.02-0.19, P = 0.02); PNETs <10 mm did not grow (P = 0.50) whilst PNETs ≥10 mm grew 0.75 mm/year (95% CI 0.41-1.09, P < 0.0001). Prevalent PNETs grew 0.21 mm/year (95% CI 0.10-0.32, P = 0.0003), while incident PNETs did not grow over time (P = 0.21). Annual growth rate of the largest prevalent PNET was 0.28 mm (95% CI 0.06-0.50, P = 0.01). Annual incidence of new PNETs was 0.78 PNETs/patient/year (95%CI 0.72-0.86). In three patients (8%), a PNET grew to ≥20 mm during surveillance EUS (number needed to test: 12.7) after 26-30 months. None of the 101 incident PNETs grew beyond 15 mm.

Conclusion: Annual growth rate of small PNETs, especially when <10 mm, is low and the interval between EUS procedures could probably be prolonged without compromising safety. Clinical relevance of new small PNETs found during surveillance appears to be limited because all PNETs ≥20 mm during surveillance EUS were already identified during the initial EUS.

Disclosure of Interest: None declared

P0111 THE PUTATIVE CANCER STEM CELL MARKER DCLK1 IS HIGHLY EXPRESSED IN PANCREATIC NEUROENDOCRINE TUMORS AND INDUCES EPITHELIAL-MESENCHYMAL TRANSITION

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Introduction: Accumulating evidence suggests that Doublecortin-like kinase 1 (DCLK1) is a putative marker for intestinal and pancreatic stem cells, including cancer stem cells (CSCs) of these organs[1,2,3]. Recently, we have reported that DCLK1 was highly and diffusely expressed in human rectal neuroendocrine tumors[4]. However the function of DCLK1 has not been investigated in detail.

Aims & Methods: The aims of the present study were to assess expression levels of DCLK1 in pancreatic neuroendocrine tumors (PNETs) and to identify critical functions of this molecule in PNET cells that are highly metastatic despite of their relatively slow growing ability. Fifteen patients (8 male, 7 female; mean age, 56) with PNETs were enrolled in this study. Informed consent was obtained from all of the patients. The tumors were surgically resected between 1997 and 2012 in the Kurume University Hospital. Mean diameter of the tumors was 30.2 mm (range, 12-93 mm). Immunohistochemistry (IHC) was employed to assess expression levels of DCLK1. QGP1, a human PNET cell line, was used in this study, and the cells were transfected with *dclk1* cDNA to establish the DCLK1-overexpressing (QGP1-DOE) cells. The QGP1-DOE cells were subjected to *dclk1* silencing of to confirm acquired cellular characteristics by DCLK1 overexpression. Protein and mRNA expression levels were analyzed by Western blot and real-time PCR (ABI PRISM 7700), respectively.

Results: In IHC, all of the 15 PNET clearly and diffusely expressed DCLK1 in the tumor areas. The protein was expressed in QGP1 cells in both protein and mRNA levels; however, the expressed protein was a short form which lacked doublecortin domains. QGP1-DOE cells robustly expressed full length of DCLK1, showing morphological alteration reminiscent of epithelial-mesenchymal transition (EMT). Indeed, extremely high expression of Slug was found in QGP1-DOE cells compared with control cells at both protein and mRNA levels. Similar upregulation was demonstrated in E2A, Twist, and N-cadherin. The QGP1-DOE cells exhibited increased cellular motility. DCLK1 knockdown restored both cellular morphological change and the expressions of the EMT-associated molecules.

Conclusion: We demonstrated high expression of DCLK1 in human PNET tissues and PNET cells. Enforced expression of DCLK1 induced EMT via upregulating Slug and other EMT regulators. Therefore, it is speculated that inhibition of DCLK1 expression is a novel therapeutic strategy for PNETs.

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MONDAY, OCTOBER 26, 2015 09:00–17:00

ENDOSCOPY AND IMAGING I – HALL 7

P0112 EVALUATION OF THE SPEED AND QUALITY OF GASTRIC ULCER HEALING AFTER ESD USING 2% REBAMIPIDE SOLUTION AS A NOVEL SUBMUCOSAL INJECTION MATERIAL

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Introduction: Rebamipide is a safe and widely used medication for oral administration to patients with gastritis or gastric ulcers. A combination therapy of proton pump inhibitor (PPI) and rebamipide was reported to effectively promote ulcer healing after endoscopic submucosal dissection (ESD).

Aims & Methods: In this preclinical study we developed a novel 2% rebamipide solution as a submucosal injection agent for ESD, used it for ESD experimentally in porcine stomachs, and examined the quality and speed of ulcer healing after the intervention.

Three domestic female pigs of about 30 kg underwent ESD. ESDs of approximately 30 mm in diameter were performed at four sites (anterior and posterior walls of both the upper body and middle body) in the stomach of each of the three pigs. An endoscopist blinded to the test agents performed the ESD with matrix alone at two sites (control group) and with the 2% rebamipide solution at the other two sites (rebamipide group). One pig was sacrificed 1 week later (pig 1) and two pigs were sacrificed 4 weeks later (pigs 2 and 3). In Examination 1 we evaluated the healing speed once a week using endoscopic ulcer staging. In Examination 2 we evaluated the quality of the ulcer scar histopathologically.

Results: Examination 1. We found no significant differences between the groups in the healing stage after resection of the gastric lesions at 1 week. Later, however, the S stage ratios in the rebamipide group and control group were significantly different: 75.0% (3/4) and 50.0% (2/4) respectively at 3 weeks and 100.0% (4/4) and 50.0% (2/4) respectively at 4 weeks. Furthermore, the folds into the centers of the ulcer scars were smoother and more uniform in the rebamipide group than in the control group at 4 weeks after the ESD. Examination 2. The ulcers at 1 week were not observably different between the two groups. At 4 weeks, mucosal healing was conspicuously better in the rebamipide group than in the control group, with a thicker and more uniform mucosal layer.

Conclusion: The use of 2% rebamipide solution as a novel submucosal injection material for ESD promoted the speed and quality of ulcer healing after ESD.

Disclosure of Interest: A. Fujimoto Financial support for research: Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan, O. Goto: None declared, T. Maehata: None declared, Y. Ochiai: None declared, T. Nishizawa: None declared, R. Nakamura: None declared, S. Sagara: None declared, T. Akimoto: None declared, M. Shimoda: None declared, T. Uraoka: None declared, N. Yahagi: None declared

P0113 PREOPERATIVE PULMONARY FUNCTION TESTS ARE USEFUL TO PREDICT ASPIRATION PNEUMONIA AFTER ESD FOR GASTRIC TUMORS

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Introduction: An experienced and skilled ESD operator enables us to perform ESD even for elderly patients with some comorbidities. Such patients whose pulmonary function is often poor may be at risk for postoperative aspiration pneumonia. However, few reports have discussed on the relationship between the pulmonary function and aspiration pneumonia after ESD for gastric tumors.
Aims & Methods: A total of 978 patients with gastric tumors who previously had received pulmonary function tests were treated by ESD between June 2006 and May 2014. ESD was performed under intravenous anesthesia using propofol. Chest radiography and blood chemistry were done on the next day after ESD. Computed tomography was added if aspiration pneumonia was suspected. Aspiration pneumonia was defined when the patients presented with lung consolidation by chest radiography or CT, in addition to respiratory infectious symptoms such as fever and oxygen desaturation. Pulmonary function tests were assessed using a spirometer. The patients were categorized into four groups according to the predicted vital capacity (%VC) and forced expiratory volume in 1 second as a percentage of forced vital capacity (FEV1.0%): normal; restrictive pulmonary dysfunction (%VC < 80%); obstructive (FEV1.0% < 70%); and combined (%VC < 80% and FEV1.0% < 70%). The factors associated with aspiration pneumonia were retrospectively analyzed using the preoperative parameters.
Results: The study subjects comprised 694 men (71%) and 284 females (29%) with a mean age of 73.6 years. Among the 268 cases (27%) with abnormal pulmonary function, 10 cases (3.7%) developed aspiration pneumonia. On the other hand, 7 cases (1.0%) with normal pulmonary function developed pneumonia. There was a significant correlation between pulmonary function and aspiration pneumonia ($p = 0.003$). The pulmonary function cases were stratified into subgroups, 2.5% of cases with restrictive pulmonary dysfunstion developed pneumonia, 5.5% with obstructive, and 7.9% with combined. Among the other preoperative parameters, serum albumin, pretreatment with glucagon, presence of antiplatelet agent, presence of cerebral vascular disease were significant factors by a univariate analysis. By multivariate analysis, pulmonary function and presence of cerebral vascular disease were identified as significant independent risk factors associated with aspiration pneumonia. The odds ratio for pulmonary function and cerebral vascular disease were 3.2 and 5.1, respectively.
Conclusion: Preoperative pulmonary function tests may be useful markers to evaluate the risk for aspiration pneumonia after ESD for gastric tumors.
Disclosure of Interest: None declared

P0114 USEFULNESS OF BLUE LASER IMAGING (BLI) FOR DETECTION OF SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: In recent years, image-enhanced endoscopy such as NBI is widely performed for detection and diagnosis of superficial ESCC. Especially, NBI has established the usefulness in detection and diagnosis of superficial ESCC. Blue LASER Imaging (BLI) is a novel image-enhanced endoscopy with two different lasers that enable us to allow narrow-band light observation. BLI-bright is a brighter BLI mode, and useful for endoscopic observation in a distant view.
Aims & Methods: The aim of this study is to evaluate the endoscopic recognition of ESCC using by four different methods (OLYMPUS white light: OWL, FUJIFILM white light: FWL, NBI, and BLI-bright). We retrospectively analyzed 25 superficial ESCCs that were examined using among OWL, FWL, NBI, and BLI-bright at Kyoto Prefectural University of Medicine (KPUM) from March 2012 to December 2014. A typical ESCC was observed as a reddish area (RA) by using OWL and FWL, or as a brownish area (BA) by using NBI and BLI-bright in a distant view. Subjective evaluation was investigated as a ranking score (RS) by three endoscopists who ranked the each image on the basis of the ease of detection of cancer area (very clear: 3 scores/ clear: 2 scores/ unclear: 1 score). As objective evaluation, we calculated the Color Difference Scores (CDS) of pixel values based on L*a*b* color spaces between each cancer and noncancerous area.
Results: There are no difference between the mean RS of OWL and FWL. The mean RS of NBI was significantly higher than OWL ($p < 0.01$) and that of BLI-bright was significantly higher than FWL ($p < 0.01$). Moreover, the mean RS of BLI-Bright was significantly the higher than NBI ($p < 0.01$). Furthermore, in the objective evaluation, the mean CDS of BLI-bright was significantly the highest than that of OWL ($p < 0.05$), FWL ($p < 0.01$) and NBI ($p < 0.01$). Therefore, BLI-bright images was significantly higher than that obtained from the other methods both RS and CDS.
Conclusion: The recognition of cancer areas using BLI-bright was the most clear than using the other methods (OWL, FWL, and NBI) both subjectively and objectively. BLI bright may be a valuable tool for identifying superficial ESCCs during screening endoscopy.
Disclosure of Interest: None declared

P0115 LONG-TERM OUTCOME AFTER BIODEGRADABLE STENT (BDS) PLACEMENT FOR THE TREATMENT OF REFRACTORY BENIGN ESOPHAGEAL STRICTURES

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Introduction: Metal stent placement has been proposed as potential treatment for refractory benign esophageal strictures. Biodegradable stents (BDS) have been used to overcome the traditional shortcomings of metal stents for benign indications. However BDS were evaluated only in small cohort studies with a short follow-up.
Aims & Methods: Aim of this study is to report long-term outcome and safety of a large group of patients treated with BDS over 6 years. Prospectively maintained database has been used to collect data on consecutive patients with refractory benign esophageal strictures (according to Kochman criteria) treated at a single tertiary level centers using a BDS since 2008. BDS have been placed under fluoroscopy; endoscopic and radiologic follow-up was planned at 3 and 6 months followed by a phone interview or outpatient appointment. Technical success was defined as uneventful placement of the BDS at the level of the stricture. Clinical success was defined as the absence of dysphagia for at least 12 months after BDS placement. Recurrent dysphagia due to stricture formation was defined as any recurrent stricture that could not easily be passed by a standard endoscope (9.8mm) together with symptoms of dysphagia for solid food (grade ≥ 2).
Results: 42 patients (28M, mean age 53.2 y) received a BDS. In 26 patients a small size (18-23 mm) BDS was used while a larger BDS (23-25 mm) was placed in the reaming. Stricture etiology was post-surgery in 12 (28.5%), post-caustic ingestion in 20 (47%), post-radiotherapy in 8 (19%) and idiopathic in 2 (4.7%). Mean number of dilation before BDS was 12.6 (range 8-17) and 17 patients were previously treated with fully covered metal stent. BDS was successfully placed in all patients. Early complications occurred in 11 patients (26%) and were mainly related to thoracic pain requiring prolonged medical therapy in 10 and stent migration in 1 patient just two weeks placement. Late complications were observed in 3 patients (2 perforation occurred respectively 4 and 6 weeks after placement and 1 bleeding requiring hospitalization 8 weeks after placement). The overall complication rate was 33%. One patient died after surgery, required because of perforation. The second perforation was managed uneventfully placing a fully covered stent. Mean follow-up was 38.3 months (range 17-68). Long-term relief of dysphagia was obtained in 11 out of 42 treated patients (26%). The median dysphagia-free period was 293 days (range 35-1688). Long-term relief of dysphagia was significantly associated to post-surgery stricture ($p = 0.001$). There was no difference in terms of BDS diameter between patients with or without complications.
Conclusion: BDS in patients with esophageal refractory strictures was associated with 26% success rate and 33% complication rate, leading to surgical intervention in 2 cases and death in 1 case. Caution is recommended when BDS is considered for treatment of benign refractory strictures related to post-caustic ingestion or post-radiotherapy.
Disclosure of Interest: None declared

P0116 UPPER GASTROINTESTINAL CANCER MISSES: COULD WE DO BETTER?

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Introduction: Endoscopy is the gold standard investigation for the diagnosis of gastro-oesophageal cancer. As occurs with lower GI malignancy, cancers can be missed at endoscopy, but this may not be appreciated by the endoscopist, nor is audit of gastroscopy as well established as that for colonoscopy. Studies have suggested that endoscopy technique may account for the majority of misses. In general, a cancer detected within 3 years following an endoscopy is considered to be a 'potential miss' and if detected within 1 year after an endoscopy, that is likely to be a 'definite miss'. This is based on the premise that early oesophageal cancers have a long natural history (1,2).
Aims & Methods: The aim of this study was to establish the proportion of missed upper GI cancers at our institution. We conducted a retrospective, case study of patients diagnosed with oesophageal and gastric cancers between January 2011 and January 2015 from our hospital cancer registry. Information regarding any gastroscopies done within 3-36 months of cancer diagnosis was obtained for each patient using our electronic endoscopy reporting tool.
Results: There were 305 new cases (Male = 207; 68%; mean age 73.8 yrs; range 26-100 yrs) of upper GI cancer, of whom 23 (7.5%) had undergone a gastroscopy within 3–36 months of the diagnosis. Only 2 patients had undergone an endoscopy procedure in the 3–12 months prior to diagnosis. Alarm symptoms were present in 11 patients (48%; information available in 20 patients) at the time of the index 'miss' endoscopy.
Conclusion: Oesophago-gastric cancers appear to have been missed at endoscopy in 7.5% of patients in our unit. This value parallels outcomes reported elsewhere

(1,2). Given the poor prognosis associated with upper GI malignancy, this study reminds us to be vigilant when examining the mucosa, particularly at the cardia, which is most vulnerable with regards to missing a cancer. The endoscopist should also have a low threshold for suspicion in patients presenting with alarm symptoms. Although there are many established performance indicators for colonoscopy, endoscopists are less familiar with gastroscopy measures of quality. We believe that addressing gastroscopy technique will have an impact on early detection of upper GI cancers and improve outcomes for these patients.

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P0117 PREDICTORS OF OUTCOMES AND LEARNING CURVE FOLLOWING PER ORAL ENDOSCOPIC MYOTOMY FOR ACHALASIA CARDIA

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Introduction: Per Oral Endoscopic Myotomy (POEM) is an effective treatment for achalasia cardia. There are no studies evaluating predictors of POEM outcome and the impact of learning curve. This single-center, retrospective study aimed at evaluation of predictors of POEM outcomes and assess the impact of learning curve.

Aims & Methods: 268 patients with achalasia cardia were subjected to POEM. POEM was done by posterior approach in first 208 patients, and anterior approach in the next 60 patients. Hybrid knife was used in 200 and triangular tip knife in 68 patients. Primary outcome measure was treatment success defined by Eckardt's score ≤ 3. Secondary measures were adverse events. Multivariate analysis was done for factors affecting outcome and learning curve determination was done.

Results: Technical success was achieved in all patients. There were 9(3.35%) treatment failures. Six failures occurred in the first 40 patients, while 3 occurred in the next 228 patients (15% vs. 1.3%, $p = 0.0005$). There were 12 adverse events (AE) in the first 40 patients (30%), and 26 (11.4%) in the next 228 patients ($p = 0.005$). On multivariate analysis, the factors adversely affecting treatment success were male gender ($p = 0.017$) and prolonged operative time ($p = 0.030$). Prolonged operative time ($p = 0.006$) and type of achalasia ($p = 0.034$) were found to be independent predictors of AE.

Conclusion: Male gender, type of achalasia and prolonged operative time are important predictors of adverse POEM outcome. The treatment success improves, and the rate of adverse events declines significantly after first 40 procedures

Disclosure of Interest: None declared

P0118 "DO WE ALWAYS HAVE WHAT WE FEEL?" - PREDICTIVE FACTORS FOR ESOPHAGEAL FOREIGN BODIES PRESENCE IN URGENT ESOPHAGOSCOPY

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Introduction: Urgent upper digestive endoscopy is frequently required in cases of suspected esophageal foreign bodies (EFD). Persistent esophageal symptoms following foreign bodies ingestion should be evaluated by endoscopy; however, absence of EFB requiring endoscopic removal when esophagoscopy is performed is frequently observed.

Aims & Methods

Aims: Identify predictive factors for EFB presence in urgent esophagoscopy.

Patients and Methods: Retrospective case-control study. All consecutive esophagoscopies performed due to persistent esophageal symptoms after involuntary foreign bodies ingestion were analyzed, during an 18 months period. Demographic and relevant clinical data from patients with presence or absence of EFB when esophagoscopy was performed were compared. Statistical analysis included *Fisher*, Qui^2 and t tests for univariate analysis and logistic regression for multivariate analysis.

Results: One-hundred and sixty-one patients were submitted to urgent esophagoscopy due to clinical suspicion of EFB impaction (mean age 60.5 ± 18.2 years, 61.2% female). Impaction of EFB was confirmed in 41.6% of patients. Most frequent foreign bodies were: meat bones 39.8%, fish bones 39.8%, pits 3.7%, dental prosthesis 3.1%, blister pills 2.4% and sharp metal objects 1.2%. Patients with EFB were significantly older than the patients without EFB (60.5 ± 18.2 *vs.* 49.7 ± 18.7 years; $p < 0.001$) and recurred earlier to the urgency (10.7 ± 15.1 *vs.* 21.0 ± 26.5 hours; $p = 0.003$). Relevant underlying diseases, namely neurological, psychiatric or otorhinolaryngological (ORL), were more prevalent in patients with EFB (17.9% *vs.* 2.1%; $p < 0.001$). Regarding specific pathology type, a higher prevalence of psychiatric (9.0% *vs.* 2.1%; $p = 0.049$) and ORL conditions (6.0% *vs.* 0.0%; $p = 0.016$) was found in patients with EFB. No differences were found between patients with or without EFB concerning gender, day of the week of ingestion, type of foreign body type ingested or underlying neurological problems. Multivariate analyses identified the following predictive factors for EFB presence in esophagoscopy: older age, earlier recurrence to urgency and underlying psychiatric or ORL diseases (OR = 7.0; IC95%:1.4-35.0).

Conclusion: In cases of persistent esophageal symptoms after involuntary foreign bodies ingestion, less than half of patients had an effective EFB. Older age, earlier recurrence to urgency and psychiatric or ORL problems were associated with EFB presence when esophagoscopy was performed.

Disclosure of Interest: None declared

P0119 ROUTINE PREOPERATIVE UPPER ENDOSCOPY IN PATIENTS UNDERGOING BARIATRIC SURGERY

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Introduction: The difficulty of endoscopic evaluation of the remaining stomach after bariatric surgery is a fact that concerns a great number of doctors. However, the performance of a routine preoperative upper endoscopy (EGD) in every patient is not consensual, because these are mostly young and healthy patients with a low risk of malignancy.

Aims & Methods: Our aim was to evaluate the findings and relevance of preoperative EGD. We performed a retrospective study including patients who had undergone EGD before bariatric surgery between January 2012 and December 2014

Results: A total of 200 patients were studied; 90% were females, with a mean age of 44.2 ± 11.2 years. The mean weight and body mass index were 109.6 ± 18.2Kg and 42.2 ± 4.9 Kg/m^2, respectively. Sixty-nine patients (34.5%) reported symptoms (heartburn/regurgitation or epigastric pain) before the EGD. There were endoscopic findings in 47% of the patients, the most common being hiatal hernia (19.5%), gastritis (19.5%), esophagitis (10%), gastric polips (3.5%) and duodenitis (3%). Gastric biopsies were performed in 186 patients with positive findings in 129 (69.4%) of them: acute and/or chronic gastritis in 100% and intestinal metaplasia in 3.8%. The presence of symptoms didn't correlate significantly with the presence of endoscopic or histologic findings.

One hundred and ninety-one proximal gastric bypasses (95.5%) and 9 sleeve gastrectomies were performed. In 4 patients, a hiatal hernia repair was done concomitantly. Postoperative complications occurred in 12 (6%) patients, the most common being anastomotic stricture, without any significant correlation with endoscopic or histologic findings.

Conclusion: Endoscopic and histologic findings were common in preoperative EGD but they did not conditioned significant changings in the planned surgical procedure nor did they correlated with postoperative complications in our study. However, in the absence of correlation between symptoms and endoscopic findings and being EGD an accessible exam, it seems reasonable to perform it in all patients before bariatric surgery.

Disclosure of Interest: None declared

P0120 GASTRIC PRECANCEROUS CONDITIONS AND LESIONS IN LYNCH SYNDROME PATIENTS

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Introduction: Gastric cancer is the second most frequent extracolonic neoplasm in Lynch syndrome (LS) patients. The majority of them are intestinal adenocarcinomas, consequent to the progression of precancerous conditions and lesions. The main groups recommend performing an upper endoscopy, but with low level of evidence and depending on local context. The objective was to evaluate the prevalence of precancerous conditions and lesions (risk phenotype) in LS patients.

Aims & Methods: Case-control study with evaluation of gastric phenotype (endoscopy with biopsy) and *Helicobacter pylori (Hp)* infection status (histology and serology).

Results

Cases: 36 patients, from 17 families, MSH2 mutations in 58%, MLH1 in 28% and MSH6 in 14%, family history of gastric cancer in 8 families.

Controls: 100 dyspeptic patients. Around 50% males (41% in controls), average age of 53.25 ± 12.62 (42.56 ± 12.34 in controls). LS patients had a higher prevalence of atrophy of the antrum (33.3% versus 19%, OR 2.13 95% CI 0.91-5.01), intestinal metaplasia of the antrum (16.7% versus 13%, OR 1.34 95% CI 0.47-3.83), extensive atrophy (8.3% versus 4%, OR 2.18 95% CI 0.46-10.26) and extensive intestinal metaplasia (2.8% versus 1%, OR 2.82 95% CI 0.17-46.44) than the controls. Patients with LS had a higher prevalence of *Hp* infection (78.8% versus 59%, $p < 0.05$).

Conclusion: Our results suggest that there is a higher tendency to precancerous gastric conditions in LS patients, although with no statistical significance, which can be due to the small sample size. Nevertheless, LS patients were older and had a higher prevalence of *Hp* infection, which can have impact on results. Larger studies are important to define if LS is indeed associated with a risk gastric phenotype and if a systematic and periodic endoscopic surveillance should be recommended.

Disclosure of Interest: None declared

Abstract number: P0123

No	Age/gender	Localization	Duration of procedure (minutes)	Size of lesion (mm)	Size of tissue (mm)	En-Block Resection	Complication	Histopathology	Complete resection
1	65,M	Duodenal bulb	33	13 x 11	21 x 15	Yes	-	Neuroendocrine tumor	Yes
2	72,M	Duodenal bulb	16	11 x 8	20 x 17	Yes	-	Neuroendocrine tumor	Yes
3	59,M	2nd part of duodenum	19	15 x 13	20 x 20	Yes	-	Tubular Adenoma (High Grade Dysplasia)	Yes
4	44,F	Duodenal bulb	29	10 x 8	14 x 12	Yes		Neuroendocrine tumor	Yes
5	38,F	2nd part of duodenum	126	28 x 19	35 x 25	Yes	Perforation	Tubular Adenoma (High Grade Dysplasia)	Yes
6	60,F	2nd part of duodenum	345	67 x 38	73 x 48	Yes	-	Intramucosal carcinoma	Yes
7	72,M	Duodenal bulb	54	12 x 11	21 x 15	Yes	-	Neuroendocrine tumor	Yes
8	66,F	Duodenal bulb	67	16 x 14	32 x 24	Yes	-	Neuroendocrine tumor	Yes

P0121 ENDOSCOPIC FULL-THICKNESS RESECTION IN THE DUODENUM - A CASE SERIES

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Introduction: Endoscopic resection of duodenal non-lifting adenomas and subepithelial tumors is challenging and harbors a significant risk of complications. We report on a novel technique for duodenal endoscopic full thickness resection (EFTR) using an over-the-scope device.

Aims & Methods: Aim of this study was to demonstrate feasibility of EFTR in the duodenum using a novel full-thickness resection device (FTRD, Ovesco Endoscopy, Tuebingen, Germany). Data of 4 consecutive patients who underwent duodenal EFTR was analysed retrospectively. Main outcome measures were technical success, R0 resection, histologically confirmed full thickness resection, adverse events.

Results: Four patients (median age: 60 y) with non-lifting adenomas (2 patients) or subepithelial tumors (2 patients) underwent EFTR in the duodenum. All lesions could be resected successfully. Mean procedure time was 67.5 min (range 50-85). Minor bleeding was observend in 2 cases; blood transfusions were not required. There was no immediate or delayed perforation. Mean diameter of the resection specimen was 28.3 mm (range 22-40). Histology confirmed complete (R0) full thickness resection in 3 of 4 cases. Endoscopic follow-up after 2 months could so far be obtained in 2 patients. In both cases, the OTSC was still in place in could be removed without complications, recurrencies were not observed.

Conclusion: EFTR in the duodenum with the FTRD is a promising technique which has the potential to spare surgical resections. Modifications of the device should be made to facilitate peroral introducability. Prospective studies are needed to further evaluate efficacy and safety for duodenal resections.

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Disclosure of Interest: None declared

P0122 CAUSTIC INGESTION, IS ENDOSCOPY ALWAYS REQUIRED? – CLINICAL AND LABORATORY MODEL FOR PREDICTING GASTROINTESTINAL LESIONS

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Introduction: The ingestion of caustic substances is one of the major areas of Gastroenterology emergency, and the endoscopic evaluation is the gold standard for assessing the grade of lesions and to define the prognosis. However, in addition to being contraindicated in severe situations, it is not risk-free and its usefulness is debatable in cases of asymptomatic patients without oropharyngeal lesions.

Aims & Methods: (1) To identify clinical and laboratory factors for predicting gastrointestinal caustic injury; (2) creation of a clinical and laboratory model that could identify patients with high-grade gastrointestinal lesions (HGGL) and low-grade gastrointestinal lesions (LGGL), without need of performing an endoscopy.

Multicentric retrospective study, that reviewed all the patients who ingested caustic and were admitted to our centers over a period of 10 years. For defining the grade of lesions, we used Zargar score system (HGGL $\geq$ 2B; LGGL $\leq$2A). We identified clinical and laboratory variables that were statistically significant associated with HGG and we calculated the correlation coefficient.

Results: We identified 133 patients, of whom 65 had a HGGL (Esophagus: 50 patients; Stomach: 43 patients).

When comparing patients with and without HGGL, we identified statistically significant differences for the variables average value of leukocytes (15.3 versus 9600 x10^9/L; p = 0.000) and CRP (73 versus 25 mg/L; p = 0.000). The variables leukocytes (rs = 0.497; p = 0.000), CRP (r = 0.485; p = 0.000) and the number of symptoms (rs = 0.667; p = 0.000) showed a significant moderate correlation to HGGL. In univariate analysis, ingestion of acid (X^2 = 6.881; p = 0.009), ulcers in the oropharynx (X^2 = 18.304; p = 0.000) and hemodynamic instability (X^2 = 19.027; p = 0.000) were also associated with HGGL.

There was no statistical association between HGGL and the variables gender, intentional ingestion, age, previous attempt, psychiatric disease and dependence of toxic substances.

The factors with the strongest relationship to HGGL (leukocytes count; CRP; symptoms; ulcers in the oropharynx and hemodinamic instability) were used to develop an objectively weighted multivariate prognostic score ranging from 0 to 14 points, with a good prognostic discrimination (area under the receiver operating characteristic curve = 0.901). The ROC curve analysis suggests for identification of HGGL, the optimal cut-off of 10 points, with a specificity of 97% and sensitivity of 64%; and for LGGL the cut-off of 5 points, with a specificity of 94% and a sensitivity of 66%.

Conclusion: Our results confirm the model as a good test (AUC = 0.901), but in need of prospective validation, preferably in international multicentric studies.

Disclosure of Interest: None declared

P0123 DUODENAL ENDOSCOPIC SUBMUCOSAL DISSECTION; SINGLE CENTER EXPERIENCE IN TURKEY

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Introduction: Endoscopic Submucosal Dissection (ESD) is an endoscopic treatment modality providing en-block and complete resection of mucosal and submucosal lesions. Duodenal ESD is technically more difficult than gastric and colorectal ESD with longer procedure duration and higher complication risk. Here we present our experience with duodenal ESD.

Aims & Methods: A total of 345 ESD procedures of the esophagus, stomach, colorectum and duodenum had been performed between April 2012 and April 2015 the data of which had been recorded prospectively. During this study the records were searched retrospectively and the results of 8 duodenal ESD were analyzed.

Results: Duodenal ESD had been performed only after performing more than 200 ESD of stomach, esophagus and colorectum. There were 8 patients with duodenal ESD, in 5 patients the lesion was in the duodenal bulb and in 3 patients the lesion was in the second part of the duodenum. The median age of patients was 59.5 years (38-72y), median length of resected tissue was 33.5 mm (14-73), median length of lesion was 16.5 mm (9-67) and median procedure duration was 31.5 min. (16-345).

All the lesions were removed en-block. On histopathological examination both lateral and vertical margins were clear in all patients. During the procedure perforation occurred in patient which was successfully treated medically and with endoscopic clipping. No recurrence was seen during endoscopic follow-up and complete resection was achieved in all patients (Table).

Conclusion: Although duodenum is a difficult localization for endoscopic interventions and duodenal ESD bears higher complication risks because of thin wall, as the guidelines suggest, we believe that after experiencing in stomach and rectal ESD, duodenal ESD can also be performed successfully when needed.

Disclosure of Interest: None declared

P0124 GRADING ATROPHIC GASTRITIS BY A NEW QUANTITATIVE METHOD USING CONFOCAL LASER ENDOMICROSCOPY PROBE (P-CLE): FIRST RESULTS OF A PROSPECTIVE COHORT STUDY

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Introduction: Atrophic gastritis (AG) is a chronic disease, associated to gastric adenocarcinoma moreover if severe AG is present. Sydney system classifies AG as mild, moderate and severe, but with moderate interobserver agreement, as this system is based on a visual analogic scale (qualitative analysis). Confocal endomicroscopy showed an accuracy of 98% for diagnosis of gastric diseases, but when grading AG still remains a qualitative measure. Recently, new software called "Cellvizio® Viewer" (CV) permits to measure in micrometers (μm) the structures observed after p-CLE studies.

Aims & Methods: Based on the hypothesis that AG severity is correlated with crypts size diminution, the ***aim*** of this study is to determine a quantitative way to classify the severity of AG measuring the crypt area and inter-crypt spaces in patients with AG. After approval by the ethics committee 200 consecutive patients that underwent to upper endoscopy (UE) evaluation were included in this prospective study. Inclusion criteria: dyspepsia >12 months, age ≥ 18, no history of UE evaluation, AG at histopathology, acceptance to participate. Exclusion criteria: use of PPIs, antibiotics or NSAIDs, gastric cancer, gastric surgery, pregnancy, contraindication to fluorescein. During UE 5 biopsy sites were performed in accordance to Sydney system first using p-CLE and then by biopsy forceps from the same site. At p-CLE normal crypt was defined by using the classification of Wang et al (1). After histopathology confirm AG, crypts were analyzed using the CV software measuring the crypts diameters, to determine the area by elliptic area formula ($A = \pi.d_1.d_2$) and measuring inter-crypt space. That space was defined as the mean of each measured distance between the studied crypt and its adjacent. The cutoff value between mild, moderate and severe AG, crypts area was classified across tertiles, expressing its distribution using a box-spot graphic. For relationship between crypt area (CA) and inter-crypt space, quadratic polynomial regression was used. Data was processed using IBM® SPSS® Statistics.

Results: 30 patients were identified to have AG, 16 females (55%) with a mean age of 47.82 ± 18.3 and 146 crypts were analyzed. Histopathology showed AG: absent in 10 (38.5%), mild 8 (30.8%), moderate 6 (23.1%) and severe 2 (7.7%) of cases. At p-CLE the mean CA was 4697 (848 – 14794), and average of mean inter-crypt distance was 33.76 (0.00 – 87.45). Minimum normal CA was 10000 μm^2. Classifying AG crypts was established as follow: mild atrophic CA (μm2) range: 5000 and <10000, moderate AG CA: 3000 and <5000. Severe AG CA was <3000. Quadratic polynomial regression established a statistically significant relationship between CA and inter-crypt space

Conclusion: Using p-CLE criteria, severity of AG could be defined through crypt area and inter-crypt space with values of $<3000\mu m^2$ and 40μm respectively.

Disclosure of Interest: None declared

P0125 CLINICAL IMPACT OF CONFOCAL LASER ENDOMICROSCOPY PROBE (P – CLE) IN THE MANAGEMENT OF GASTROINTESTINAL NEOPLASIC AND NON-NEOPLASIC LESION

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Introduction: It has been demonstrated that endoscopic and histopathology findings don't have good correlation, leading sometimes to diagnostic and therapeutic doubts. Confocal laser endomicroscopy probe (p-CLE) is a new technology which permits in-vivo cellular view of gastrointestinal mucosa. It includes esophagus, stomach, small intestine, colon, biliary tract and pancreas. Studies showed a diagnostic accuracy above 90% for neoplastic (N) and non – neoplastic (NN) lesions, with specific characteristics and classifications. However, few studies have been oriented to determine the clinical impact of p-CLE for diagnosis and management in patients with diagnostic doubts.

Aims & Methods: The aim of this study is to put in evidence the clinical impact of p-CLE in this group of patients. Prospective study, performed from November 2013 to November 2014, in consecutive patients in whom p-CLE (Cellvizio®, Mauna Kea Technology) was indicated due to diagnostic doubts (absence of endoscopic–histological relationship). Baseline characteristics, indications, previous diagnosis studies, findings at p-CLE, clinical management and histopathological outcomes were evaluated. Indications for p-CLE were N and NN lesions. Lesions include: adenomas, dysplasia or cancer located in any gastrointestinal tract level, Barrett's esophagus, inflammatory bowel disease or pancreatic cysts. Previous diagnostic studies included: high definition magnification with digital chromoendoscopy, ERCP with brushing, EUS. Other studies were: CT-scan, cholangiography by MRI, tumor markers. Interventions based on the findings of p-CLE were analyzed according to the records, and included: drug treatment, other diagnostic studies, endoscopic or surgical treatments. The diagnostic yield was determined thought sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and match measurement. Diagnostic and therapeutic management, redirection of biopsies and need of other diagnostic methods were evaluated.

Results: 43 patients were included. 51% were male (22/43) with mean age of 49 ± 19 years. N lesions were 37% (15/43) of cases, located at: stomach (6), esophagus (4), bile duct (3) and colon (2). The sensitivity was 87% and specificity of 93%,(AUC = 0.9582) with a PPV of 87% and NPV 93%. p value <0.05. The observed concordance was 90.6% with a Kappa value of 0.80, corresponding to a force of substantial agreement according to Landis & Koch criteria. Changes in diagnostic and therapeutic approach were evident in 39.5% of cases (17/43), directing the sampling in 100% of cases (17/17) and avoiding diagnostic or therapeutic methods in all cases.

Conclusion: p-CLE is an essential diagnostic tool for patients with diagnostic doubts, as it allows in-vivo display cell and helps to direct biopsies. It has a significant clinical impact on the diagnosis and treatment of patients.

Disclosure of Interest: None declared

P0126 PERIODIC ENDOSCOPIES DID NOT INCREASE THE DETECTION OF EARLY GASTRIC CANCER IN A YOUNG POPULATION

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Introduction: Screening endoscopies in individuals 40 years or older in regions where gastric cancer is prevalent increase the diagnosis of gastric cancer at an early stage. However, the benefits of screening endoscopies in a young population (<40 years) have not been evaluated.

Aims & Methods: We reviewed data from patients less than 40 years old who underwent endoscopic submucosal dissection (ESD) or surgery for initial-onset gastric. We also administered a questionnaire to gather information concerning periodic endoscopic inspections and the period from the penultimate endoscopy to diagnosis.

Results: Of the 564 patients in this study, 101 (17.9%) and 36 (6.4%) patients had undergone screening endoscopies within 24 months and 60 months of gastric cancer diagnosis, respectively. The proportion of patients with early gastric cancer (EGC) was 67.6%, 83.3%, and 64.3% in the ≤ 24 months, 24 to 60 months, and >60 months groups, respectively ($P = 0.063$). On multivariable analysis, periodic endoscopies did not influence early diagnosis of gastric cancer (with >60 months as the reference group: ≤ 24 months, odds ratio [OR] = 0.992, 95% CI = 0.614–1.603; 24–60 months, OR = 2.238, 95% CI = 0.891–5.625). However, the proportion of lesions treated with ESD did differ according to the interval between endoscopic examinations ($P = 0.048$).

Conclusion: Although periodic endoscopies increased the proportion of patients with EGC that was treated with ESD, they did not increase the proportion of patients diagnosed with gastric cancer that was determined to be EGC in a young population.

Disclosure of Interest: None declared

P0127 CLINICAL OUTCOME OF ABSOLUTE VERSUS EXPANDED INDICATION OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER: SINGLE CENTER STUDY

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Introduction

Background: The treatment of early gastric cancer (EGC) by endoscopic submucosal dissection (ESD) has been rapidly gaining popularity in Korea. Current guidelines for endoscopic management such as EMR and endoscopic submucosal dissection (ESD) in early gastric cancer (EGC) are in evolution, with broader indication criteria. In Korea, indication of ESD for early gastric cancer have been still one of big issue.

Aims & Methods

Aim: The purpose of this retrospective comparative study was to evaluate clinical outcome of ESD for EGC, based on absolute indication and expanded indication criteria,

Method: ESD was performed on 1102 cases of early gastric neoplasm (cancer: 631, dysplasia: 471) from Jan 2002 to Aug 2011 at Soon Chun Hyang University Bucheon Hospital.

According to final diagnosis, EGCs below were enrolled by two groups (absolute vs expanded) and followed up: absolute: differentiated intramucosal (IM) cancer less than 20 mm, expanded: differentiated-type intramucosal cancer less than 30 mm in diameter or minute sm invasion (<500 μm from the muscularis mucosa) or undifferentiated IM cancer less than 10 mm.

Results: En bloc and complete resection rate in absolute and expanded group were 94.1% vs 90.7%, 93.7% vs 88.5% (*NS*). Size of lesion was 12.7 ± 4.8 mm, 26.6 ± 13.0 mm ($p < 0.05$). Complication such as bleeding and perforation was no statistical difference ($p > 0.05$). There was no between-group difference in the local recurrence rate (1.4% vs1.8%; NS) at a median follow-up period of 28 months (interquartile range 6-48 months).

Conclusion: Higher en bloc resection and complete resection rate, lower complication and recurrence in expanded group of ESD for EGC revealed as absolute group.

We concluded indication of ESD for EGC can be expanded.

Disclosure of Interest: None declared

P0128 CAUSTIC INGESTION: PREDICTIVE FACTORS FOR ESOPHAGEAL STENOSIS DEVELOPMENT - A MULTICENTER EXPERIENCE

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Introduction: There is an increasing incidence of caustic substances ingestion in the Western Countries, carrying a high risk of luminal strictures.
Aims & Methods: Identify predictive factors for the development of esophageal stenosis, and evaluate the effect of corticoteraphy and antibiotic therapy in reducing that risk. Multicentric retrospective study, that reviewed all the patients who ingested caustic substances and were admitted to our centers over a period of 10 years. Demographic, clinical, analytical, endoscopic (Zargar score) data were obtained. Univariate and multivariate logistic regression analysis was performed.
Results: 133 patients, 67 females, mean age 49, of whom 100 were hospitalized (median: 6 days). During follow up, 20 patients developed strictures, (esophagus: 90%), predominantly after alkaline substances ingestion (83%). Strong alkali ($p = 0.000$), esophageal lesions Zargar 2B ($p = 0.002$) and Zargar 3A ($p = 0.001$), invasive ventilation ($P = 0.012$), oral feeding after 48h ($p = 0.003$) and total parenteral nutrition (TPN) ($p = 0.000$) were independent risk factors for esophageal stenosis. Delay in the oral feeding had a moderate correlation for stricture development ($rs = 0.422$;$p = 0.00$). Corticotherapy ($p = 0.031$) and antibiotic therapy ($p = 0.001$) were not associated with risk reduction. Age, strong acid, intentionality and recurrence of ingestion were not associated with stricture risk ($p > 0.05$). Multivariate analysis revealed that only strong alkali (OR = 18,81), TPN (OR = 6,6) and esophageal lesions Zargar-2B (OR = 7,18) and Zargar-3A (OR = 12,12) maintained statistical significance.
Conclusion: There was a higher risk of esophageal stenosis with strong alkali ingestion and with higher severity of endoscopic lesions. Corticotherapy and antibiotic therapy were not associated with risk reduction. Our study suggests a potential cytoprotection effect of early oral feeding in esophageal stenosis risk reduction.
Disclosure of Interest: None declared

P0129 IS ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SPORADIC NON-AMPULLARY DUODENAL ADENOMA/CARCINOMA ESSENTIAL IN TERMS OF LONG-TERM CLINICAL OUTCOMES?

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Introduction: The number of endoscopic submucosal dissections (ESD), as well as endoscopic mucosal resection (EMR), performed for sporadic non-ampullary duodenal adenoma/carcinoma (SNADA) has recently increased. EMR for SNADA is a comparatively safe procedure, but there are concerns regarding local recurrence, due to a non-R0 resection or piecemeal resection. On the other hand, ESD for SNADA is excellent for en-bloc resection; however, the rate of complications in the duodenum, such as perforation, is much higher than that in the rest of the digestive tracts. Moreover, the indications for duodenal ESD are highly controversial. We therefore analyzed the necessity of ESD for SNADA from the perspective of long-term clinical outcomes and complications.
Aims & Methods: We retrospectively evaluated 82 patients, who underwent endoscopic resection, and who were histopathologically diagnosed as SNADA between May 2004 and February 2015 at our institution. Of 87 lesions, the final pathological diagnoses were low-grade dysplasia, high-grade dysplasia, and adenocarcinoma, in 23, 30, and 34, respectively; in all cases of adenocarcinoma, the disease had invaded up to the mucosal layer. The mean size of the lesions was 10.5 ± 5.7 mm. The numbers of lesions resected by polypectomy, EMR, strip biopsy, EMR with a cap-fitted panendoscope (EMR-C), and ESD were 1, 35, 9, 31, and 11, respectively.
Results: Eighty lesions were endoscopically followed up at least once after endoscopic resection (mean follow up period [months], 32.9 ± 28.5; range, 3–111), and 67 were followed up endoscopically for more than 1 year (mean follow up period [months], 38.2 ± 28.2; range, 12–111). The overall rate of R0 resection was 46.0% (40 of 87), and that of en-bloc resection was 77.0% (67 of 87). The rate of intraprocedural perforation was 3.4% (3 of 87), all of which occurred during ESD; the rate of intraprocedural perforation of ESD was 27.3% (3 of 11), which was significantly higher than that of the rest of the procedures (vs. 0% [0 of 76]; $p < 0.001$, chi-square test). There was only 1 case (1.3%) of local recurrence after resection; this was a case of piecemeal EMR for intramucosal carcinoma in 2 segments, and the recurrent lesion was resected by EMR 3 months after the initial resection, with no re-recurrence. Of the 67 lesions which were endoscopically followed up for longer than 1 year, the recurrence-free rate was 98.5% (66 of 67); the recurrence-free rates for cases of non-R0 and piecemeal resection were 97.5% (39 of 40, 12–95 months) and 91.7% (11 of 12, 12–89 months), respectively. There were no cases of distant recurrence or death from SNADA.
Conclusion: In terms of long-term clinical outcomes, the prognosis of the patients who underwent resection of SNADA with ESD was excellent; the patients who underwent resection of SNADA with non-R0 or piecemeal resection also had a favorable long-term prognosis, because of the rarity of recurrence. We think that reconsideration of the indications for ESD for SNADA is necessary, given the high frequency of complications with ESD.
Disclosure of Interest: None declared

P0130 INTRAGASTRIC MIGRATION OF LAPAROSCOPIC ADJUSTABLE GASTRIC BANDING. ENDOSCOPIC TREATMENT IS ALWAYS FEASIBLE. THE EXPERIENCE OF A SPANISH NON TERTIARY HOSPITAL

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Introduction: Intragastric band migration is an uncommon complication of Laparoscopic Adjustable Gastric Banding (LAGB) (0.5-11%) usually resolved by a surgical approach. We describe our experience .
Aims & Methods: Since 2001 we treated 127 morbid obese patients (pts) by LAGB. Patients with migration of gastric band into stomach more than 50% of circumference were able to be treated. The procedure was performed under general anesthesia. It is not necessary to use fluoroscopy.
Procedure: The band is cut using the wires from mechanical lithotripsy basket (MTW) or a 0.035 standard guidewire. Second the wire is looped about the visible band, grasped by the alligator forceps and brought out through the patient's mouth. Then the guidewire two ends are placed into the metal sheath of the mechanical lithotriptor (MTW) in order to cut it. The surgeon excised and removed the tubing and external port. Finally the split band is removed using a polypectomy snare, usually with a gentle pulling back from the esophagus.
Results: We found that 11 out of 127 LAGB (8.6%) become symptomatic due to gastric migration. 88.8% were females with average age of 42.6 yo. The time between the band placement and endoscopic removal was 60.5 months.
The symptoms were epigastric pain and weight regain as a sign of band dysfunction. Three pts were operated, one refused endoscopic treatment and the others were operated by band dysfunction finding out the gastric migration. 7 out of 9 LAGB (77.7%) were endoscopically removed in one session. We had two failures, 1 out of 9 LAGB (11.1%) was not possible to cut and the other (11.1%) was split but not removed due to difficulties with ventilation by excessive gas insufflation. His recovery from the attempt was uneventful and she remains well after 7 years of follow up, waiting for their possible complete migration. No complications were noticed after the endoscopic removal and pts were discharged in average of 2.6 days (17). The band removal was accomplished in three steps: a) cutting the band of silicone in the middle part avoiding the plastic part near the external tube, b) seizing the end of the split band near the external tube, coming from the port and c) pulling the endoscope out steadily and forcefully to liberate the band from the gastric wall.
Conclusion: More than 8.6% of LAGB will have gastric migration and develop symptoms. The endoscopic removal of LAGB is feasible, safe, but not easy, being a good alternative to surgery. We were able to remove 77.7% of LAGB, but the band should be migrated more than 50%. It is important to know very well the removal technique and their tricks. It is not necessary the use of intraoperative fluoroscopy and it seems to be safe to cut the band without its removal.
Disclosure of Interest: None declared

P0131 ENDOSCOPIC TREATMENT OF FISTULAS AFTER BARIATRIC SURGERY: EXPERIENCE OF A SINGLE CENTER

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Introduction: Bariatric surgery is the most effective treatment for long-term resolution of obesity and its co-morbidities. The complexity of the procedure and the surgical risk in obese patients is associated with significant morbidity and mortality. Fistulas in suture sites are the most serious complications and their best therapy approach is not yet defined. In the literature there are several small series and descriptions of cases in which self-expandable metallic stents (SEMS) are used for fistulas' treatment, proving to be an effective and safe alternative to surgery.
Aims & Methods: The authors aim to evaluate the efficacy and safety of SMES in the treatment of fistulas after bariatric surgery.
Retrospective analysis of patients who underwent SEMS (uncovered or partially covered) placement for treatment of fistulas after bariatric surgery between 01/01/2010 and 31/12/2014.
Results: Ten patients (p) were included, 80% women, mean age 40 years (26-62). Sleeve was performed in 9p and gastric-jejunal bypass in one. Mean time between the surgery and fistula diagnosis was 34 days (10-67). In 6p uncovered SEMS was used and in 4p partially covered SEMS. Completed fistula closure in 9p (90%), being necessary to relocate the SEMS in one case and to place a second stent in other. Surgery was performed in one patient in which the fistula persisted 49 days after the stent placement. SEMS remained in situ for a mean time of 70 days (24-105). In the patient submitted to gastric-jejunal bypass stent late migration occurred with obstruction and consequent removing by double-balloon enteroscopy. SEMS withdrawal in the remaining cases was performed by traction (5p) or by placement of a plastic stent with extraction in bloc after 2 weeks (3p), without complications.
Conclusion: The endoscopic treatment of fistulas after bariatric surgery is an effective and safe alternative to surgery, with clinical sucess of 90% in this series.
Disclosure of Interest: None declared

P0132 TOO MANY PREDICTIVE SCORES FOR UPPER GASTROINTESTINAL BLEEDING – SHOULD WE USE THEM AT ALL?

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Introduction: Despite the irreplaceable role of esophagogastroduodenoscopy (EGD) in the diagnosis of upper gastrointestinal bleeding (UGB), it is frequently hard to establish the ideal timing to perform it. The need of therapeutic intervention and the risk of relapse are also often difficult to predict. Several scores have been described with this purpose, but a comparison between them is seldom considered.

Aims & Methods: To identify clinical predictors of the need to undertake therapeutic endoscopic procedures, the best timing to execute them and the risk of relapse.

From January to April 2014, all patients submitted to EGD due to suspected UGB were included. Clinical and endoscopic variables from 141 patients were collected. Endoscopic scores such as Rockall, Glasgow-Blatchford and AIMS65 were calculated.

Results: A total of 141 patients were included, with an average age of 68.1 ± 16.3 years old, 65.2% being males. Endoscopic therapeutic intervention was needed in 62 patients (44%), 16 had a relapse (10.6%) and 3 eventually died (2.1%).

The need to perform therapeutic maneuvers was bigger in patients presenting with hematemesis (69.4% *vs.* 38.6%; $p = 0.003$), chronic liver disease (62.2% *vs.*37.5%; $p = 0.009$), hypoalbuminemia (69.4% *vs.* 38.6%; $p = 0.003$) e in those with significant rise in blood urea nitrogen (BUN) levels (41.8 ± 24.1 vs. 34.4 ± 26.0mg/dL; $p = 0.009$). In multivariate analysis, only hematemesis and elevated BUN kept their predictive value. In ROC curves, only pre-endoscopic Rockall score had an acceptable performance: AUC 0.664 (CI:0.561-0.768).

As for relapse, multivariable analysis showed that patients presenting with hematemesis (18.5% vs. 3.9%; $p = 0.005$) and hypoalbuminemia (22.2% vs. 2.9%; $p = 0.001$) had considerably bigger risk of rebleeding.

Conclusion: Clinical presentation with hematemesis, a bigger rise in BUN levels and pre-endoscopic Rockall score showed the ability to predict the need of endoscopic therapy. The best predictors of UGB relapse were AIMS65 score, hypoalbuminemia (< 3g/dL) and altered mental status.

Disclosure of Interest: None declared

P0133 FLEXIBLE ENDOSCOPIC MYOTOMY IS SAFE AND EFFECTIVE FOR ZENKER'S DIVERTICULUM (ZD): RESULTS FROM A TERTIARY REFERRAL CENTER

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Introduction: Flexible endoscopic treatment for Zenker's diverticulum (ZD) aims at performing a myotomy of the cricopharyngeal muscle on the septum in symptomatic patients. Because this technique is still not widely spread, data regarding its real efficacy in routine practice are still lacking. Our aim was to assess the feasibility, complication rates and the efficacy of flexible endoscopic treatment in patients referred for symptomatic ZD.

Aims & Methods: Medical records of all patients referred to our Department for flexible endoscopic treatment of ZD were retrospectively reviewed. Procedures were performed with a flexible gastroscope (Fujifilm EG530, Japan or Olympus Gif 180/190, Japan). After performing a diagnostic endoscopy, a soft overtube (ZDO-22-30, Cook, Ireland) was inserted over the scope to stabilize the gastroscope over the septum. Under endoscopic surveillance, a myotomy of the cricopharyngeal muscle was performed using a Zimmon needle connected to a surgical generator. After performing the myotomy, 2 clips were placed on the distal edge of the myotomy to prevent leakage into the mediastinum. Patients were discharged on the following day with oral antibiotics and alimentary recommendations. Patients' clinical characteristics, occurrence of complications as well as evolution of digestive symptoms were analysed.

Results: Between 2009 and 2014, 16 patients (8M/7F; mean age 73 years, range 54-97years) underwent flexible endoscopic treatment of ZD at the University Hospital of Nantes, France. Mean size of ZD was 36 mm (range 20-60mm). One case of mediastinitis occurred, which was successfully treated with radiological drainage. No other complication was noted. Prevalence of dysphagia, regurgitation and chronic cough dropped from 80%, 67% and 47% of patients to 27%, 27% and 7%, respectively. Odynophagia and/or dysphonia were initially present in 13% of patients and completely disappeared (0%) after endoscopic treatment. In 3 patients, symptoms recurrence (1 to 7 months) led to further treatment, either by 1-2 endoscopic session(s) ($n = 2$) or surgical ZD resection ($n = 1$).

Conclusion: Flexible endoscopic myotomy was relatively safe and effective for Zenker's diverticulum in this single centre study. Provided multicenter studies confirm these results, flexible endoscopic myotomy might be used as a first-line therapy in symptomatic patients in centers performing interventional endoscopy.

Disclosure of Interest: None declared

P0134 EFFICACY AND SAFETY OF ENDOSCOPIC MUCOSAL RESECTION (EMR) IN SUPERFICIAL OESOPHAGEAL SQUAMOUS CELL CARCINOMA (SCC): RESULTS FROM A MULTICENTER STUDY

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Introduction: Squamous cell carcinoma (SCC) is frequent but data are scarce regarding endoscopic mucosal resection (EMR) in these patients. Data from studies on EMR in Barrett's oesophagus are specifically different and cannot be transposed to SCC because 1) SCC patients generally have severe specific comorbidities and 2) SCC lesions have a higher risk of lymph node invasion. Therefore, our aim was to specifically evaluate the complication rate and efficacy of EMR in a large cohort of patients referred for superficial SCC.

Aims & Methods: We retrospectively selected all patients undergoing esophageal EMR for SCC at the University Hospitals of Nantes and Brest, France. EMR was performed on lugol-negative lesions with previous biopsies showing dysplasia or carcinoma. Clinical, endoscopic and histologic data were analyzed using medical records. Complication rates, recurrence and overall survival were reviewed as the main outcome measurements.

Results: In total, 78 patients (62M/16F; mean age 65 years) with SCC were treated by EMR from 1998 to 2014. Three complications occurred (2 perforations, 1 delayed bleeding), which were all successfully managed by endoscopy. Histological assessment of the EMR specimen confirmed epithelial carcinoma ($n = 27$), intramucosal carcinoma ($n = 8$), muscularis mucosae invasion ($n = 15$) or submucosal invasion ($n = 22$). The deep margin was R0 in 78% of cases. Due to submucosal invasion, 4 and 11 patients underwent subsequent surgery or radiochemotherapy, respectively. During follow-up (mean duration 35 months), recurrence occurred in 24% of cases. Overall survival rates at 1, 3 and 5 years were 90%, 74% and 59%. The 3-year disease free survival was 74%. Only 7.7% of patients died from an evolution of the oesophageal cancer.

Conclusion: In our study, EMR had a very low rate of complications and allowed curative resection in more than 75% of cases, with good long-term overall survival and disease-free survival in patients with SCC. In case of submucosal invasion, EMR was also useful to discuss surgery or radiochemotherapy. Therefore, EMR should be considered as a first-line modality to stage and potentially cure superficial SCC. Future prospective studies should establish the exact role of other promising endoscopic techniques such as endoscopic submucosal dissection in comparison with EMR.

Disclosure of Interest: None declared

P0135 SAFETY AND EFFICACY OF GLYCOPYRROLATE AS A PREMEDICATION FOR ENDOSCOPIC SUBMUCOSAL DISSECTION: A PRELIMINARY REPORT (A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY)

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Introduction: Endoscopic submucosal dissection (ESD) requires a high level of technique as well as a longer procedural time than conventional endoscopic procedures. Occasionally large amount of salivary and bronchial secretion can induce hypoxemia or sudden coughing during endoscopic procedure. Therefore there is a necessity to reduce oral or bronchial secretion. Anti-muscarinic anticholinergics suppress salivary and bronchial secretion and glycopyrrolate is one of the potent anti-muscarinic anticholinergics.

Aims & Methods: In the present study, a double blind, randomized, placebo-controlled trial, we investigated the efficacy and safety of glycopyrrolate premedication for ESD at a single tertiary medical center. A total of 59 patients undergoing ESD at a single tertiary medical center, from December 2014 to April 2015 were randomly allocated to receive one of the two premedications: glycopyrrolate (0.004 mg/kg, IM); or placebo (2.0ml of normal saline solution, IM). All patients received premedication 30 minutes before ESD in double-blind manner. The endoscopist reported the amount of secretions, cough, hypoxemia, procedure time and other procedure related adverse events after the procedure. The secretion assessment of the endoscopist was reported with predefined grading scale from zero indicating no secretion to four indicating large amount of secretion which cannot be controlled with suction.

Results: A total of 28 patients received glycopyrrolate, and 31 patients received placebo. ESD was successfully conducted in all patients without serious adverse events related to sedation or ESD. The proportion of the patients with the secretion score more than three points was lower in the glycopyrrolate group than in control group. (14.3% vs 32.3%), which was not statistically significant ($p = 0.133$). The hypoxemia during ESD was observed in 9.7% of the control group and 10.7% of the glycopyrrolate group, which was not statistically significant ($p = 1.0$). The proportion of the patients with cough during procedure was 41.9% for the glycopyrrolate group and 25% for the control group, which was not statistically significant ($p = 0.170$). No other procedure or premedication related complications were observed in both groups.

Conclusion: In this preliminary report, the use of glycopyrrolate as a premedication for the ESD reduced the salivary and airway secretion, however there was no statistically significant difference between two groups. Similarly incidence of hypoxemia and cough was not significantly different. Further studies with larger sample sizes are necessary to investigate the safety and efficacy of glycopyrrolate as a premedication for endoscopic procedure.
Disclosure of Interest: None declared

P0136 ROUTINE ENDOSCOPIC SCREENING FOR SYNCHRONOUS ESOPHAGEAL NEOPLASM IN PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA: A PROSPECTIVE STUDY

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Introduction: Early detection of synchronous esophageal squamous cell neoplasm (ESCN) in head and neck squamous cell carcinoma (HNSCC) patients can significantly affect their prognosis.
Aims & Methods: Subjects who were diagnosed as HNSCC from May 2010 to January 2014 were eligible. All patients underwent conventional white light endoscopic examinations with narrow band imaging and Lugol chromoendoscopy.
Results: Among 458 subjects screened, 28 synchronous ESCN, including 18 dysplasias and 10 squamous cell carcinomas, were detected in 24 patients (5.2%). The incidence of ESCN was greatest in patients with hypopharyngeal cancer (20.9%), followed by laryngeal cancer (3.8%), oropharyngeal cancer (2.8%), and oral cavity cancer (0.9%). In multivariate analysis, pyriform sinus involvement was independent risk factor for developing synchronous ESCN (odds ratio 171.2, $p<0.001$). Most patients with synchronous ESCN (22/24, 91.7%) were early stage, and 16 patients (66.7%) received treatment with curative intent. During the follow-up period (median, 24 months), the 3-year overall survival rates was significantly lower in patients with ESCN than in patients without ESCN (54.2% *vs.* 78.3%, $p=0.0013$).
Conclusion: Routine endoscopic screening for detecting synchronous ESCN should be recommended for patients with HNSCC, especially those with pyriform sinus involvement.
Disclosure of Interest: None declared

P0137 ENDOSCOPIC PAPILLECTOMY: FEASIBILITY, SAFETY AND EFFICACY DATA FROM A SINGLE UK CENTRE

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Introduction: Endoscopic papillectomy is an alternative to radical surgery (10% mortality risk) in the management of ampullary adenomas. Very few centres in the UK have the expertise or experience of performing this procedure and there is certainly no published literature from the UK.
Aims & Methods: We aim to report outcomes after endoscopic papillectomy in a single tertiary endoscopy unit in the UK. The prospectively collected data of all patients who underwent endoscopic papillectomy between 2005 and 2015 in Queen Alexandra Hospital, Portsmouth were reviewed. All procedures were carried out by PB (papillectomy) and PG (ERCP) using a standard duodenoscope. The pancreatic and biliary ducts were cannulated. A dilute methylene blue dye was injected into the pancreatic duct prior to papillectomy. Submucosal injection was performed in all cases prior to snare resection of the ampullary neoplasia. 5 Fr pigtail pancreatic stent insertion was attempted in all cases after resection of the neoplasia.
Results: A total of thirty-five patients were referred for papillectomy but only twenty-two patients (13 female, median age 72 years) underwent a total of 24 papillectomies. En-bloc resection was achieved in 17 patients (77%) with lesion sizes ranging from 8 - 25mm (Median 16mm). Pancreatic stent placement was successful in 82% of all papillectomies. Three patients experienced complications (12.5%); 2 bleeding and 1 acute pancreatitis. There was no procedure-related deaths and no one required emergency surgery. There were no local recurrences in 77% of patients. Two patients required 2 attempts to achieve complete clearance of their adenomas. Histology of the resected lesions revealed low grade dysplasia (54.6%), high grade dysplasia (27.2%), cancer (9%), gangliocytic paraganglioma (4.6%), and neuroendocrine tumour (4.6%). Of the two patients who were found to have invasive cancer, the first patient went on to have a pancreaticoduodenectomy and subsequently died of post-operative complications and the second patient was palliated. The total curative resection rate was 86%.
Conclusion: This is the largest reported UK series of endoscopic papillectomy. Our data demonstrates that this method is a feasible, safe and efficacious means of treating ampullary neoplasia in expert hands. It obviates the need for pancreaticoduodenectomy with its inherent morbidity and mortality. Complications can be serious and expertise is required to deal with them.

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P0138 DEVELOPMENT AND VALIDATION OF AN ONLINE TRAINING MODULE IN THE USE OF ACETIC ACID TO DETECT BARRETT'S NEOPLASIA

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Introduction: Acetic acid enhances the ability to correctly identify Barrett's neoplasia and is increasingly used by both expert and non-expert endoscopists. However, despite its increasing use, there is no validated training strategy to achieve competence.
Aims & Methods: The aim of our study was to develop a validated online training tool for acetic acid assisted Barrett's neoplasia detection and prospectively evaluate its impact and effectiveness. Video libraries of acetic acid assisted chromoendoscopy (AAC) were analysed. The best still images and videos were identified and correlated to histology. These images and videos were validated for quality and accuracy by 3 independent experts in AAC and 3 AAC naïve endoscopists. An online training module was developed.
13 Endoscopists with varying degrees of experience in the use of AAC participated in the study. Participants initially completed an online test consisting of 40 still images and 20 videos of Barrett's oesophagus with and without neoplasia. No feedback was given. Following this, the participants completed an online training module on the use of AAC. Having completed the training module, participants then repeated the test.
Results: We observed a significant difference in accuracy ($p=0.006$) between experts (0.93; 95% CI, 0.84-1.00) and novices (0.76; 95% CI, 0.70-0.82) during the validation exercise. The training tool led to a significant improvement in accuracy for all endoscopists with a mean pre-training score of 76% rising to 83% ($p=0.013$) after training. The training intervention with our tool led to a significant improvement in the confidence of the endoscopist in the use of acetic acid with the mean pre-training confidence level rising from 2.5 (5 point scale) to 3.9 post-training ($p < 0.001$). The training module led to a significant shift to the willingness of the endoscopists in changing practise from Cleveland clinic protocol to acetic acid guided targeted biopsy protocol with mean pre-training score of 2.6 (5 point scale) rising to 3.8 post-training($p < 0.001$).
Conclusion: 1. We were successful in developing and validating an online training and testing tool for acetic acid chromoendoscopy for Barrett's neoplasia.
2. Low pre-training scores amongst users and non-users demonstrated the need for training tool.
3. Training intervention with our tool improves the accuracy of endoscopists in the use of acetic acid to detect Barrett's neoplasia proving the efficacy of this tool.
4. The training tool increases the endoscopist's degree of confidence in the use of AAC.
5. The training tool also leads to shift in attitudes of endoscopists from Cleveland clinic protocol towards AAC guided biopsy protocol for Barrett's surveillance.
Disclosure of Interest: None declared

P0139 ENDOSCOPIC OVER-THE-SCOPE CLIP SYSTEM FOR TREATMENT OF PERFORATED PEPTIC ULCER: FIRST CLINICAL EXPERIENCES

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Introduction: Perforated peptic ulcer disease is a severe surgical emergency that carries high mortality and morbidity rates. The standard treatment has been prompt surgical closure of the perforation and control of extraluminal fluid collections. Hereby we report on 12 patients with gastric or duodenal peptic ulcer perforations who were managed by a novel therapeutic concept, i.e. endoscopic over-the-scope clip (OTSC) system.
Aims & Methods: All patients were treated at the OR under general anesthesia with readiness for laparotomy if endoscopic management would fail. The endoscopic OTSC system (10 mm) was combined with a twin-grasper (Ovesco Endoscopy AG, Tübingen Germany) in order to approximate the edges of the ulcer, whereupon the OTSC was applied. The procedure was supplemented with intra-abdominal lavage using 2 litres of lukewarm saline instilled through an infra umbilical drain and subsequently evacuated. The efficacy of the closure was documented by installing some methylene blue through a naso-gastric tube during the procedure and on the first postoperative day (POD). If there were no signs of blue colour in the drainage at POD 1, the drain and the naso-gastric tube were removed and per oral feeding started. A follow-up endoscopy was performed on POD 4. During 2010-2015 we treated 12 patients (median age 72, range, 33-89; 9 men, 3 women) with intention to treat at the time when CT-scan revealed free air in the abdominal cavity.
Results: Ten out of twelve patients (83%) were successfully treated with endoscopic closure at the first attempt. Two patients were directly converted to surgery due to complex perforation and hard surrounding tissue, which made it impossible to grasp the edges. Follow-up endoscopy at POD 4 demonstrated intact closure in all 10 cases.
In patients ($n=5$) with a short perforation history and mild degree of abdominal contamination, the postoperative period was smooth and associated with short hospital stay (4-5 days). In elderly and frail patients and in those with extensive

abdominal contamination a greater need for additional percutaneous drainage of fluid collections, intensive care and prolonged antibiotic treatment were required. No mortality was recorded.
Conclusion: Endoscopic OTSC closure of perforated peptic ulcer disease can be an alternative in selected cases, particularly in patients with short medical history of perforation irrespectively of comorbidity and age.
Disclosure of Interest: None declared

P0140 SAFETY AND EFFICACY OF A NEW THERAPEUTIC LASER SYSTEM FOR HEMOSTATIC TREATMENTS IN LUMINAL GI ENDOSCOPY – FIRST RESULTS IN AN ESTABLISHED ANIMAL MODEL

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Introduction: The Thulium laser system is an established therapeutic technology for surgical resection [1-3]. The wavelength of 2μm is strongly absorbed by water present in soft organic tissues, thereby providing constant speed of cutting and vaporization (i.e. ''vaporesection'') regardless of vascularization, with high degree of control on the penetration depth (0.2-0.4mm) to reduce the risk of inadvertent deep injury. However, no study has yet reported its use for achieving hemostasis in the luminal gastrointestinal (GI) tract.
Aims & Methods: We conducted a pilot study in an established animal model to test for the first time the safety and efficacy of the Thulium Laser system (Cyber TM®, Quanta System, Varese, Italy) for hemostatic treatment in luminal GI-endoscopy. Therefore, various optical fibers (365 and 550 um) were evaluated with different power settings (10, 15, 20, and 25 watts), and diverse configurations (continued laser shaping or pulse modality). Study endpoint was to assess the impact of the device in terms of depth penetration and lateral tissue damage under a laser exposure prolonged for 3, 5 and 7 seconds at fixed distance (0.5-1 cm) from the mucosal surface. Results were compared to the effect of Argon Plasma Coagulation (APC) generated by an established standard electrosurgery system for hemostatic therapy in the luminal GI-tract with a 2.3 mm catheter using 20, 40 and 60 watts. All procedures were performed using a standard video-gastroscope and digitally recorded. Histopathological analysis based on the whole stomach were performed by an expert GI pathologist.
Results: Neither transmural perforation, nor any muscular layer damage was observed with both systems used. A progressive penetration depth and tissue damage was observed with increased laser power and APC settings, as well as with prolonged tissue exposure. Nonetheless, both the fiber diameter and the configuration modality of the laser system were found to have no impact on depth penetration and tissue damage, with only marginal effect on the lateral spread of vaporization. Overall, the laser system has been correlated with comparable degree of vertical tissue injury (from 0.1 to 2.0 mm), with a much more precise effect on target according to a lower lateral spreading damage (0.1-0.3mm and 0.2-0.7mm using the 365 and 550um fiber, respectively) compared to APC (1.1-1.6 mm).
Conclusion: The Thulium laser system appears to be safe and effective for hemostatic therapy in an ex vivo animal model of the upper GI-tract. In vivo studies should now confirm these initial results in a prospective setting.

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P0141 ENDOSCOPIC PREDICTION OF RECURRENCE IN PATIENTS WITH EARLY GASTRIC CANCER AFTER MARGIN-NEGATIVE ENDOSCOPIC RESECTION: IS FOLLOW- UP BIOPSY NECESSARY AT ENDOSCOPIC RESECTION SCAR AFTER MARGIN-NEGATIVE RESECTION?

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Introduction: Although follow-up endosocpy is routinely performed after endoscopic resection for early gastric cancer (EGC), it has not been determined which endoscopic findings are suggestive of recurrence and when we take a biopsy at resection scar.
Aims & Methods: We aimed this study to predict local recurrence at resection scar with endoscopic criteria after margin-negative resection of EGC and to determined the necessity of follow-up biopsy at resection site.
Among 3037 cases of margin-negative endoscopic resection (including endoscopic mucosal resection and endoscopic submucosal dissection) for EGC between June 1995 and December 2011, a consecutive 22 patients with recurrent carcinoma at the site of endoscopic resection were identified. For each case, 4 controls were matched by age, sex and resectability (en-bloc or piecemeal). Endoscopic review was performed by consensus of 2 endoscopists based on the characteristic endoscopic criteria categorized as gross morphology (evenly elevated, unevenly elevated and flat), hyperemic change, mucosal defect (erosion or ulcer) and spontaneous bleeding.
Results: The mean age was 63.8 years and male was 72.9%. En-bloc resection was achieved in 100/110 (90.9%) cases. The mean interval between endoscopic resection and the diagnosis of recurrence was 16.8 months. Using endoscopic criteria of 'elevated gross morphology (both evenly and unevenly) or hyperaemic change at resection scar, the sensitivity, specificity, and positive and negative predictive values of recurrence rate at resection site were 95.5%, 68.2%, 2.6% and 99.94%, respectively. When applying these criteria to histologically differentiated and en-bloc resected EGCs, the values were 100%, 71.4%, 3.0% and 100%, respectively.
Conclusion: Recurrence at endoscopic resection scar after margin negative resection of EGC is very rare. Routine follow-up biopsies may be unnecessary when the follow-up endoscopy shows flat mucosa without hyperaemic changes at the scar especially, for the en-bloc resected and differentiated EGCs.
Disclosure of Interest: None declared

P0142 FIRST STUDY ON A NEW THERAPEUTIC LASER SYSTEM FOR PER-ORAL ENDOSCOPIC MYOTOMY IN AN EX VIVO ANIMAL MODEL

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Introduction: Therapeutic laser systems are established for surgical and endourological interventions [1-2]. Most recently, a new therapeutic laser system with a wavelength of 2μm has been developed to provide constant speed of cutting and vaporization (i.e. ''vaporesection'') with a precise control on depth and lateral tissue penetration to avoid inadvertent injury. To date, no study has assessed the efficacy of the new device for luminal gastrointestinal endoscopy.
Aims & Methods: We conducted the first pilot study to test the feasibility of the newly introduced Thulium laser system (Cyber TM®, Quanta System, Varese, Italy) for POEM by using an established experimental setting (EASIE model). The POEM procedure was performed in standard technique. All steps were performed just by using the new Laser system. Subsequent to the endoscopic procedure, specimens were evaluated by an expert pathologist.
Results: A complete POEM by using the Thulium laser took approximately 20 minutes. No perforation to the luminal side (i.e. mucosal) occurred. For laser power settings the most effective choice was 25-35 watts for mucosal excision and 15-25 watts for submucosal and muscular excision. Histopathology confirmed a clean and safe cutting of the different layers.
Conclusion: This is the first study of the newly introduced Thulium laser system showing the safety and efficacy of the new device for performing POEM procedures. These initial results should now be confirmed in additional in vivo studies.

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Disclosure of Interest: None declared

P0143 EFFICACY AND LEARNING CURVE OF A NEW SCISSOR-LIKE DEVICE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD)

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Introduction: ESD has become the standard technique for early cancerous lesions, particularly in Asian countries. However, current limitations of ESD include the complication rate, a distinct learning curve and the need of various devices, resulting in substantial costs of the procedure.
Aims & Methods: Aim was to prospectively assess the efficacy and learning curve of a new alligator scissor-like device for ESD. Accordingly, a prospective ex vivo study was performed in an established experimental setting. Ex vivo porcine models were utilized in the EASIE endoscopic simulator of interventional endoscopy. First, artificial lesions, each 2x2 cm in size, were created in fresh ex vivo porcine stomachs at the fundus, corpus and antrum. Two beginners with less than 10 ESD procedures each participated in the study. All study parameters were independently recorded. ESD was performed after marking of the lesions with the closed ESD-instrument, followed by lifting of the mucosa with submucosal injection of saline. Afterwards, circumferential incision of the lesions was performed with the new ESD-instrument. For resection, the submucosa was grasped with the scissor-like device, elevated and cut. Resection specimens were retrieved to evaluate if all marks were included (R0).
Results: Average size of removed lesions was 35 mm. En-bloc resection rate was 100% and R0 resection rate was 86%. After the initial three cases, R0 resection was achieved in all cases. The total procedure time improved significantly during the study (52.4 minutes versus 21.10 minutes; $p < 0.05$). One perforation occurred which could be managed with endoclips. Endoscopists satisfaction was high throughout all cases.
Conclusion: The new scissor-like device for ESD appears to be a safe and efficient new instrument for ESD which can relatively easy being learned.

Further studies should now focus on in vivo studies to confirm these initial results.

Disclosure of Interest: None declared

P0144 CAPNOGRAPHY DURING SEDATION FOR ENDOSCOPIC TREATMENT USING CARBON DIOXIDE SUPPLY SYSTEM

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Introduction: A respiratory monitoring during sedation for endoscopy has an important role. Pulse oximetry is one of the most common ways for respiratory monitoring, however, unexpected adverse effect may occur with pulse oximetry only. In the cases of deep sedation, visual examination, auscultation and monitoring by capnography may be recommended. However, only few studies reported about the capnography during sedation for endoscopic treatment of lesions located in upper gastrointestinal tract using endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR) technique, with deep sedation and carbon dioxide supply system.

Aims & Methods: The aim of this study is to evaluate the stability of respiratory monitoring by capnography during deep sedation for ESD/EMR using carbon dioxide supply system.

Twenty-six patients with successfully monitored both capnography and respiratory monitoring system by breath sounds (Rad87®, Masimo, Japan) among 52 consecutive patients who underwent endoscopic treatment (ESD/EMR) under deep sedation without intubation by anesthesiologist from December 2013 to October 2014 were analyzed. Oxygen saturation (SpO_2) was measured by pulse oximetry. Respiratory rate per minute (RR) was measured by side stream capnography and recorded every 8 seconds. RR was also measured from breath sounds by Rad-87® as gold standard and recorded every 2 seconds. We compared the average value of RR for every 8 seconds with RR by capnography and calculated Pearson's correlation coefficient. We also defined ''outlier'' when the value of RR by capnography was more or less than RR range of ±50% by Rad87®.

Results: In this study, 23 of 26 patients were male and median age was 72.5 years old (IQR: 62.5-80.0). Mean BMI was 22.1(±4.5). Patients who had cardiovascular or pulmonary disease were 26.9% and 19.2%, respectively. Location where patients had the lesions was follows; 17 patients have lesions in esophagus, 5 patients in normal stomach, 2 patients in gastric tube, one patient in gastric remnant. Mean size of the resected specimens was 39.3mm (± 8.8mm). Median time of procedure is 126 minutes (IQR: 91.5 – 167.8 min). Anesthesiologist used fentanyl and propofol for all patients. Mean amount of total administered agent is 0.14mg and 1220mg, respectively. The average of SpO_2, RR by Rad87® and RR by capnography during procedure was 97.6%, 9.6/min and 13.8, respectively. Four cases showed transient hypoxia (SpO2 < 90%). One of four cases showed hypoxemia for few minute, and this adverse effect could be detected by capnography as apnea before pulse oximetry detection. One case showed relatively strong correlation ($r = 0.511$), and three cases showed weak correlation ($0.2 < r < 0.4$), while other 22 cases showed no correlation between RR measured by capnography and by Rad87®. Median frequency of outlier for RR by capnograhpy was 35.2% (IQR: 26.5 – 48.8%).

Conclusion: Respiratory monitoring by capnography during deep sedation for endoscopic treatment with carbon dioxide supply system may be unstable and need some improvement in some situation.

Disclosure of Interest: None declared

P0145 THREAD TRACTION WITH A SHEATH OF POLYPECTOMY SNARE FACILITATES ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCERS

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Introduction: Endoscopic submucosal dissection (ESD) has been established as a standard therapy for early gastric neoplasms. During ESD, the mobility of the lesion increases as submucosal dissection proceeds and it becomes difficult to attain effective counter traction. To overcome this problem, various traction methods have been developed. Recently, the thread-traction (TT) method has been developed. However, in TT method, the movement of the thread was interfered with the movement of the endoscopy, and it resulted in disturbing to make the appropriate traction which the operator required. Moreover, in TT method, the lesion can be pulled only to the mouth side but not to the anal side by the thread. Therefore, we modified TT method and developed novel TT method using a sheath of polypectomy snare (TTSPS) method. The TTSPS method enabled the comfortable ESD procedure that did not disturb the thread movement without the interference with the endoscopy and could pull the lesion towards not only to the oral side but also to the anal side regardless of lesion locations.

Aims & Methods: This study aimed to evaluate usefulness of TTSPS method during ESD. Thirty-four consecutive patients who underwent conventional ESD between May 2013 and December 2013 and 54 consecutive patients who underwent ESD with the TTSPS method between January 2014 and March 2015 were included in the study. We compared counter traction ESD with the TTSPS method and conventional ESD that did not involve the new traction system in terms of the duration, the number of times regarding the arterial bleeding and the times regarding the local injection all after completion of circumferential mucosal incision until completion of dissection of the specimen.

Results: The median dissection duration after completion of circumferential mucosal incision until completion of dissection of the specimen for all lesions significantly differed between conventional ESD and ESD with method [conventional ESD, 90 min (range 30-320 min) vs ESD with TTSPS method, 60 min (range 15-160 min); $p = 0.015$]. The median number of times regarding the arterial bleeding after completion of circumferential mucosal incision until completion of dissection of the specimen was significantly less in ESD with TTSPS method than in conventional ESD [conventional ESD, 3 times (range 0-25) vs ESD with TTSPS method, 2 times (range 0-7) ; $p = 0.015$]. The median number of times regarding the local injection after completion of circumferential mucosal incision until completion of dissection of the specimen significantly differed between the two groups [conventional ESD 10 times (range 3-51), vs ESD with TTSPS method, 8 times (range 1-27) $p = 0.04$]. There was no significant difference in complications between conventional ESD and ESD with TTSPS method.

Conclusion: Our study suggests that TTSPS method is straightforward, safe, easy, noninvasive, cost-effective and uses readily available instruments to enhance visualization of cutting lines. Our TTSPS method can be universally applied to conventional ESD.

Disclosure of Interest: None declared

P0146 DEVELOPMENT OF A NOVEL ENDOSCOPIC SUTURING DEVICE USING NEW RECIPROCATING CURVED NEEDLE: AN EX VIVO COMPARISON STUDY

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Introduction: Endoscopic Suturing Device has been developing rapidly for not only Natural orifice transluminal endoscopic surgery (NOTES) but also minimally invasive obesity treatment. However, some issues remain involving the complex approach to the suturing site and the many additional instruments required that render the procedure more difficult. The complex suturing mechanism and tools not only increase the operation time but also decrease the feasibility of minimally invasive surgery. The authors have developed a novel endoscopic suturing devices to continuously suture a viscerotomy of stomach to overcome limitations of previous suturing devices.

Aims & Methods: The goal of this study is to develop an endoscopic suturing device and to demonstrate the feasibility of the device by showing the strength of closure. New endoscopic suture device is composed of main body, suturing-arms, curved needle, protective tube, and control device. This endoscopic closer (EN-closer) device sutures wound with a curved needle using back and forth movement. The endoscopic suturing device with new closure mechanism was compared with two other closure techniques; endoscopic clips and hand-sewn in porcine stomach. After closure, air leakage pressure was used to determine the strength of the perforation closure by an automated pressure gauge.

Results: After the mechanism design and implementation, we carried out a feasibility study on 10 porcine stomach models. In a comparative experiment, each endoscopic clip (endoclip) method and full-thickness stitches involved hand suturing was used 10 times to increase reliability. The average leakage pressure for the En-closer was 43.25mmHg. The average closer strength of the En-closer does not significantly differ from that of the endoclip, but standard deviation of the En-closer is significantly smaller than that of the endoclip treated stomachs. The En-closer that is capable of multiple stitches with a single endoscope insertion had similar closure strength to that of the endoclips but showed a more consistent sequence than the endoclips.

Conclusion: New suture device competently produced a tight, reliable, and consistent closure. Our instrument platform could be an important basis for future developments of not only gastric NOTES devices but also endoscopic bariatric surgery device. This research showed a new approach for endoscopic suturing devices.

Disclosure of Interest: None declared

P0147 WHEN SHOULD WE USE HEMOSPRAY? A SINGLE CENTRE EXPERIENCE

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Introduction: Hemospray is an inorganic nanopowder produced by Cook Medical and is licensed in Europe and Canada for the management of nonvariceal upper gastrointestinal bleed (NVUGIB). The powder adheres to liquid and forms a coagulum which concentrates clotting factors and stimulates the internal clotting cascade. There are numerous reports of successful haemostasis with hemospray, some reporting success rates of 85%[i]. However, the knowledge of which lesion is most suitable for hemospray use remains unclear. We report our experience at Guys and St Thomas' NHS trust to establish the lesions most likely to benefit from hemospray either as a primary intervention or an add-on strategy.

Aims & Methods: A retrospective review of endoscopic procedures that required hemospray was performed and the data was extracted from our endoscopy reporting system between December 2013 and February 2015 (14 months). We

Abstract number: P0147

Results of hemospray use	Procedure induced upper GI	Forrest 1a	Forrest 1b	Forrest 2a	Forrest 2b	Distal ileum (Enteroscopy)	Colonic bleed
Primary haemostasis achieved and sustained	9	0	5	2	3	1	1
Haemostasis not sustained	0	2	5	0	0	1	0
Unsuccessful	0	4	1	0	0	1	1

identified 32 patients who received hemospray, and excluded 2 where hemospray was applied blindly and the bleeding lesion was missed. The primary outcome was achieving primary haemostasis. Cases of recurrent GI bleed requiring further endoscopic or radiological intervention within 72 hours were considered unsuccessful.
Results: The 30 procedures were divided according to the procedure performed.
1. Procedure induced bleeding: 9/30 (7 post Barrett's endoscopic mucosal resection (EMR), 1 post gastric polypectomy and 1 iatrogenic bleed post nasojejunal tube insertion).
2. NVUGIB: 17/30
3. Enteroscopy small bowel bleed: 2/30
4. Colonoscopy: 2/30
Primary haemostasis was achieved in 77%, of which 7% required further endoscopic procedure or interventional radiological intervention within 72 hours (Table). The coagulum was not seen on second endoscopy.
Conclusion: Hemospray provides good hemostasis for post procedure, in particular post EMR bleed, as a single agent or where coagulation alone failed. Bleeding from Forrest 1b, 2a and 2b responded well to hemospray as a second modality, or single modality when the lesion was inaccessible. Forrest 1a had a poor response to hemospray and all cases required further endotherapy or interventional radiology. Further evidence is required to establish the value of hemospray in colonic and variceal bleed.

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Disclosure of Interest: None declared

P0149 ENDOSCOPIC MANAGEMENT OF POST-OPERATIVE LEAKAGES AND FISTULAS AFTER ESOPHAGEAL ONCOLOGIC SURGERY: EVALUATION OF EFFICACY IN A LARGE RETROSPECTIVE STUDY

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Introduction: Anastomotic leakages or fistulas are among the most common and severe complications of esophagectomy for esophageal cancer, with high grade of mortality. Recently the endoscopic management has taken a growing place in the treatment of digestive post-operative complications (1). The aim of this study was to evaluate the effectiveness and the characteristics of the endoscopic management in this indication.
Aims & Methods: This is a monocentric study on consecutive patients treated surgically in our institution between 2010 and 2014 for esophageal carcinomas. During this period, on 126 patients operated, 35 developed post-operative fistulas or leakages (27%), endoscopically managed and included in this study. All the procedures were performed in our endoscopy unit, by interventional endoscopists, in intubated patients under general anesthesia, using a large operating channel gastroscope (3.8mm, Pentax, Japan) and fluoroscopy. The patients were systematically controlled endoscopically 6 weeks after the endoscopic treatment to check the efficacy out and to evaluate the need for an additional treatment. The primary or secondary efficacy, the time between surgery, diagnostic and endoscopy, the number of procedures, the material used (stents, clips, or drains), the complications, and the death rate were recorded, and uni- and multivariate analysis was carried out to determine predictive factors of success.
Results: There were 4 women and 31 men, with a median age of 61.7 years $\pm$ 8.9 [43-85]. The surgical techniques were in majority Lewis-Santi for 48.6% of cases, Akiyama for 45.7%. 71.4% patients have undergone neo-adjuvant chemo radiation therapy and 77.1% were hospitalized in intensive care unit. The median delay between surgery and first endoscopy was 8.5 days [6.00-18.25]. 88% of the patients were treated using metallic (double type) esophageal stents, with a removability rate of 100% and a migration rate of 18%. The other ones were treated by Over-the-scope clips, naso-cystic drain or combined approach. The mean number of endoscopy per patient was 2.6 $\pm$ 1.57 [1-10], with a mean number of 1.6 $\pm$ 1.35 [0-7] stents placed. The primary efficacy of the endoscopic treatment was 48.6%, the final efficacy was 68.6%. The mortality rate in patients endoscopically managed was 17%, none being related to procedures. No predictive risk factor of success or failure of the endoscopic treatment (CRT, type of surgery, fistula size, age...) could be identified in univariate as well as in multivariate analysis.
Conclusion: The endoscopic management of leakages or fistulas after esophageal surgery is feasible, and lead to an overall effectiveness rate of 68.8%. There were no significant complications related to the procedures, and the mortality rate was decreased to 17% compared to 40 to 100% rate in the literature (2). Self-expandable metallic stents are the most common used treatment with a removability rate of 100% and a migration rate of 18%.

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Disclosure of Interest: None declared

P0150 CONFOCAL LASER ENDOMICROSCOPY IMAGING OF NEOANGIOGENESIS USING FITC-CD105 ANTIBODIES IN COLORECTAL CANCER: HUMAN IN VIVO TESTING

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Introduction: To date, the determination of neoangiogenic status and its dynamic assessment in real time has been challenging and, therefore, has made treatment optimization in colorectal cancers difficult. One strategy for antiangiogenic therapy is the long-term suppression of forming new blood vessels. Recent developments in endoscopic imaging technologies such as confocal laser endomicroscopy (CLE) have contributed to the progress from macroscopic evaluation to *ex vivo* molecular experiments and consequently to promising *in vivo* imaging by using fluorescently labeled antibodies.
Aims & Methods: The aim of this study was to evaluate the feasibility of *in vivo* acquisition of microscopic images using fluorescent CD105 antibodies for molecular imaging in human colorectal cancer. The current approach builds on our previous study in which we proposed *ex vivo* CLE examination and CD105 immunostaining of fresh tissue samples as a more reliable tool for evaluation of neoangiogenesis in rectal cancer [1]. Tumor was washed with saline solution and it was evaluated from a stable position using an eCLE system, before undergoing surgery. After excluding the presence of tissue autofluorescence, 1 ml fluorescent antibody solution (FITC-labeled anti-CD105/Endoglin antibody, Exbio, 1:5) was topically administered through a spray-catheter. After 10 min of incubation, the targeted area was analyzed by CLE and images were recorded. The fractal dimension of tumor vessels was calculated offline using "fractal box count" tool in Image J software. Grid method was applied to determine the vessel density. Before *in vivo* testing, multiple attempts were made at establishing the optimal antibody-tissue contact time using paraffin-embedded tissue sections under fluorescence microscopy conditions. Immunohistochemistry staining with CD105 was used as a gold standard.
Results: In vivo CLE analysis of CD105 expression in human colorectal cancer enabled the study of vascular network, revealing a chaotic structure. Both good and medium quality images were eligible for clinical analysis. Fractal value was 1.57, indicating the chaotic architecture (with 2 being the fractal value for normal vessels). Average vessel density was 46.09$\pm$ 7.06 vessels/mm^2.
Conclusion: *In vivo* molecular imaging of human colorectal cancer neoangiogenesis using CLE and FITC-CD105 antibodies is feasible. Future *in vivo* applications of immunoendoscopy using CD105 could provide a more specific analysis of tumor microvascular architecture in order to improve diagnosis, patient stratification and monitoring of antiangiogenic therapy.

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Disclosure of Interest: None declared

P0151 THE EFFECTIVENESS OF A CUSTOMIZED MOBILE APPLICATION IN COLONOSCOPY PREPARATION: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Colonoscopy preparations are generally poorly tolerated. Compliance with dietary instructions and proper use of the prescribed purgative solution are essential in achieving an adequate bowel preparation.
Aims & Methods: The study aims at assessing the effect of a customized mobile application (with dietary instructions, illustrations, reminders and push notifications) on the compliance and adherence to instructions and diet and consequently on the quality of bowel cleansing.
Consecutive patients scheduled for elective colonoscopy and having on-hand personal smartphones were randomly assigned to one of two groups. The first group (Paper) received face-to-face detailed paper instructions while the second group (App) received the same paper instructions and had the customized application downloaded onto their phone including the scheduled date and time of their colonoscopy appointment. The preparation consisted of split-dose sodium picosulfate/magnesium citrate (SPS) (Picoprep®, Ferring, Saint-Prex, Switzerland) and a 3-day diet consisting of a low-fiber diet for the first 2 days, and a clear fluid diet on the last day before colonoscopy (day -1). The first dose of SPS was to be taken the eve prior to colonoscopy, and the second dose a minimum of 4 hours before the procedure. Colonoscopy appointments were scheduled between 10 am and 3 pm. Patients were interviewed prior to colonoscopy about compliance with the 3-day diet and use of the SPS solution as well as their assessment of the preparation and the provided instructions. The colonoscopist, blinded to assignment, was asked to grade the bowel cleanliness after the examination using the Aronchick, Ottawa, and Chicago bowel scales. The primary endpoint was overall compliance with dietary and purgative solution instructions. Quality of the preparation was a secondary endpoint.
Results: 160 patients were enrolled (80 in each arm)**.** The average age was 54 (SD = 13), 55.6% were males, and 27.5% of patients had a BMI of $\geq$30. No difference in overall patient compliance and bowel cleanliness (on all 3 scales) was observed between the Paper and App groups. An adequate bowel preparation defined as either excellent or good on the Aronchick scale was noted in 82.5% and 77.2% of Paper vs. App group respectively ($p = 0.68$). Gender, age, BMI, and time of colonoscopy (am vs. pm) did not influence bowel cleanliness or patient compliance. Full compliance with clear fluids on day -1 was seen in 93.9% of patients with a BMI < 30 vs. 77.3% of those with a BMI $\geq$ 30 ($p = 0.009$). SPS was very well tolerated by 81.9% of patients as evidenced by their willingness to use it again in the future. The application was deemed user-friendly and helpful/indispensable by 96.2% and 87.3% of patients in the App group respectively.
Conclusion: Split-dose sodium picosulfate with dietary modification is well tolerated and highly effective for bowel cleaning prior to elective colonoscopy. A detailed face-to-face explanation of bowel preparation instructions leads to comparable results regardless of the instruction method used. Customized smartphone applications may replace traditional paper instructions in this information technology era.
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P0152 EARLY AND LONG-TERM OUTCOME OF A SINGLE-CENTER DATABASE ON ESD FOR COLORECTAL LESIONS WITH SPECIAL EMPHASIS ON LEARNING CURVE IN WESTERN SETTING

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Introduction: ESD for colorectal lesion is well established in Japan while has limited application in western countries.
Aims & Methods: The aim of present study was to report the early and long-term outcome as well the learning curve of a tertiary referral center that has established a database for colorectal ESD since 2008. Information on all patients who underwent ESD for colorectal lesions at our institution since 2008 have been prospectively collected in a database and patients followed-up with endoscopy on regular basis according to the lesion histology and standard guidelines. Collected data included size, morphology, location, technique of ESD, en-bloc rate, R0 rate, complication and recurrence. Part of these data have been previously reported in 2 papers. Results were compared between three consecutive study periods (2 years each until end of 2014) in order to determine the effect of learning curve on outcome.
Results: Overall data on 286 patients (167M, mean age 68.3 y) were recorded in the data base. Lesions were located in the rectum in 187 cases (68.8%) and mean diameter was 3.9 mm (range 15 to 110). ESD was aborted because of technical difficulties in 29 (10.1) with 12 of these patients switched to multipiece EMR and 17 referred for surgery. Hybdrid-knife technology was used in 105 cases (36%) while different types of knife (Flush-knife, Hook-knife, Dual-knife and Flex-knife) have been used in the remaining cases. Median operative time 108 minutes. En-bloc resection and R0 resection were respectively 82% (235 out of 286) and 72% (208 out of 286). Perforation occurred in 20 patients (6.9%) while bleeding occurred in 7 (2.4%) with all bleeding cases successfully treated with conservative management in 2 cases or endoscopic intervention in 5. Perforation required surgery in 7 cases while was managed conservatively in the remaining. No mortality associated to the procedure was observed. Histology has demonstrated intramucosal cancer or submucosal cancer in 110 cases (38.4%) and surgery was required because of advanced histology in 26 patients (9%). The mean follow-up was 32.7 months with 11 patients lost during follow-up and 4 patients died because of unrelated disease. The overall recurrence rate was 6.2% with most of these patients successfully treated with additional endoscopic therapy and 2 patients requiring surgery. Mean operation time (152 minutes vs 88 minutes, $p = 0.001$), en-bloc resection (62% to 92%, $p = 0.05$), R0 (56% to 85%, $p = 0.001$) significantly improve from period 1 (2008-2010) to period 3 (2012-2014). Perforation rate decreased from 11% in period 1 to 6.5% even though did not reach the statistical significance.
Conclusion: Data coming from a single European center experience confirm that ESD for colorectal lesions can be safely and effectively performed in western setting. However a long-training period with progressive learning curve is required to obtain results comparable with Japanese experts in terms of efficacy and perforation rate.
Disclosure of Interest: None declared

P0153 NON-ANESTHESIOLOGIST ADMINISTERED PROPOFOL SEDATION IN COLONOSCOPY – RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: Propofol allows the best sedation in colonoscopy. There is only one Randomized Controlled Trial (RCT) comparing Non-Anesthesiologist Administered Propofol Sedation (NAAPS) to sedation by an anesthesiologist.
Aims & Methods: Our goal was to compare the incidence of sedation related adverse events (AE), colonoscopy quality and patient satisfaction between NAAPS and anesthesiologist sedation. We performed a single blinded RCT with two parallel intervention groups (group A – NAAPS; group B – anesthesiologist sedation). The primary endpoint was the incidence of AE as defined by the World SIVA International Task Force on Sedation. Secondary endpoints were propofol dose, patient satisfaction and pain assessed by a 10 point visual analogue scale, procedure and recovery time and colonoscopy quality indicators (cecal intubation rate, withdrawal time, adenoma detection rate). Based on the AE incidence of our preliminary experience a sample size of 320 (1:1) was calculated with a non-inferiority margin of 15% for a power of 90% at a 5% level of significance. Patients aged 18-80 with low anesthetic risk (ASA I-II) were included. Statistical analysis was performed with SPSS version 21. Chi-square, Fischer's exact, t-tests and logistic regression were used as indicated.
Results: A total of 277 colonoscopies were performed (table 1). The incidence of AE was 39.3% on group A and 39.0% on group B (OR1.013; IC95% 0.622-1.651; $p = 0.959$). There were no severe (sentinel) AE events. The following interventions were necessary: atropine administration (0% vs 5.5%; $p = 0.004$); airway repositioning (8.7% vs 4.7%; $p = 0.196$); increase in O2 administration (6.7% vs 4.2%; $p = 0.317$); increase in fluids rate (2.6% vs 0.8%; $p = 0.242$). Mean propofol dose: group A 215 ± 92 mg vs group B 230 ± 97 mg ($p = 0.205$). Procedure times was 21.59 ± 12.967 and 18.64 ± 9.859 min ($p = 0.033$), withdrawal time was 11.37 ± 9.839 vs 9.84 ± 7.509 min ($p = 0.154$) and recovery time was 58 ± 33 min vs 67 ± 29 min ($p = 0.032$). Patients had no pain (0) in 83.5% vs 88.9% ($p = 0.208$) and reported complete satisfaction with the sedation in 82.4% vs 85.1% ($p = 0.887$). Procedural amnesia was reported in 83.9% vs 90.8% ($p = 0.093$). All but 2 patients (group B) were willing to repeat the colonoscopy under propofol sedation. Cecal intubation rates were 94.7% vs 96.1% ($p = 0.584$), adenoma detection rates were 28.4% vs 23.2% ($p = 0.331$).

	Group A (n = 150)	Group B (n = 127)
Male sex, n(%)	61 (40.7)	50 (39.4)
Mean age, years(sd)	58.6 (13.8)	55.4 (15.4)
ASA I/II, n	13/137	18/107
Cardiovascular disease, n(%)	20 (13.4)	12 (10.4)
Smoking, n(%)	24 (18.0)	20 (17.5)
Snoring history, n(%)	17 (13.1)	24 (21.8)

Conclusion: NAAPS is equivalent to anesthesiologist sedation in the rate of adverse events in a low risk population. Clinicaltrials.gov (NCT02067065).

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Disclosure of Interest: None declared

Abstract number: P0154

BBPS Score	8-9 (634 p) *	≥7 (1232 p) #	≥5 (2268 p) °	?5 (144 p)?	
Number of cases with polyps	163 (25.7%)	219 (17.7%)	420 (18.5%)	30 (20.8%)	* vs. # p = **0.0001*** vs. ° p = **0.0001*** vs. ? p = 0.2617# vs. ° p = 0.5894# vs. ? p = 0.4230° vs. ? p = 0.5640
Significant polyps (polyp > 1cm)	32 (5%)	73 (5.9%)	152 (6.7%)	12 (8.3%)	* vs. # p = 0.4871* vs. ° p = 0.1438* vs. ? p = 0.1761# vs. ° p = 0.3953# vs. ? p = 0.3416° vs.? p = 0.5693

P0154 IS THERE A RELATION BETWEEN BOSTON BOWEL PREPARATION SCALE AND THE DETECTION RATE OF POLYPS AT SCREENING COLONOSCOPY?

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Introduction: Colonoscopy is the most sensitive method for colorectal cancer screening, but inadequate bowel preparation can result in both missed pathological lesions and cancelled procedures.

Aims & Methods: We prospectively followed up the quality of colonic preparation at screening colonoscopy and tried to establish if there is a potential association between the bowel preparation and the polyp detection rate in screening colonoscopy.

We evaluated prospectively the bowel preparation during colonoscopy, using the Boston bowel preparation scale (BBPS) (a scoring system applied to the 3 broad regions of the colon: right colon, transverse colon and left colon, each part being evaluated from 0 and 3 as follows: 3 = entire mucosa of the segment seen well, 2 = minor amount of residual staining, 1 = segments not well seen due to residual stool or/and opaque liquid, 0 = unprepared segment), with a maximum of 9 points (perfectly cleaned colon). The bowel preparation was performed either with split or non-split regimens using PEG solution.

Results: We evaluated 2412 patients in whom screening colonoscopy was performed: 1377 women (57%) and 1035 men (43%). The mean BBPS score was 6.6 ± 1.3. Considering an excellent bowel preparation for the colonoscopy a BBPS score of 8 or 9 points, a good bowel preparation a BBPS score ≥ 7 points, and a score of ?5 points as an inadequate bowel preparation, we obtained the following BBPS score distribution: excellent preparation in 634 (26.3%) patients, good preparation in 1232 (51%) patients, and an inadequate preparation in 144 (6%) patients. In 450 (18.6%) patients we found one or more colonic polyps and in 166 (6.8%) patients significant polyps (polyp $\geq$1cm). We compared the polyp detection rate and significant polyp detection rate in relation with the BBPS score and we obtained the following results:

Conclusion: The polyp detection rate increased with the increasing of BBPS score; for significant polyps this association was not found.

Disclosure of Interest: None declared

P0155 MARKED VARIATION IN ENDOSCOPIC MUCOSAL RESECTION OUTCOMES WITHIN THE UK BOWEL CANCER SCREENING PROGRAMME

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Introduction: The use of endoscopic mucosal resection (EMR) is established as first-line treatment for the treatment of large non-pedunculated colorectal polyps (LNPCP), with practice now widespread in both the district general and tertiary setting. A large proportion of LNPCPs in the UK are managed within the Bowel Cancer Screening Programme (BCSP)[1] and recent data demonstrating increased variation in endoscopic polypectomy outcomes with increased polyp size[2] has led to concerns that the quality of endoscopic LNPCP management also varies widely between BCSP clinicians and centres, irrespective of procedure volume, with many patients potentially subject to suboptimal therapy.

Aims & Methods: Retrospective analysis was conducted on LNPCPs [MDR1] managed using EMR in the England Bowel Cancer Screening Programme (BCSP) within the North East region between 2011-14. A comparison of 12 month recurrence, an internationally recognised marker of successful endotherapy[3], was made between the four North East screening centres. Statistical analysis was performed using the Fisher's exact test.

Results: A total of 135 lesions were subject to 12 month surveillance with recurrent/residual polyp (RRP) identified in 8.1% of cases. RRP incidence was 8.4%, 0%, 29.2% and 3.9% at the 4 screening centres respectively, with screening centre location strongly associated with the probability of a finding of unsuccessful endotherapy ($p = 0.001$).

		12 month recurrence (%)		Total (n)
		n	y	
Screening Centre	A	91.6	8.4	24
	B	100	0	36
	C	70.8	29.2	24
D	96.1	3.9	51	
Total		**91.9%**	**8.1%**	**135**

Conclusion: A vast difference was demonstrated in the quality of endotherapy undertaken within a wide geographical area, with 12 month RRP varying between 0% and 29.2%. The results from this series are especially noteworthy given that the endoscopists concerned were all BCSP accredited, and therefore highly experienced and subject to a strict certification process. These findings indicate that advanced polypectomy is not a universal skill and that endoscopist quality varies markedly irrespective of experience. In addition, they highlight the importance of accurate lesion management and the identification of endoscopists with the requisite expertise to manage these complex lesions.

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Disclosure of Interest: None declared

P0156 CAECAL LOCATION IS ASSOCIATED WITH INCREASED LESION RECURRENCE FOLLOWING ENDOSCOPIC MUCOSAL RESECTION OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS

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Introduction: Large caecal polyps over 2cm in size are considered amongst the most complex lesions to achieve successful endoscopic resection, with recent data suggesting a significantly increased risk of post procedure bleeding and perforation associated with their endoscopic removal compared with elsewhere in the colon.[1,2] There is however a paucity of data assessing whether caecal location affects successful (R_0) clearance of lesions.

Aims & Methods: Retrospective analysis was conducted on large non-pedunculated colorectal polyps (LNPCPs) managed with endoscopic mucosal resection in the English Bowel Cancer Screening Programme (BCSP) between 2011-14. A comparison of 12 month recurrence rates, an internationally recognised marker of treatment success,[3] was made between caecal and non-caecal LNPCP groups. Statistical analysis was performed using the chi-squared test.

Results: A total of 135 lesions were identified, with 12 month recurrence identified in 8.1% of cases. Caecal location demonstrated a strongly significant association with recurrence compared with non-caecal location (27.8% vs 5.1%, p = 0.007)

	12 month recurrence (%)		Total (n)
	no	yes	
Caecal location?	94.9	5.1	117
	72.2	27.8	18
Total	**91.9%**	**8.1%**	**135**

Conclusion: Caecal location was associated with over a 5-fold increase (28.7% vs 5.1%) in the incidence of 12 month recurrence. The results from this series confirm the increased technical demands associated with the endoscopic resection of caecal LNPCPs, and are especially noteworthy considering that our study involved experienced BCSP endoscopists only. In view of the increased risk of endoscopic treatment failure, in addition to the established increased risk of adverse endoscopic events, caecal LNPCPs may benefit from multidisciplinary discussion and managed by a select group of advanced endoscopists.

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Disclosure of Interest: None declared

P0157 THE DEVELOPMENT OF A MINIMUM DATASET PROFORMA FOR THE MULTIDISCIPLINARY ASSESSMENT AND MANAGEMENT OF LARGE NONPEDUNCULATED COLORECTAL POLYPS

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Introduction: The lack of any structured framework internationally for the assessment and management of large non-pedunculated colorectal polyps (LNPCPs) appears to have resulted in a wide variation in decision making with regards to endoscopic and surgical management and suboptimal outcomes.[1] Multidisciplinary team discussion has been advocated to better coordinate management. The development of an evidence based and expert approved minimum dataset proforma may complement this process and encourage optimal management resulting in improved outcomes.

Aims & Methods: Following an extensive literature review, various patient and polyp parameters relevant to LNPCP assessment and management were selected. A 14 person British Society of Gastroenterology (BSG) approved multidisciplinary panel participated in Delphi consensus methodology to vote anonymously on the proposed parameters with ≥80% agreement required for consensus to be achieved. The draft proforma was then assessed on a sample of 20 LNPCP cases, resulting in modification after a further voting round.

Results: The final proforma comprised of 17 parameters encompassing all patient and lesion factors considered essential to the decision making process in LNPCP management. Patient parameters included patient symptoms, treatment preferences and comorbidity. Lesion parameters included morphology and surface characteristics (e.g. Paris classifications and Pit pattern) and the specification of any lesion features associated with increased complexity such an increased risk of malignancy, unsuccessful endoscopic resection or adverse endoscopic events[2]. Parameters regarding relevant histology and radiology results and guidance on obtaining adequate lesion imaging were also agreed.

Conclusion: The development and validation of a BSG/ACPGBI minimum dataset proforma allows for structured and comprehensive multidisciplinary discussion in LNPCP management, ensuring that all important factors are discussed and resulting in more coordinated and robust decision-making. This proforma can be used to structure discussions during a multidisciplinary team meeting and all related discussions such as referral to the tertiary setting, in addition to being used as a checklist for comprehensive lesion assessment.

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Disclosure of Interest: None declared

P0158 INCREASED PROCEDURE VOLUME LEADS TO IMPROVED ENDOSCOPIC MANAGEMENT OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS

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Introduction: Confirmation of lesion eradication at least 12 months after endoscopic mucosal resection (EMR) of large non-pedunculated colorectal polyps (LNPCPs) is an internationally recognised marker of therapeutic success[1]. Variable outcomes have been reported in international case series, with reported figures of up to 10% recurrent/residual polyp (RRP)[2]. Whilst various technical factors been attributed to the variable outcomes in treatment success, there is a paucity of evidence linking endoscopist advanced endotherapy procedure volume with successful curative resection of LNPCPs.

Aims & Methods: Retrospective analysis was conducted on LNPCPs managed with endoscopic mucosal resection in the North East NHS Bowel Cancer Screening Programme (BCSP) between 2011-14. A comparison of 12 month RRP was made between high volume (≥30 procedures per year) and low volume (<30 procedures per year) endoscopist groups. Statistical analysis was performed using the chi-squared test.

Results: A total of 135 lesions were identified, with 12 month RRP identified in 8.1% of cases. The incidence was higher in the low volume endoscopist group (12.3% (9) vs 3.2% (2),p = 0.064).

		12 month recurrence (%)		Total (n)
		no	yes	
Endoscopist procedure number	≥30	96.8	3.2	62
	<30	87.7	12.3	73
Total		**91.9**	**8.1**	**135**

Conclusion: A level of 12-month RRP comparable with international series (8.1%), suggests effective LNPCP management within the NHS BCSP. Whilst no statistical association was found between endoscopic volume and curative resection, an almost four-fold increase in failed curative resection was seen in the low volume endoscopist group (12.3% vs 3.2%). It can be argued that our study may be underpowered and that the results indicate clinical relevance. These outcomes also indicate that limiting advanced endotherapy to a select number of experienced therapeutic endoscopists may result in a further improvement in outcomes.

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P0159 ENDOSCOPIC REMOVAL OF DEFIANT COLORECTAL LESIONS: A RETROSPECTIVE STUDY IN A TERTIARY MEDICAL CENTER

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Introduction: Endoscopic mucosal resection [(EMR) en-block and piecemeal] has been recognized as an effective and less invasive curative endoscopic treatment procedure for large and nonpedunculated colorectal lesions (LNLs) > 20 mm.

Aims & Methods: The aims of the current study were to evaluate EMR complete resection and complication rate for LNLs > 20 mm and to estimate the long-term local recurrence rate afterwards. Data were collected retrospectively by use of the Electronic Endoscopy Report Data Base at our center. A total of 158 patients (84 men, 71.1 ± 7.52 years and 74 women, 70.58 ± 7.49 years) with 158 LNLs > 20 mm were enrolled. All endoscopic resections were performed by experienced endoscopists. All patients underwent standardized follow-up colonoscopy after 3.23 ± 2.43 months and 9.58 ± 6.26 months based on the lesion diameter, location, configuration, histopathology, type of EMR and endoscopic assessment of complete resection, respectively. The resection was regarded as incomplete if histopathologic examination revealed a residual/recurrent adenomatous tissue at the EMR scar site.

Results: En block resection was performed in 43/158 LNLs (27.21%) and piecemeal resection in 115/158 LNLs (72.78%). LNLs mean size was estimated at 34.9 ± 14.5 mm. Histological examination of LNLs showed 30 tubular adenomas (18.98%), 5 villous adenomas (3.26%), 102 tubular-villous adenomas (64.55%), 1 serrated adenoma (0.63%) and 20 adenocarcinomas (12.65%). High-grade

dysplasia was detected in 35 LNLs (22.15%) and low-grade dysplasia in 123 LNLs (77.84%). The first follow-up demonstrated 40/102 LNLs (39.21%) with residual/recurrent adenomatous tissue at the EMR scar site while the second revealed 23/87 LNLs (26.43%). The overall post-polypectomy complication rate was 4.43% (major complications 0.63%, one case of bowel perforation, minor complications 3.79% two cases of minor bleeding and three cases of postpolypectomy syndrome). Although, there was no statistically significant correlation between the size of the LNLs and the rate of residual/recurrent neoplasia after the first surveillance colonoscopy (t-test, $P = 0.052324$, $p < 0.05$), subsequent statistical analysis showed a strong correlation between the initial size of LNLs and the total rate of late recurrent and residual lesions after the second follow-up examination (t-test, $P = 0.0249$, $p < 0.05$). Finally, the use of chi-square test indicated that piecemeal resection is equally effective to en-block resection in LNLs related to recurrent/residual lesions at the previous EMR scar site ($\chi 2$ test, $P = 0.083$, $p < 0.05$).

Conclusion: EMR is safe and effective for treatment of LNLs > 20 mm. Nonetheless, a substantial portion of residual/recurrent adenomas at the previous EMR scar site can be detected. Therefore, an appropriate very strict follow-up surveillance colonoscopy protocol is necessitated in order to obtain biopsies from previous polypectomy scar sites.

Disclosure of Interest: None declared

P0160 EUROPEAN COLONOSCOPY QUALITY INVESTIGATION GROUP: IMPROVING STANDARDS IN COLONOSCOPY THROUGH A PRACTICE LEVEL AUDIT TOOL

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Introduction: Colorectal cancer is a major cause of morbidity and mortality worldwide. Colonoscopy remains the investigation of choice for both diagnosis and screening, and many countries have implemented screening programmes to allow for early detection. The European Society of Gastrointestinal Endoscopy quality in colonoscopy position statement highlights key quality indicators in colonoscopy and concluded that the success of screening programmes is related to the prompt provision of high quality, patient centred colonoscopy service. The European Colonoscopy Quality Investigation (ECQI) group of leading European clinicians developed a practical tool to enable audit of current clinical practice across Europe to assess whether quality standards are being achieved, and to identify, test, and implement practical ways of improving quality in colonoscopy.

Aims & Methods: The aim was to understand how quality is evaluated in current clinical practice via the development and implementation of an online tool to audit colonoscopy practice. At the inaugural meeting in 2013, the ECQI group recommended a clinical practice level audit tool to be developed to enable colonoscopists to audit their own practice. The audit tool was designed to encourage improvement in overall outcomes (e.g. adenoma detection rate), and to ensure consistency and high standards across clinical practice, within countries and across Europe, and was validated by the group in September 2014. A phase 1 pilot to test this tool was performed in November 2014, with early outputs discussed by the group in December 2014. The audit tool was further revised to improve usability via a collaborative iteration process.

Results: The online audit tool was piloted at centres across 10 European countries with 313 patient visits recorded on the initial questionnaire during a 1-week period. Questions included: patient demographics, the status and experience of the practitioner performing the endoscopy, details of the bowel preparation procedure used and the quality of bowel cleansing achieved, colonoscopic findings, and follow up arrangements. Following the review of the phase 1 pilot, consensus from the ECQI group resulted in the refinement of the tool to create an updated version which included three separate sections: Practitioner, Centre and Patient level questionnaires to improve efficiency of use. This will form part of a second phase pilot planned for 2015.

Conclusion: The creation of the ECQI Group enabled the development of a validated, practice level audit tool to enable clinicians to audit their own practice. This tool will be tested in a second pilot phase, and its value will be further evaluated by the Group in order to make recommendations for its use across Europe. The range of experience and geographical spread of the participants allows for quality evaluation to be compared across practices and countries. The longer term aim of this project is to enhance the quality of colonoscopy at a practice level by enabling clinicians to be involved in improving their own practice.

Disclosure of Interest: J. Riemann Consultancy: Advisory board participant for Norgine, I. Demedts Consultancy: Advisory board participant for Norgine, A. Agrawal Consultancy: Advisory board participant for Norgine, R. Jover Consultancy: Advisory board participant for Norgine, A. Ono Consultancy: Advisory board participant for Norgine, P. Amaro Consultancy: Advisory board participant for Norgine, E. Toth Consultancy: Advisory board participant for Norgine, P. Eisendrath Consultancy: Advisory board participant for Norgine, A. Naidoo Conflict with: Employee of Norgine

P0161 UNDERWATER ENDOSCOPIC MUCOSAL RESECTION: THE THIRD WAY FOR EN BLOC RESECTION OF COLONIC LESIONS? A CASE SERIES

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Introduction: Underwater endoscopic mucosal resection (UEMR) has been described since 2012 for removing large colorectal non polypoid lesions[1,2,3,4]; it is based on filling the colonic lumen with water and it differs from traditional endoscopic mucosal resection since it does not require sub-mucosal injection.

Aims & Methods: To evaluate the reproducibility of this new endoscopic technique in terms of ease of implementation, safety and efficacy. UEMR prospectively performed in a community hospital were gathered.

Results: From September 2014 to February 2015 20 colorectal non polypoid lesions (median size 24.7 mm, range 10-50mm) have been removed in 20 patients (12 women; median age 62.2 years). Two of the lesions were adenomatous recurrences on scar of previous resection and one was a recurrence located on a surgical anastomosis. Five lesions were located in the cecum, seven in the ascending colon, two in the transverse colon, one in the descending colon, one in the sigmoid colon and three in the rectum.

In 16 lesions (80%) the resection was performed en bloc, whereas 4 (20%) were removed by piece-meal resection. At the pathological examination six lesions had non advanced histology, 10 lesions had advanced histology and 4 were SSA, one of which with high grade dysplasia.

Complete resection was observed in all the sixteen lesions removed en bloc.

A complication (intra-procedural bleeding, endoscopically managed with no consequences) was observed in the first two UEMR.

Conclusion: UEMR appears an easy, safe and effective technique also in community setting. Further studies comparing UEMR and conventional EMR in terms of complete resections and evaluating the early and late recurrence are needed.

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P0162 IS WATER-ASSISTED COLONOSCOPY SUPERIOR TO CARBON DIOXIDE ASSISTED STANDARD COLONOSCOPY: RESULTS OF AN OBSERVATIONAL STUDY

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Introduction: Water-assisted colonoscopy [WAC] is known to reduce patient discomfort and improve the adenoma detection rate [ADR] [1]. In this retrospective observational study, we compared water assisted colonoscopy against standard colonoscopy [SC] using CO2 in a bowel cancer screening positive population.

Aims & Methods: This was a retrospective review of prospectively collected data. The population studied was undergoing colonoscopies following a positive faecal occult blood test as part of the bowel cancer screening programme [BCSP]. Endoscopist A preferred to intubate the caecum using the water exchange method and endoscopist B would insufflate the bowel using carbon dioxide. Sedation and analgesic use was at the discretion of the endoscopist. The primary outcome was the adenoma detection rate and the comfort scores in the two groups. Secondary outcomes included caecal intubation rate, mean withdrawal time, sedation use and polyp retrieval rate.

Results: Data from two hundred and seven colonoscopies performed from April 2014 to December 2014 [9 months] were analyzed. 102 colonoscopies were performed using the water exchange method [group A] and 105 colonoscopies were performed using CO2 [group B].

Primary outcomes:

Adenoma detection rate [ADR] in group A was 53% compared to of 36% in group B.This was statistically significant [difference in rate = -0.1868 [95% CI 0.0052- 0.3685 $p = 0.0438$].

The proportion of patients experiencing none [score 1] or minimal [score2] discomfort [based on modified Gloucester comfort score] were more in group A [n = 74] compared to group B [n = 62]. This was found to be statistically significant [$Z = 2.046$, $p = 0.0408$].

Secondary outcomes:

Indicator	Group A	Group B
Caecal intubation rate	95%	97%
Mean withdrawal time	8.4 minutes	7 minutes
Polyp retrieval rate	93%	95%
Intravenous sedation	68	87
Entonox only	30	13

Conclusion: Our finding of a significant improvement in ADR and better tolerability in the WAC group supports similar conclusions by Hsieh et al. This may have potential implications for the bowel cancer screening programme since the perception of colonoscopy can influence public participation and improve uptake in the BCSP. Improved ADR may be due to combination of factors like improved bowel preparation, flattening of mucosal folds and floating effect of polyps with water irrigation.

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P0163 EFFECT OF HIGH BMI ON ADEQUACY OF BOWEL PREPARATION & COLONOSCOPY PERFORMANCE

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Introduction: There is limited evidence regarding the effect of high body mass index (BMI) on colonoscopy performance. Given the prevalence of high BMI in regional communities, this association may impact on the already limited resources within regional hospitals [1,2].

Aims & Methods

Objective: To determine if there is an effect of high BMI on bowel preparation and colonoscopy performance.

Design: A single centre prospective study at a teaching hospital in Ballarat, Victoria, Australia between May 2012 and November 2014. Patients undergoing colonoscopy for any indication were included.

Method: Patients were divided into two groups, BMI $\geq$25 or BMI $<$25. Colonoscopies were performed by 17 experienced endoscopists and the data collected by trained endoscopy nurses. Bowel preparation was assessed using the Ottawa Bowel Preparation Scale. Colonoscopy performance was assessed using caecal intubation times (short up to 6 minutes, intermediate = 7-9 minutes and long $\geq$ 10 minutes). Chi-square statistical analysis was used to determine significance ($p = <0.05$).

Main outcome measurements: Adequacy of bowel preparation and caecal intubation time.

Results: A total of 2026 colonoscopies were performed during the study period. 74% of participants had a BMI $\geq$25. Both the low BMI and the high BMI groups has similar adequacy of bowel preparation (93%, $p = 0.16$). Short caecal intubation time (up to 6 minutes) was 29% for patients with normal BMI, and 35% for patients with high BMI. 28% of patients with a normal BMI had an intermediate caecal intubation versus 23% for patients with high BMI. For patients with a long caecal intubation time, 41% had a normal BMI, compared to 42% of patients with a high BMI, which was not statistically significant ($p = 0.37$).

Discussion: In this study we found that high BMI is extremely prevalent in the Ballarat population. However, high BMI did not contribute to a statistically significant difference in the quality of bowel preparation or colonoscopy performance. This prospective study, showing important negative results, has a good sample size and was conducted by 17 experienced colonoscopists. However being a single-centre study, the generalizability of the results is limited.

Conclusion: The study has shown that there is no correlation between high BMI and colonoscopy performance. A multicentre study may be helpful in further establishing significance of high BMI and colonoscopy performance.

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P0164 PROSPECTIVE RANDOMIZED COMPARISON OF THE SAFETY AND EFFECTIVENESS OF ANESTHESIOLOGIST-ADMINISTERED PROPOFOL ALONE VERSUS PROPOFOL AND NALBUPHINE DEEP SEDATION FOR OUTPATIENT COLONOSCOPY

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Introduction: Colonoscopy is nowadays routinely carried out under propofol deep sedation. Nalbuphine is a widely used major analgetics and is an ideal drug to reduce the given propofol dose during outpatient colonoscopy. The aim of our present prospective, randomized study was to evaluate the safety and effectiveness of 397 ambulatory colonoscopies carried out under propofol versus propofol and nalbuphine deep sedation with respect to endoscopic success rate, complications and patient satisfaction.

Aims & Methods: 190 patients received nalbuphine and propofol and another 207 patients received propofol alone in a randomized manner. The cecal intubation rate, the incidence of major and minor cardiovascular and respiratory complications during deep sedation in terms of the mean of the highest and lowest blood pressure and heart rate values were prospectively measured (BPmax and BPmin mean, Pmax and Pmin mean) as well as changes in oxygen saturation (SpO2) were calculated. The propofol induction and total dose, the time from induction to spontaneous awakening, the recovery time and Post Anesthetic Discharge Scoring System (PADSS) were also compared.

Results: No significant differences in the cecal intubation rate was demonstrated in the nalbuphine and propofol vs. propofol groups: 98.4% vs. 96.8% ($p = 0.4$). No major cardio-respiratory complications lasting more than 2 minutes occurred. The induction propofol dose was 40 ± 13 mg vs. 74 ± 45 mg, and the corresponding mean total doses of propofol was 80.5 ± 32.7 mg and 142.9 ± 88.1 mg in the two groups, respectively ($p < 0.05$). Comparison of patients groups with nalbuphine and propofol versus propofol administration alone depicted no significant differences regarding to the mean awakening time 30.4 min $\pm$ 10.7 vs. 29.3 min $\pm$ 9.4, ($p = 0.3$), and the mean recovery time 51.7 min $\pm$ 23.3 vs. 68.1 min $\pm$ 29.5 ($p = 0.4$). However, and the results of PADSS was significantly different, and demonstrated more gastrointestinal symptoms to prevent timely patient discharge in some of patients in the nalbuphine group ($p < 0.05$).

Conclusion: Colonoscopy procedures implemented in propofol deep sedation administered by an anesthesiologist turned out to be completely safe procedure, with excellent coecum intubation rate and optimal patient satisfaction. Low-dose nalbuphine combined with propofol is an effective and economic alternative in the reduction of propofol needs, but gastrointestinal side effects of morphine agonists significantly reduce the PADSS and may prevent timely patient discharge.

Disclosure of Interest: None declared

P0165 RELATIONSHIP BETWEEN THE POSITION OF THE ILEOCAECAL VALVE IN THE COLONIC CIRCUMFERENCE AND THE FEASIBILITY OF ITS INTUBATION

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Introduction: Ileal intubation is an important goal in colonoscopy practice.
We have studied if the position of the ileocaecal valve in the colonic circumference can determine a feasible and prompt ileal intubation.

Aims & Methods: We randomized 177 consecutive patients (mean age: 56 yrs; range: 13-87 yrs; 52% males) in which we reached a clean caecum to supine (62.7%) and right-lateral decubitus posture (37.3%).
This two postures resulted in different positions of the ileocaecal valve: 5.7% in the quadrant I (2 o'clock: 2.3%, 3 o'clock: 1.1% and 4 o'clock: 2.3%); 20.3% in the quadrant II (5 o'clock: 3.4%, 6 o'clock: 5.6% and 7 o'clock: 11.3%); 43.5% in the quadrant III (8 o'clock: 7.9%, 9 o'clock: 15.3% and 10 o'clock: 20.3%) and 30.5% in the quadrant IV (11 o'clock: 20.9%, 12 o'clock: 7.3% and 1 o'clock: 2.3%).
With the scope shortened and de-looped we moved it back to the ileocaecal valve, trying to get into the ileum (at least 3 cm) with the tip.

Results: Successful ileal intubation was achieved in the first attempt (16.9%), in the first three attempts (71.7%), or in the first five attempts (89.2%).
We did not find statistically significant difference in accomplishment ileoscopy in the first attempt depending on quadrant ($p = 0.158$) nor o'clock position ($p = 0.189$), because of the low percentage of success in this case, but we did for the first three attemps ($p = 0$ for quadrant; $p = 0$ for óclock position) and for the first five attemps ($p = 0.005$ for quadrant; $p = 0$ for o'clock position).
Quadrant III and 10 o'clock position were the best locations for a quick ileoscopy.

Conclusion: The exact position of the ileocaecal valve in the colonic circumference, a modifiable condition by changing the patient's posture, can determine success in its intubation and promptness to get it.
This is a scarcely analyzed point that could improve safety and comfort for patients undergoing in colonoscopy.

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Disclosure of Interest: None declared

P0166 PREDICTORS OF INADEQUATE BOWEL PREPARATION FOR COLONOSCOPY: A PROSPECTIVE STUDY

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Introduction: Inadequate bowel preparation remains a common problem on our daily clinical practice and is associated with canceled procedures, prolonged procedure time, incomplete examination, but most importantly, with missed pathology.
Aims & Methods: This prospective study was designed to assessment the quality of intestinal preparation and evaluate potencial factors associated with an inadequate level of bowel preparation.
Methods: We prospectively studied consecutive outpatients who had colonoscopies performed at our hospital between March and December 2013. Patients' data were analyzed and a questionnaire was applied to the gastrenterologist after the examination. The grade of intestinal preparation was evaluated using the Aronchick preparation assessment scale.
Results: A total of 196 patients were enrolled into the study (51.2% male; with a mean age of 64 ± 13 years). Only 10.6% of patients were not able to follow the bowel preparation instructions and 34.0% described a poor tolerability to the bowel preparation. An excellent or good bowel preparation was achieved in 61.7% and a fair, poor or inadequate intestinal preparation was reported in 38.3% of observed colonoscopies. An earlier colonoscopy start time ($p < 0.034$), age greater than 65 years ($p < 0.014$), male gender ($p < 0.001$) and higher weight ($p < 0.034$) were independent predictors of an inadequate intestinal preparation. There was no significant difference in the quality of bowel preparations among the types of bowel preparations administered to the patient, the tolerability of bowel preparation and the quality of preparation instructions ($p > 0.05$).
Conclusion: This prospective study identified several factors that may predict inadequate bowel preparation irrespective of bowel preparation type, compliance with preparation instructions and tolerability. This information may help to identify patients at an increased risk for inadequate colonic preparation for whom the personal education would be appropriate.

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P0167 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION IN A WESTERN TERTIARY REFERRAL CENTRE. ANALYSIS OF 173 CASES: LONG-TERM RESULTS AND IDENTIFICATION OF POSSIBLE RISK FACTORS FOR TECHNICAL DIFFICULTY

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Introduction: Colorectal endoscopic submucosal dissection (CR-ESD) enables en-bloc resection of lesions > 2 cm which would otherwise require piecemeal removal. However, CR-ESD is still considered as a technically challenging procedure and is not widespread outside Asian expert centres.
Aims & Methods: Our aim was to assess efficacy, safety and long-term results for CR-ESD and identify possible risk factors for technical difficulty. We analysed charts from 173 consecutive patients who underwent CR-ESD between May 2006 and July 2013. Efficacy and safety endpoints were complete en-bloc resection rates, endoscopic and histological remission and post-procedural complications.
Results: Median age of patients was 67 years (IQR 58-76). Lesions were located throughout the colon with predominance for the caecum and rectum: ileo-anal pouch (1.2%), ileo-caecal valve (4.6%), caecum (21.4%), ascending colon (11.6%), hepatic flexure (6.9%), transverse colon (4%), splenic flexure (2.3%), descending colon (1.7%), sigmoid colon (6.4%) and rectum (39.9%). Median longest and perpendicular diameter of lesions was 35mm (range 10-150mm) and 30mm (range 8-130mm) respectively. Most lesions were classified as Paris 0-IIa (45.1%), 0-Is (29.5%) and 0-IIb (17.3%). Forty-eight percent of lesions were classified as LST-NG according to the Japanese classification. In 15.6% of cases a previous resection had been attempted elsewhere. Full ESD was performed in 117 (68%) patients; the remainder was treated using a hybrid technique of circumferential submucosal incision, dissection and finally followed by en-bloc snare resection. Median procedure duration was 109 minutes (IQR 70-157). The en-bloc resection rate was 74.6% (129/173). Previous attempt at resection was a significant risk factor for en-bloc resection failure (40.8% vs. 22.7%; $p < 0.05$). Twenty-one (12.1%) perforations occurred during ESD, which were all successfully managed by endoscopic clip closure. One or more post-procedure complications occurred in 46 patients (26.9%) of which 15 delayed perforations (8.6%). The complication rate decreased significantly with growing experience (e.g. 14 delayed perforations for the first 87 cases vs. 1 for the last 86 cases; 16% vs. 1%; $p < 0.05$). Two patients required surgery for post-procedural perforation salvage. Median hospital stay was 2 days (IQR 2-2). The majority of lesions (114/173; 65%) contained high-grade dysplasia or more advanced histopathology (Table 2). Free vertical margins were achieved in 92% (160/173) of patients. Fourteen patients underwent additional surgical resection because of incomplete resection or unfavourable histology. Endoscopic follow-up was available in 154 patients. During the median follow-up period of 13 months (IQR 3-24), 2 small mucosal recurrences occurred which were resected endoscopically.
Conclusion: CR-ESD is effective with very low local recurrence rates. Previous attempts at snare resection are predictive for en-bloc resection failure. In general, post-procedural course is favourable with short hospitalisation stays. Complications (especially delayed perforation) have to be considered, but usually can be managed conservatively. A growing level of experience significantly reduces the post-procedural complication rate.
Disclosure of Interest: None declared

P0168 THE USEFULNESS OF BALLOON OVERTUBE-ASSISTED COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION WITH A RUBBER BAND TISSUE TRACTION DEVICE

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Introduction: The gastroscope is often used even for colorectal ESD on a priority basis because operational performance is suitable to procedure in our facility. However, anatomic variability in the colon may hinder any endoscopic intervention. In cases which access to the lesion with a gastroscope was difficult, we used a balloon overtube as an endoscopic channel for colorectal ESD. In addition, to enable a more safe and efficient procedure, we combined balloon overtube- assisted ESD with a rubber band tissue traction device (RTD), designed to be fixed on freed edges of a mucosal overlay with clips to deflect the diseased mucosa away from the dissection plane.
Aims & Methods: We aimed to evaluate the utility of balloon overtube- assisted colorectal ESD with a RTD as needed. At The Jikei University Hospital from April 2012 to December 2014, we performed ESD in colorectal lesion for 311 patients. In the preoperative evaluation of accessibility with a gastroscope, thirty one patients were identified as difficult, and were enrolled in the balloon overtube- assisted ESD and retrospectively examined.
Conclusion: There were little practical differences between the standard ESD method using a gastroscope without the overtube and the balloon-assisted ESD method in term of outcome for therapy. This result suggested that use of the balloon overtube is an effective for colorectal ESD, when lesions are located at difficult positions in the right side colon. Furthermore, as the situation demands, using the RTD for colorectal ESD was also suggested to effective procedure.
Disclosure of Interest: None declared

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	Ratio of the use of RTD	M or SM slightly cancer/SM deeply cancer	Protoruded/ Flat elevated/ Others	Cecum/Right colon/Left colon/Rectum	Mean size of specimen	Mean time of procedure	Ratio of curative resection	Ratio of complication Perforation/Bleeding
Standard (n: 280)	33.2%	261/19	114/158/8	27/115/64/74	39.9mm (18-150)	62.8min (5-560)	91.1%	1.4%/2.9%
Overtube (n: 31)	29.0%	30/1	12/18/1	10/21/0/0	40.1mm (25-71)	63.7min. (20-212)	83.8%	0%/0%

P0169 CECAL INTUBATION RATE (CIR) CORRELATES WITH ADENOMA DETECTION RATE (ADR) BUT HAS NO IMPACT ON ADVANCED ADENOMA DETECTION RATE (AADR)

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Introduction: Incomplete screening colonoscopy can result in missing precancerous lesions, such as adenomas. By a study of Kaminski et al., cecal intubation rate (CIR) as a major quality indicator, showed to be not associated with higher risk of interval cancer.

Adenoma detection rate (ADR) is considered a main quality measure in screening colonoscopy and should be at least 20%. Advanced adenomas (AA) carry greater risk for progression to cancer than non-advanced adenomas and should be detected early.

Because of lack association between CIR and the risk of interval cancer, our primary aim was to investigate whether there is a correlation between CIR and ADR. Further we wanted to assess if CIR correlates with AADR and if findings differ between high (≥95%) and low CIR-group (<95%).

Aims & Methods: Within the Austrian quality assurance program, 148.284 colonoscopies performed by 197 endoscopists were analyzed. Spearman rank-order was used to assess correlation between CIR and ADR, as well as AADR.

Results: Median CIR was 97.38% [Interquartile range (IQR) = 94.24% > 98.65%] and ranges from 72.95% > 100%. Median ADR was 21.37% (IQR = 16.25% > 27.78%) with a minimum of 4.45% and a maximum of 43.06%. Median AADR was 5.43% (IQR = 3.71% > 8.40%) with a range from 0.00% to 20.93%.

Spearman rank order coefficient (r_s) of 0.222 showed a significant correlation between CIR and ADR ($p < 0.001$). AADR was independent of CIR ($R_s = -0.024$; $p = 0.735$) within both groups of endoscopists, those with CIR <95% ($r_s = 0.152$; $p = 0.251$; $n = 59$) as well as within high (≥95%) CIR-group ($r_s = -0.036$; $p = 0.679$; $n = 138$).

Conclusion: CIR correlates with ADR but has no impact on participants' detection of advanced adenomas, which could explain the lack of impact of CIR and the risk of interval cancer in the study of Kaminski et al.

Disclosure of Interest: None declared

P0170 IDENTIFICATION OF COLONOSCOPY COMPLICATIONS RATE IN 6 SPANISH COLORECTAL CANCER SCREENING PROGRAMMES

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Introduction: In Spain, colorectal cancer screening programmes (CRCSP) are being progressively implemented, with 28% coverage (for all Spanish population) in 2014. The regions of Canarias, Cantabria, Cataluña, Murcia, País Vasco and Valencia participate in the CRIBEA Project with the aim to identify CRC screening benefits and warms (FIS PI12/00944, financed by FEDER funds). The programmes are directed at men and women between 50 and 69 years of age with the aim to reduce CRC incidence and mortality. The screening test is a biennial faecal occult blood test (FOBT), and the confirmation test is a colonoscopy. Colonoscopy complications are one of the adverse effects of screening, and could be immediate (during the exploration) or deferred (post-exploration). Immediate complications are easy to identify and register but deferred ones not, because of ignorance of the time that occurs.

Aims & Methods

Aim: To estimate the severe complications rate (immediate and deferred at 30 days) in the context of further investigation colonoscopies (after positive FOBT) in the context of 6 Spanish CRCSP according to the European definition of severe complication (severe bleeding that requires transfusion, intestinal perforation, severe vagal syndrome, similar to peritonitis syndrome).

Method: Retrospective population-based cohort study, defined by the population with colonoscopy performed in 6 regions of Spain with CRCSP from 2000 to 2012. Information sources: the screening information system and the Minimum Set Basic Data (MDS) information system (mandatory in all hospitals). The identification process of complications is managed by crossing the personal identifiers of people with screening colonoscopy and the hospital admissions 30 days after the colonoscopy performance. Matched people are identified using CIE-9 codes.

Results: A total of 2.15413 million invitations and 959 249 people participated in these regions. People with positive FOBT were 52.913, and 47.008 colonoscopies were performed. The complication rate for both sexes was 5.02 per thousand colonoscopies (236/47008), men being 5.51% (151/27402) and women 4.34% (85/19606). Complication rate for the age group 50-59 was 3.76%, and for 60-69 was 4.57%.

Conclusion: A significant number of deferred screening colonoscopy complications need to be identified in hospital registries. The severe complications rate is 5.02 per 1000 colonoscopies. The complication rate was higher in men versus women and in the age group of 60-69 years versus 50-59.

Disclosure of Interest: None declared

P0171 THE IMPACT OF "BEHIND FOLDS VISUALIZING" COLONOSCOPY – A POOLED ANALYSIS OF RANDOMIZED BACK-TO-BACK TANDEM COLONOSCOPY STUDIES

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Introduction: The Third Eye Retroscope, Full Spectrum Endoscope (FUSE) and EndoRings have been developed to improve visualization behind colonic folds and have individually been shown to reduce overall adenoma miss rates. Using a pooled analysis, we evaluated for which adenoma characteristics and in which patient subgroups "behind folds visualizing" techniques are most optimal to reduce miss rates.

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Table. Ade: noma miss rate per adenoma characteristic and patient subgroup.

Adenoma characteristics		Standard colonoscopy	"Behind folds visualizing" technique	
		Missed/total (%)	Missed/total (%)	P-value[a]
All adenomas[b]		93/255 (36)	37/264 (14)	<0.001
Localization	*Proximal colon*	51/135 (38)	21/156 (13)	<0.001
	Distal colon	42/119 (35)	16/108 (15)	<0.001
Adenoma size	*≤5mm*	71/189 (38)	34/203 (17)	<0.001
	6-9mm	19/43 (44)	3/38 (8)	<0.001
	≥ 10mm	3/23 (13)	0/23 (0)	0.233
Morphology	*Pedunculated*	3/24 (13)	1/39 (3)	0.150
	Sessile	73/195 (37)	34/209 (16)	<0.001
	Flat	14/27 (52)	1/11 (9)	0.014
Histology	*Tubular (Tubulo) villous*	84/223 (38)	35/238 (15)	<0.001
		4/19 (21)	0/16 (0)	0.109
Advanced adenomas[c]		6/35 (17)	1/32 (3)	0.108
Serrated lesions[d]		4/8 (50)	1/14 (7)	0.039
Patient subgroups				
Gender	*Female*	27/61 (44)	11/61 (18)	0.002
	Male	66/194 (34)	26/203 (13)	<0.001
Age	*<50 years*	4/11 (36)	3/18 (17)	0.375
	50-60 years	40/103 (39)	14/102 (14)	<0.001
	> 60 years	49/141 (35)	20/144 (14)	<0.001
Indication	*Screening*	30/103 (29)	18/113 (16)	0.020
	Surveillance	43/98 (44)	15/111 (14)	<0.001
	Diagnostic workup	20/54 (37)	4/40 (10)	0.003

[a]Calculated using chi-square or Fisher's exact test where appropriate. [b]Including 2 adenocarcinomas. [c]Any adenoma with villous features, high-grade dysplasia or ≥10mm. [d]Serrated lesions are counted separately from adenomas.

Aims & Methods: Data of three independent multicentre randomized trials (NCT01044732; NCT01549535; NCT01955122) were combined. Patients underwent same-day, back-to-back tandem examinations with both standard colonoscopy and Third Eye Retroscope, FUSE or EndoRings colonoscopy, respectively. In a pooled analysis we determined adenoma miss rates stratified by adenoma characteristics and patient subgroups.
Results: A total of 650 patients (60% male, mean age 57.5 ± 9.7 years) were randomized, of which 320 patients underwent standard colonoscopy first and 330 patients underwent ''behind folds visualizing'' colonoscopy first. Adenoma miss rates with ''behind folds visualizing'' colonoscopy were significantly lower compared to standard colonoscopy for proximally and distally located adenomas, for ≤5mm and 6-9mm adenomas, for sessile, flat and tubular adenomas, and for serrated lesions (Table). The miss rates were not statistically significantly different for ≥10mm, pedunculated, (tubulo)villous and advanced adenomas. Adenoma miss rates were significantly lower with ''behind folds visualizing'' colonoscopy independent of gender and indication, and in all persons ≥50 years.
Conclusion: ''Behind folds visualizing'' colonoscopy reduces miss rates in all segments of the colon for 1-9mm adenomas; no significant differences were found for larger (≥10 mm) and advanced adenomas. Whether the detection of more small (<10mm) adenomas indeed reduces CRC incidence and mortality remains to be determined.
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P0172 ENDOSCOPIC SUBMUCOSAL DISSECTION LEARNING CURVE: EXPERIENCE OF A LARGE VOLUME COLONOSCOPY CRC ITALIAN SCREENING CENTER

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Introduction: endoscopic submucosal dissection (ESD) is an advanced endoscopic technique that allows for curative resection of superficial neoplasms in GI tract. The vast majority of experience and guidelines for ESD resection comes from Japan, where this technique was developed more than 10 years ago. In East countries the training curve is done on gastric GI lesions with expert supervision before starting on esophageal and colon lesions. In West countries EGC is a rare desease and expert guidance is not commonly available, so the learning courve of this tecnhique has to be developed in a different way.
Aims & Methods: To demonstrate that the ESD learnig curve performed on rectal lesions is a good way to practice on these difficult procedure in European countries. We retrospectovely included in the study all the ESD performed in our Endoscopy Unit in Padua from february 2012 to april 2015. None neplastic lesions come frome other endoscopy units. We considered the learning curve of a single dedicated endoscopist that before starting on humans performed 10 ESD on in vivo animal models under expert guidance. All the dissections were performed using Hybridknife needle and ERBEJET2 (ERBE®). Complications after procedure like bleeding and perforation were managed with hemoclips, Over the scope clips and hemostatic forceps. ESD was performed if the neoplastic lesion was considered susceptible to ESD regardless to the size. T test for unpaired data and Pearson chi-test were used for ststistical analysis.
Results: 40 ESD were performed, 22M(55%) and 18F(45%), mean age 63yr. 27 rectum (68%), 9 sigmoid tract (23%), 1 trasverse colon (2%), 3 ascending colon (7%). The neoplastic lesions were: 31 laterally spreading tumors (77%), 2 polipoid lesions 0-Is (5%), 3 recurrent tumor on scar (8%), 4 polipoid lesion 0-Isp(10%). Mean polyp area was 17.5 cm^2. Mean intervention time 107 min. En-bloc dissection was successful in 25/40 (63%) and R0 was reached in 18/24 (75%). Polyps hystological features were: 10 LGD (25%), 21 HGD (53%), 6 pT1 (15%), 3 pT2 (7%). Procedural complications accurred in 12/40 (30%): perforation in 8/40(20%), delayed bleeding 2/40(5%), rectal stenosis 2/40(5%). No deaths or surgical interventions followed the procedural complications. From the 12th procedure onwards the en-bloc performance became acceptable 22/27(81%) vs 3/12(25%) ($p < 0.001$). From the 30th procedure onwards the en-bloc performance became good 9/10 (90%, $p < 0.05$) and the mean execution time was significantly lower 55 vs 122 min ($p < 0.0001$) with no significant difference in the mean area of the lesions 15.6 vs 18.2 cm^2 (p = ns). Only 1 complication occurred after the 30th procedure (p = ns).
Conclusion: In our experience to reach an acceptable confidence with ESD procedure starting the training from in vivo animal model (at least 10 procedures) and then to colo-rectal neoplasms no less than 12 procedures had to be performed, but we still probably havent yet reached the learning curve plateau also after 40 procedures.
Disclosure of Interest: None declared

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	Standard Group (n = 20)	PCM-t Group (n = 15)	p
Lesion size, (median;range),mm	58.5; 50-104	66; 51-170	0.364
Tissue size, (median;range),mm	68.5; 50-123	74; 58-198	0.131
Time of procedure, (median;range),min	104; 46-321	107; 47-540	0.987
Dissection speed, (median;range),mm^2/min	26.6; 11-65.3	33.7; 22-78.2	**0.046**
Hemostatic Forceps Use	5;3-15	4;0-21	**0.044**
En-Bloc Resection, n(%)	18(90)	15(100)	0.319
Complete Resection, n(%)	18(90)	15(100)	0.451
R0 Resection	1(5)	0(0)	
R1 Resection	1(5)	0(0)	
Rx Resection			
Complication,n			0.241
Delayed bleeding	0	1	
Perforation	1	0	
Localization,n			0.155
Rectum	11	9	
Sigmoid colon	0	3	
Descending colon	3	0	
Transverse colon	1	0	
Hepatic Flexura	2	0	
Ascending colon	1	2	
Ceacum	2	1	
Pathology,n			0.46
Carcinoma	11	7	5
-Intramucosal	10	0	
-Sm1 invasion	1	0	
Tubular Adenoma	1	0	
Tubulovillous Adenoma	5	7	
Villous Adenom	4	1	

P0173 A NEW TECHNIQUE IN TREATMENT OF GIANT LATERAL SPREADING TUMORS WITH ENDOSOCPIC SUBMUCOSAL DISSECTION; POCKET CREATION TUNNELING METHOD

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Introduction: Endoscopic submucosal dissection (ESD) has been widely accepted as an effective and minimally invasive treatment for patients with premalignant lesions. ESD allows en-bloc resection of a lesion, irrespective of the size lesion. However, en-bloc resection of large laterally spreading tumors (LST) with ESD is difficult technically because of anatomical features of the colon including its longer length, narrower lumen, and thinner walls and needs longer procedure time in the colon. The pocket-creation method (PCM) is a new technique in overcoming these difficulties of ESD in the treatment of colorectal lesions ≥3cm in size. But for larger lesions both the vascular structures and submucosal area to be dissected is larger. We investigated the efficacy of pocket creation tunneling method (PCM-t) in giant (≥5 cm) LSTs.
Aims & Methods: A total of 345 ESD procedures, which were performed in the esophagus, stomach, colorectum and duodenum between April 2012 and April 2015, were recorded prospectively before and after the procedure. 191 ESD procedures were performed in the colorectum. Lesions <5 cm in size and those removed with PCM were excluded from the study. The data of the rest 35 patients with lesion size ≥5cm were analyzed retrospectively. The patients were divided in to two groups; namely the ESD and PCM-t, according to the technique performed. The en-bloc and complete resection rates,complications, size of lesions, pathological results, length of procedure and dissection speed, and frequency of hemostatic forceps use in both groups were compared.
Results: Standard ESD was performed in 20 patients and PCM-t in 15 patients. There were no statistically significant differences between the two groups regarding age, gender, duration of procedure, size and type, endoscopic view, localization and pathological results of the lesions ($p > 0.05$).The dissection rate was higher in the PCM-t group and the frequency of hemostatic forceps use was less (p = 0.046 and 0.044, respectively). En-bloc and complete resection rates were higher in PCM-t group and complication rate was less.
Conclusion: The dissected lesion can completely block the lumen as the diameter of colon is small and generally the lesions are more vascular. This may lead to difficult dissection and a long procedure time.When the lesion diameter is large, dissection of the submucosal area as a tunnel helps in dissecting with control by providing a better notice of the vascular area.Using PCM-t in giant colorectal lesions can increase en-block resection rate, help in controlled dissection, decrease use of forceps besides decreasing the length of duration and increasing dissection rate.
Disclosure of Interest: None declared

Abstract number: P0174

Gender, Male/Female, n	103/82
Age, years, mean (SD) (median; range)	62.16 (11.55) (63; 26-88)
Lesion size, mm, mean (SD) (median; range)	37.88 (22.72) (33; 7-170)
Tissue size, mm, mean (SD) (median; range)	45.52 (24.58) (40; 10-198)
Duration of procedure, min, mean (SD) (median; range)	78.49 (70.11) (61; 6-540)
Dissection speed, mm^2/min, mean (SD) (median; range)	21.49 (13.92) (17.66; 1.74-79.55)
En-Bloc Resection , N (%)	172 (90.1)
Complete Resection, N (%)	
R0 Resection	169 (88.5)
R1 Resection	16 (8.4)
Rx Resection	6 (3.1)
Paris Classification, N (%)	3 (1.6)
1s	101 (52.9)
1s + 2a	58 (30.4)
2a	26 (13.6)
2a + 2c	3 (1.6)
SMT	
Adverse Events, N (%)	
Delayed bleeding	2 (1.0)
Perforation	5 (2.6)
Localization, N (%)	
Rectum	86 (45.0)
Sigmoid colon	31 (16.2)
Descending colon	14 (7.3)
Splenic Flexura	6 (3.1)
Transverse colon	8 (4.2)
Hepatic Flexura	18 (9.4)
Ascending colon	13 (6.8)
Cecum	11 (5.8)
Ileocecal valve	4 (2.1)
Pathology, N (%)	
Carcinoma	80 (41.9)
-Intramucosal	61 (31.9)
-Sm1 invasion	3 (1.6)
-Sm2 invasion	16 (8.4)
Tubular Adenoma	16 (8.4)
Tubulovillous Adenoma	68 (35.6)
Villous Adenoma	14 (7.3)
Serrated Adenoma	10 (5.2)
Neuroendocrine tumor	3 (1.6)
Dysplasia, N (%)	
None	3 (1.6)
Mild	5 (2.6)
Moderate	11 (5.8)
Severe	172 (90.1)

P0174 ENDOSCOPIC SUBMUCOSAL DISSECTION IN COLORECTAL LESIONS: EXPERIENCE OF 191 CASES FROM A TERTIARY REFERENCE CENTER IN TURKEY

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Introduction: Endoscopic submucosal dissection (ESD) is a minimally invasive technique, providing en-bloc resection of premalignant lesions and early stage gastrointestinal (GI) cancers. This procedure is commonly used in Far East countries like Japan and Korea; however, it has come into use in western countries in recent years. Additionally, ESD is not as widely performed in the colorectum compared with gastric ESD. In the present study, we present our results of colorectal ESD procedures.

Aims & Methods: A total of 345 ESD procedures, which were performed in the esophagus, stomach, colorectum and duodenum between April 2012 and April 2015, were recorded prospectively before and after the procedure. Patient data were analyzed retrospectively. We began to perform colorectal ESDs after 30 gastric ESD procedures and proximal colon segment procedures were performed only after 15 rectal ESD procedures had been completed. The results of 191 ESDs performed in colon and rectum were analyzed retrospectively.

Results: In a total of 185 patients, 191 colorectal ESDs were performed. The overall en-bloc and complete resection rates were 90.1% and 88.5%, respectively. Histopathology revealed carcinoma in 80, adenoma in 108 and neuroendocrine tumor in 3 patients. Complete resection was not achieved in 8.4% patients with positive vertical border. Perforation occurred in 4 patients which were treated successfully with endoscopic clip without the need for surgery except for one patient with delayed perforation (Table). Although cover type knife was generally preferred during the first cases non-cover type knife was used for later procedures. Surgical treatment was performed in all patients with deep submucosal (sm2) invasion, however neoplasia was observed in none of these patients.Table.Demographic data and colorectal ESD results Lesion (**N**) = 191

Conclusion: ESD is a safe and effective method to provide en-bloc and curative resection of premalign or malign colorectal lesions.

Disclosure of Interest: None declared

P0175 SALVAGE ENDOSCOPIC RESECTION OF SCARRED POLYPS AFTER FAILED PREVIOUS ENDOSCOPIC RESECTION ATTEMPT: SENSE STUDY

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Introduction: Current standard of care for recurrent/residual polyps after previous endoscopic resection is surgery which can be associated with significant morbidity and cost.

Aims & Methods: This study analyses the outcomes of salvage endoscopic resection of polyps with severe scarring following a previously failed endoscopic resection. Prospective cohort study of patients referred to a Tertiary-centre for resection of scarred polyps with failed previous endoscopic resection attempts. Resection techniques: ESD knife & Snare combination (Knife Assisted Resection, KAR) or Snare & APC assisted resection (SAR).

Results: We identified 64 consecutive patients referred to us following a previously failed endoscopic resection attempt. All these patients had severely scarred polyps which were being considered for surgery at the referring centre. The mean polyp size 46mm (20-150mm). 83% were left-sided and 17% right–sided. 67% of resections were performed by KAR with mean polyp size 50mm. 33% of resections were by SAR with mean polyp size 38mm.

Referral to surgery: 2/64 for technically difficult so no attempt made, 5/64 for cancer.

Endoscopic follow up & cure: mean follow up of 3 years (range: 1-8 years), 97% overall cure rate which was the same for left and right sided lesions as well as KAR and SAR. The only complication was bleeding seen in 3 patients (4.6%).

Cost saving: Had all 64 patients been sent for surgery the total cost would have been £343,224. The total cost of the endoscopic approach, including the cost of patients requiring surgery, was £149,820 representing an average cost saving of £3021.94 per patient.

Conclusion: Severely scarred polyps due to failed previous endoscopic mucosal resection attempts can be successfully treated by experts. The techniques of KAR and SAR are equally effective when used for appropriate polyps. The complication rate is low. Further recurrence after first salvage resection can be treated successfully. Surgery can be avoided in most patients and an endoscopic approach is very cost effective. We would therefore, advocate an aggressive endoscopic resection strategy over surgery when dealing with severely scarred polyps.

Disclosure of Interest: None declared

P0176 COLON CLEANSING FOR COLONOSCOPY IN PATIENTS WITH IBD COLITIS: EFFICACY AND ACCEPTABILITY OF 2 LITER PEG VS 4 LITER PEG

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Introduction: Low-volume preparations are gaining attention for higher acceptability, but their use in IBD patients has never been evaluated. This study compares the efficacy, safety and tolerability of a 2L PEG solution plus bisacodyl with a 4L PEG solution in patients with ulcerative colitis.

Aims & Methods: This is a multicenter, randomized, single-blind, non-inferiority study. Adult outpatients with ulcerative colitis undergoing colonoscopy received either 2L PEG plus bisacodyl or 4L PEG. Bowel cleansing was assessed using the Ottawa Scale and rated as adequate if the score was ≤ 2 in each colon segment. Patient acceptance, satisfaction, and related symptoms were recorded.

Results: 211 patients were included. Overall, preparation was adequate in 80% patients without any differences between groups. Mean Ottawa scores for whole and right colon were similar in the two groups. As concern tolerability, 83% patients in 2L PEG bisacodyl arm and 44.8% in 4L PEG arm reported no/mild discomfort ($p < 0.0001$) and 94.3% and 61.9% expressed their willingness to repeat the preparation ($p < 0.001$). Palatability was better with 2L PEG-bisacodyl, whereas related symptoms occurred more frequently with 4L PEG. Regardless of preparation, split dosage was associated to better cleansing. Further predictors of poor cleansing were moderate/severe discomfort during preparation, and more than 6 hrs between end of preparation and colonoscopy. Extension and severity of colitis did not influence quality of preparation.

Conclusion: Low-volume PEG plus bisacodyl is not inferior to 4L PEG for bowel cleansing in IBD, but it is better tolerated and accepted by patients. The time interval from solution intake and colonoscopy is the most important factor affecting quality of cleansing also in IBD.
(ClinicalTrial.gov number NCT02248337).

Disclosure of Interest: None declared

P0177 COMPUTER-ASSISTED INSTRUCTION BEFORE COLONOSCOPY IS AS EFFECTIVE AS NURSE COUNSELLING, A CONTROLLED TRIAL

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Introduction: Better patient education prior to colonoscopy, for instance through nurse counselling, improves adherence to instructions for bowel preparation and probably leads to cleaner colons. We hypothesized that computer assisted instruction (CAI) supported by video and 3D animations improves the effectiveness of nurse counselling, with potential operational advantages.
Aims & Methods: To assess the effectiveness of CAI for patient education prior to colonoscopy in terms of bowel cleanliness and patient knowledge, comfort and anxiety.
We included patients > 18 years who were referred for colonoscopy in an endoscopy unit in a general teaching hospital in the Netherlands. Exclusion criteria were illiteracy in Dutch and audiovisual handicaps. Patients were divided into two consecutive groups, one which received nurse counselling and one which received CAI, followed by a brief contact with a nurse shortly before colonoscopy. The CAI had been reviewed by expert endoscopists. For the main outcome measure, cleanliness of the colon during examination, data was collected using a physician questionnaire including the Ottawa Bowel Preparation Scale (OBPS) and the Boston Bowel Preparation Scale (BBPS). We assessed patient anxiety, patient comfort and general information using three questionnaires validated by expert consensus, which were issued after counselling or CAI and shortly before and after colonoscopy. We assessed knowledge of information provided earlier through a pre-colonoscopy test consisting of 10 questions. Statistical analyses were performed, including Mann-Whitney and T-test.
Results: We included 385 patients, 197 in the nurse counselling group and 188 in the CAI group. Overall response rates for the three patient questionnaires were 99%, 76.4% and 69.9% respectively. The physician questionnaire had an overall response of 60.8%. Baseline characteristics were similarly distributed among groups. Bowel cleanliness did not differ significantly between the two groups; on the OBPS, the counselling group scored 6.07 (SD 2.53) and the CAI group 5.80 (SD 2.90), and on the BBPS the scores were 6.54 (SD 1.69) and 6.42 (SD 1.62) respectively. Anxiety scores did not differ significantly. Patient comfort scores were significantly lower after CAI only. But in combination with a brief nurse contact comfort scores were significantly higher shortly before the colonoscopy. Scores on the knowledge test were similar, with 7.08 (SD 1.17) and 7.31 (SD 1.11).
Conclusion: CAI is a safe and practical modality for instructing patients before colonoscopy. This study found no difference in bowel cleanliness and patient knowledge with respect to the two groups. However, brief personal contact yielded significantly better patient comfort scores. We therefore recommend the combination of CAI with a brief nurse contact for daily practice.
Disclosure of Interest: None declared

P0178 SAFETY AND EFFICACY OF A NOVEL BALLOON SYSTEM FOR DIFFICULT COLONOSCOPY

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Introduction: Colonoscopy is the gold standard for colorectal cancer screening. However, total colonoscopy may be impeded by several factors, including extensive diverticulosis, elongated transverse colon, female gender, low body mass index, or prior abdominal or pelvic surgery.
Aims & Methods: Aim was to evaluate the safety and efficacy of a novel balloon system which will be introduced at UEGW 2015 for difficult colonoscopy. Therefore, patients (mean age 75 years; Range 21-78 years; 40% female) referred for colonoscopy after failure of previous colonoscopy were prospectively enrolled in a pilot cohort study whose primary end point was device safety. Other study endpoints included success rate and time of cecum intubation, withdrawal times, total procedure times, and success of therapeutic procedures.
Results: Among the enrolled patients one was excluded due to a technical problem of the device. Ileocolonoscopy was performed in all (100%) patients using the novel balloon-system without any complications. Cecal intubation rate was 100%. Mean times to reach the cecum, withdrawal, and total procedure times were 11.05 minutes, 15 minutes, and 32 minutes, respectively. All therapeutic endoscopic interventions that were required were performed without any complications. Success rate of therapeutic procedures was 100%.
Conclusion: The novel introduced balloon-system for difficult colonoscopy appears safe and effective to use. Final data will be presented at UEGW.
Disclosure of Interest: None declared

P0179 PROSPECTIVE 1:1 RANDOMIZED STUDY TO ASSESS THE PERFORMANCE CHARACTERISTICS OF COLORECTAL FULL SPECTRUM ENDOSCOPY (FUSE)

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Introduction: The newly introduced Full Spectrum endoscope (FUSE) provides a 330° field of view thereby potentially allowing endoscopists to see more anatomy of the colon as compared to standard forward viewing endoscopes (FVE). Recent data has indicated that FUSE significantly reduced adenoma miss rates.
Aims & Methods: The aim of this prospective randomized study was to assess the performance characteristics of FUSE in comparison to FVE. Therefore, patients were randomly assigned at a one-to-one ratio to undergo colonoscopy with FUSE or FVE after a previous sample size calculation. Performance characteristics including time to cecum, withdrawal time, total examination time, medication, patient and endoscopists' satisfaction, and polyp detection rates were recorded.
Results: Among 109 patients, 19 patients were excluded (11 inadequate bowel preparation; 5 hemicolectomy, 2 stenosis, 1 severe inflammation). 90 patients were finally randomized at a 1:1 ratio to undergo FUSE or FVE. Time to cecum (minutes, mean ± SD) was 4.05 ± 0.68 minutes for FUSE and 5.48 ± 0.67 minutes for FVE ($P < 0.001$). Withdrawal times were 12 ± 4.16 minutes and 15 ± 4.28 minutes for FUSE and FVE, respectively ($p < 0.01$). Total examination time was 16.30 ± 4.72 minutes in the FUSE group and 20.48. ± 4.39 minutes in the FVE group ($p < 0.001$). Sedation was less required in the FUSE group as compared to FVE (mean propofol dosage, 170 mg vs. 200 mg). Significantly more patients needed analgesia in the FVE group (meperidine; $P = 0.002$). Patient and endoscopists satisfaction were high throughout the cases and not different between both groups. Polyps were detected in 36% and 24% of patients in the FUSE and FVE group, respectively.
Conclusion: Advancement times of the scope to the cecum and withdrawal times were faster with the FUSE scope as compared to standard FVE. Satisfaction rates of patients and endoscopists were similar in both groups while patients needed more sedation and analgesia in the FVE group. Although more polyps were found in the FUSE group the study was not designed to compare adenoma detection rates between both groups.
Disclosure of Interest: None declared

P0180 RISK FACTORS FOR POSTPOLYPECTOMY BLEEDING AND ITS ASSOCIATION WITH HEPARIN BRIDGE THERAPY

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Introduction: Postpolypectomy bleeding (PPB) is the most common complication of colonic polypectomy. The risk of PPB is associated with increasing age, anticoagulation therapy, hypertension, large polyp size, proximal location, and polyp morphology. According to American Society for Gastrointestinal Endoscopy (ASGE) and Japanese Society of Gastrointestinal Endoscopy (JSGE) guidelines, for patients taking anticoagulants (e.g. warfarin), bridge therapy with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) is recommended to reduce the risk of thromboembolic events during high-risk procedures like polypectomy. However, little is known about the risk of PPB with heparin bridge (HB) therapy. We investigated the association between HB therapy and PPB.
Aims & Methods: We retrospectively reviewed 1659 polypectomies performed on 906 patients from January 2007 to December 2014 at our institution. A total of 728 patients did not take any antithrombotic agents (control group), and 45 patients underwent colonic polypectomy while receiving HB therapy (HB group). We analyzed the risk factors for PPB related to both the patients and the polyps, and we determined the rate of PPB in the HB group.
Results: PPB occurred in 33 lesions (2.0%) of 30 patients (3.3%). Eleven of 30 (36.7%) PPB patients were in the HB group ($p < 0.0001$), and the incidence of PPB in the HB group was 24.4% (11 of 45 patients). Polyp size ≧10 mm (20 of 33 [60.6%] vs. 639 of 1626 [39.3%], $p = 0.015$), pedunculated polyps (12 of 33 [36.7%] vs. 288 of 1626 [17.7%], $p = 0.012$), and location in the cecum (10 of 33 [30.3%] vs. 111 of 1626 [6.9%], $p < 0.0001$) were significant risk factors for PPB. In the control group, size ≧10 mm, pedunculated polyps, and location in the cecum were also significant PPB risk factors ($p = 0.0042$, $p = 0.014$, and $p = 0.0029$, respectively), although in the HB group, these were not significant ($p = 0.39$, $p = 1.0$, and $p = 0.053$, respectively). PPB in small polyps (≧10 mm) was higher in the HB group (15.4%, 10 of 65 lesions) than in the control group (0.73%, 7 of 963 lesions) ($p < 0.0001$), as was the recurrent bleeding rate (27.3% [3 of 11 patients] vs 0% [0 of 15 patients], respectively) ($p = 0.064$).
Conclusion: HB therapy, polyp size ≧10 mm, pedunculated polyps, and location in the cecum are risk factors for PPB. The incidence of PPB was higher in the HB group, and PPB occurred even if the polyp size was small (≧10 mm).
Disclosure of Interest: None declared

P0181 THE VALIDITY AND SAFETY OF THE COLORECTAL ESD FOR THE LESIONS SPREADING TO THE APPENDICEAL ORIFICE

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Introduction: Colorectal ESD has not been widely performed for colorectal tumors because of the high frequency of complications. Especially, ESD for the lesions spreading to the appendiceal orifice needs higher skill because of the confrontation to the muscle layer, narrow working space or spontaneous fibrosis. It is still unknown about the validity or effective strategy for these lesions.

Aims & Methods: 163 consecutive cases who underwent ESD in Omori Red Cross Hospital from 2012 April to 2015 March were analyzed. We use needle knife (Flex or Dual knife, Olympus Co Tokyo, Japan) for colorectal ESD. The main strategy for the lesions in the appendiceal orifice was shown as follows; we do the first injection from the tip of the vermiform appendix so that the tumor does not sink to the end of the vermiform appendix. This first injection should be minimum volume, and we make an enough endpoint around the appendiceal orifice as soon as possible. After this, we can continue ESD while using a counter traction of the gravity. We assessed the clinical findings and outcomes of ESD for the 6 lesions spreading to the appendiceal orifice (group A), compared to the other 157 lesions as control (group B).

Results: Mean age, sex, antithrombotic agents and past history were similar between two groups and there was no case of post appendicitis in group A. All ESD in group A was performed by one experienced endoscopist (≧150 colorectal ESD cases).Tumor shape was Is0/LST-G5/LST-NG1 in group A, and Is8/LST-G58/LST-NG84/SMT4 in group B, respectively. In addition, tumor size, specimen size, the area of the resected specimen, rate of en-bloc resection, and rate of curative resection were also similar: 35.8mm, 41.8 mm, 1187.9 mm^2, 6/6(100%), and 6/6(100%) in group A, and 28.4mm, 36.8mm, 1022.7mm^2, and 156/157 (99.4%) in group B, respectively. The number of mild or sever fibrosis was more often in group A (non; 3, mild; 3) than in group B (non; 127, mild; 25, severe; 5) ($p = 0.077$), but the mean operation time (group A: 42.5min, group B: 42.9min) was about the same. Pathological findings were adenoma2/M3/SM-slight 1 in group A, and adenoma71/M73/SM-slight3/SM-massive6/SMT4 in group B, respectively. The number of post bleeding or perforation was no case in group A and 2 perforations in group B. After ESD, WBC(/μl), CRP(mg/dl), a number of having a high fever(≧38°C), and taking a painkiller had no significant difference.

Conclusion: ESD for the lesions spreading to the appendiceal orifice was safe and there were no significant differences of outcomes, compared to the lesions in the other positions. Our strategy for these lesions will be appropriate. However, the existence of the spontaneous fibrosis around appendiceal orifice is not a little and the working space is very narrow, so we have to understand the characteristics of the appendiceal orifice.

Disclosure of Interest: None declared

P0182 PITFALL OF PIT PATTERN DIAGNOSIS AND MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING -PREDICTION OF THE DEPTH OF SUB MUCOSAL INVASION FOR COLORECTAL NEOPLAS

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Introduction: In Japanese Society for Cancer of the Colon and Rectum guidelines 2014, the intramucosal or superficial submucosal (depth of invasion < 1000 μ m:T1a) invasion is important to determine appropriate for ESD. On the other hand, size and macroscopic type both do not matter. So it is important for us to evaluate the depth of submucosal invasion because there have been reports of significantly increased risk factors for lymph node metastasis of early colorectal cancers in cases where the lesions invaded the deep submucosa (depth of invasion ≥ 1,000 μ m:T1b). When we evaluate the depth of invasion for colorectal cancer, we usually use pit pattern classification and magnifying narrow band imaging (NBI) adding white light observation and magnifying chromo-endoscopy.

Aims & Methods: The aim of this study is to evaluate diagnostic accuracy in estimating the depth of submucosal invasion of colorectal neoplasms using both pit pattern classification and NBI, and to extract endoscopic features for misdiagnosis patients. We enrolled the 522 patients who performed colorectal ESD from January 2011 to December 2014. Among them, 286 patients (57.3%, 164 men, 42.7%, 122 women, Median age ±SD: 66 ±11.3 years) that we could confirm type V pit pattern were enrolled for this study. Type V pit patterns include areas with irregular crypts (type V_I) and areas of apparent non-structure (type V_N). Type V_I pit patterns are further subdivided into areas of mild irregularity (type V_I mild) and areas of severe irregularity, which exhibit destroyed and damaged pits (type V_I severe). We evaluated the ability of differential diagnosis between Tis-T1 cancer and T1b cancer using type V pit pattern and NBI, and extract endoscopic features for misdiagnosis patients.

Results: In macroscopic type, polyploid type was 31.1% (88/286), and depressed or laterally spreading type were 68.9% (LST-G:106?LST-NG and depressd:92). In the relationship between type V pit pattern and the depth of invasion, sensitivity, specificity, and accuracy were 96.0%, 33.3%, and 88.1%, respectively. On the other hand in the relationship NBI and the depth of invasion, sensitivity, specificity, and accuracy were 89.4%, 32.3%, and 82.5%, respectively. Endoscopic features of misdiagnosis patients of type V mild shrunk in size of villous component, depressed area, and more than 30mm in max diameter. Furthermore, expansiveness, constitutive of the focal fold, and white spots in the polyploid type appeared with higher frequency than in the depressed or laterally spreading type. In contrast, the frequency features of a large nodule in the depressed lesion or laterally spreading type was higher than in the polyploid type. For the patients of type V severe, 5 patients had loss of dyeing and this was the factor of over diagnosis. The remaining 5 patients high frequency of endoscopic features were severe redness, elevation, depressed component, and the area of type V severe within 5mm in diameter.

Conclusion: Endoscopic findings suggest that there are some limitations of the diagnosis of the depth of submucosal invasion for colorectal cancer using pit pattern classification and NBI. We should utilize the findings of the lesions invaded with deep submucosa in the white light and chromo-endoscopic observation and evaluate submucosal fibrosis of the cancer when performing ESD.

Disclosure of Interest: None declared

P0183 A VISIBILITY STUDY USING NARROW BAND IMAGING IN THE COLORECTAL FLAT AND DEPRESSED LESIONS

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Introduction: Background: In conventional observation using white light, miss rate of adenoma was 10–30% through colonoscopy. It is difficult to detect flat lesions, especially laterally spreading tumors of non-granular type (LST-NG) and depressed lesions with higher malignant potential. In many detection studies for all colorectal lesions including polypoid, flat, and depressed lesions, no significant difference as seen in detection rate between narrow band imaging (NBI) and white light imaging, however, there have been no reports regarding visualization of LST-NG and depressed lesion in NBI observation.

Aims & Methods

Aim: To investigate the visibility of LST-NG and depressed lesions by using NBI.

Methods: We intended consecutive patients with LST-NG and IIc lesions that were endoscopically or surgically resected in our hospital between August 2011 and July 2013. These lesions were classified into four groups as followed: ''Brownish area (BA)'', ''Brown of only margins (O-ring sign)'', ''Same color as normal mucosa (SC)'' and ''Whitish area (WA)'' by appearance of NBI, and reveal each ratio. Furthermore, we compared pathological findings in individual groups of LST-NG and IIc lesions.

Results: Result: A total of 19 IIc lesions and 180 LST-NG lesions were analyzed. In IIc lesions, BA was 6 lesions (31.5%), O-ring sign was 11 lesions (57.9%), SC was 1 lesion (5.3%) and WA was 1 lesion (5.3%). In LST-NG lesions, BA was 120 lesions (66.7%), O-ring sign was 26 lesions (14.4%), SC was 34 lesions (18.9%) and WA was no lesions. The pathological findings of IIc lesions as followed: in BA, 1 lesion (16.7%) of high grade dysplasia (HGD), and 5 lesions (83.3%) of low grade dysplasia (LGD). In O-ring sign, 2 lesions (18.1%) of invasive cancer, and 9 lesions (81.9%) of LGD. In SC and WA, LGD were 1 lesion (100%). The pathological findings of LST-NG lesions as followed: in BA, 25 lesions (20.8%) of invasive cancer, 45 lesions (37.5%) of HGD, and 50 lesions (41.7%) of LDG. In O-ring sign, 8 lesions (30.8%) of invasive cancer, 4 lesions (15.4%) of HGD, and 14 lesions (53.8%) of LGD. In SC, 3 lesions (8.8%) of invasive cancer, 8 lesions (23.6%) of HGD, and 23 lesions (67.6%) of LGD.

Conclusion: Conclusions: Since most of IIc lesions were visualized as brown by NBI, there would be clinical benefit for the visibility. On the other hands, approximately 20% of LST-NG lesions were recognized in same color as surround normal mucosa, so the visibility was inferior to that of IIc lesions.

Disclosure of Interest: None declared

P0184 USEFULNESS AND SAFETY OF COLD SNARE POLYPECTOMY FOR REMOVING COLONIC POLYPS IN JAPANESE PATIENTS

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Introduction: Colorectal cancer is a major health problem worldwide. Polypectomy of small colonic polyps has been an effective procedure for reducing the risk of colon cancer development by interrupting the progression of adenoma to carcinoma. Cold snare polypectomy (CSP) which can treat small colonic polyps without electrocautery has been recently reported to be useful for removing small colonic polyps in European countries, and CSP has become one of the common procedures for resecting colonic polyps. In Japan, CSP has been gradually utilized although endoscopic mucosal resection (EMR) has been a most common method for removing small colonic polyps. However, there has been few reports regarding the usefulness and safety of CSP in Japanese patients.

Aims & Methods: To verify the usefulness of CSP, we analyzed the complete resection rate and the complication between EMR and CSP. Subjects were 423 consecutive patients with 1010 lesions (ranges of polyp sizes, 3 mm-15 mm; average of polyp size, 6.8 mm; macroscopic type, Is or Isp) resected by EMR, and 106 patients with 175 lesions (ranges of polyp sizes, 3 mm-10 mm; average of polyp size, 5.0mm; macroscopic type, Is or Isp) resected by CSP at Aichi Medical University School of Medicine between May 2014 and February 2015. Moreover, 175 lesions resected by CSP were divided into two groups; 58 lesions resected by CSP using short snare (diameter of the snare, 13 mm) and 117 lesions resected by CSP using long snare (diameter of the snare, 27 mm). The complete resection rate was histologically compared between the two groups.

Results: There was no significant difference in complete resection rate between EMR (99.5%) and CSP (99.4%). There were no significant difference related with complications such as perforation and post-operative bleeding between EMR (perforation: 0, post-operative bleeding: 2) and CSP (perforation: 0, post-operative bleeding: 0). Histological examination revealed that complete resection rate of CSP using short snare (60.3%) is significantly higher than that of CSP using long snare (33.7%) ($p < 0.05$). There were no significant difference in complications between CPS using short-snare and CPS using long-snare.
Conclusion: CSP is a safe method for removing colonic polyps without complication. The complete resection rate in CPS using short snare is significantly higher than that in CPS using the long snare. Our study demonstrates that the short snare is considered to be useful for removing colonic polyps compared with the long snare in CPS. Thus, CSP using the short snare should become widely applicable to Japanese patients.
Disclosure of Interest: None declared

P0185 DEVELOPMENT OF NOVEL TECHNIQUE FOR IDENTIFICATION OF COLONOSCOPE SHAPE USING ULTRATHIN SHAPE SENSOR: A PILOT STUDY

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Introduction: During colonoscopy, procedural completion, accuracy, comfort, and safety are important factors. Uncontrolled looping of the colonoscope shaft during insertion can cause abdominal pain and could lead serious complications. Scope guided endoscopy using ultrathin shape sensor can reduced unnessessory tactile pressure or torque.
Aims & Methods: The aim of this study is to simulate 3D structure of colonoscope using ultrathin shape sensor. We conducted a prospective pilot study. Three-dimensional (3D) shape of the colonoscope shaft was obtained by using ultrathin shape sensor of fiber Bragg gratings. It detect strains and bending angles and provides real-time continuous 3D imaging of the colonoscope without radiation hazard. We reconstructed the shape of colonoscope and measured bending curvature and error of tip position.
Results: Total 10 patients underwent colonoscopy using ultrathin shape sensor. The results show that the shape sensor is reliable at a maximum bending curvature of $80mm^{-1}$. The average tip position error was 1.722 ± 1.678mm, which corresponds to $1.50 \pm 1.46\%$ of the total length of the sensor.
In this approach, the endoscopists performance may enhanced by providing using a kinetic model that provides information such as the shape of the scope, direction of the colon and forces.
Conclusion: Scope guided endoscopy using FBG sensor can be successfully used to display colonoscope configuration by reconstruction of the high curvature bending and low tip position error. This Flexible, thin and almost weightless shape sensor would be a novel technique for identification of colonoscope shape.

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Disclosure of Interest: None declared

P0186 PROSPECTIVE, OBSERVATIONAL STUDY TO EVALUATE THE ACCURACY OF ELECTRONIC ISCAN CHROMOENDOSCOPY TO PREDICT HISTOLOGY OF COLORECTAL LESIONS IN NON-EXPERT HANDS

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Introduction: Accurate detection and characterization of colorectal lesions are important for optimal treatment and follow-up strategies. Electronic chromoendoscopy may be helpful in this setting, but scientific evidence is inconclusive. The usefulness of chromoendoscopy may differ according to the expertise of endoscopists. We hypothesized that i-Scan, the electronic chromoendoscopy available in Pentax endoscopes, improves the characterization of colorectal lesions in non-expert hands.
Aims & Methods: Aim of the present study was to assess the impact of different iScan profiles for the accurate characterization of colorectal lesions in non-expert hands.
Material and methods: A prospective, observational study of colorectal lesions detected in patients referred to our Endoscopy Unit for diagnostic colonoscopy from February to April 2015 was designed. Three experienced endoscopists collected four images from every lesion by applying HD-white light (HDWL) and three different iScan profiles (iScan1, iScan2 and iScan3), respectively before endoscopic removal for histological evaluation. Total collected images from all lesions were presented unlabeled in a randomized order to a young staff member with a two years' experience in diagnostic and therapeutic endoscopy, and with a limited experience in advanced imaging, for predicting histological diagnosis. The accuracy to predict histology with the different iScan profiles compared to HDWL was calculated according to the size of the lesions. The prediction confidence was also evaluated and classified as low and high. Statistical analysis was performed using the chi-square test and Fisher exact test, as appropriate.
Results: A total of 444 images from 111 lesions were analyzed. Final histological diagnosis was adenoma in 73 cases and serrated lesions in 38 cases. Global accuracy for predicting histology increased from 69.4% with HDWL to 85.6% with iScan ($p < 0.05$). Accuracy was similar with any of the three iScan profiles (75.7%, 80.2% and 82.9% for iScan 1, 2 and 3, respectively) (n.s.). For non-serrated adenomas, accuracy to predict histology was 57.5% for HDWL compared to 82.2% with iScan ($p < 0.05$). Again, no statistical difference was observed among different iScan profiles, although accuracy tended to be higher with iScan3 (69.8%, 76.7% and 79.4% for i-Scan1, 2 and 3, respectively) (n.s.). Accuracy for serrated lesions was equal with HDWL and i-Scan (92.1% in both cases). Usefulness of iScan was greater for predicting histology in case of diminute and small lesions (19.3% and 11.9% diagnostic improvement with regard to the accuracy with HDWL, respectively) ($p < 0.05$). iScan also allowed to increase significantly the prediction confidence, and high prediction confidence was more frequent with iScan (78.4%) than with HDWL (51.3%) ($p < 0.05$).
Conclusion: i-Scan allows improving significantly the accuracy of optical diagnosis of colorectal lesions compared to HDWL in non-expert hands. This is mainly true for diminute and small adenomatous lesions. iScan also helps to increase the prediction confidence of these lesions.
Disclosure of Interest: None declared

P0187 THE FACTORS ASSOCIATED WITH COMPLETE ENDOSCOPIC RESECTION OF COLORECTAL ADENOMAS IN EXPERTS AND FELLOW-TRAINEES

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Introduction: The complete removal of adenomatous polyps is important for reducing the incidence and mortality of colorectal cancer. However, little information is available on the rate of incomplete polypectomy for intermediate sized lesions (5–20 mm) in clinical practice and on the affecting factors, and there are no guidelines addressing the issue of incomplete resection.
Aims & Methods: The aims of this study were to identify factors affecting the completeness of colonoscopic polypectomies and to evaluate the experience level of fellows who achieve competence compared with that of experts. Medical records of the patients who underwent at least one polypectomy for an adenomatous polyp at a single tertiary hospital between March 2011 and February 2013 were retrospectively reviewed. The lateral and deep margins of the resected polyps were evaluated to check the resection completeness.
Results: A total of 3,671 adenomatous polyps from 1,945 patients were included. Of these polyps, 1,591 (43.3%) were removed by three experts and 2,080 (56.7%) were removed by seven fellows. In the expert-treated group, polyp size ≥ 20 mm (odds ratio [OR] 3.07, 95% confidence interval [CI] 1.87-5.05, $P < 0.001$), right-sided location (OR 1.35, 95% CI 1.09-1.67, $P = 0.006$), and sessile type (OR 1.67, 95% CI 1.10-2.54, $P = 0.017$) was associated with incomplete resection. In the fellow-treated group, not only polyp characteristics (right-sided location [OR 1.41, 95% CI 1.18-1.69, $P < 0.001$]), but the cumulative number of procedures was also related to resection completeness. After 300 consecutive polypectomies, the complete resection rate of the fellows was comparable to that of the experts.

Conclusion: In the fellow-treated group, the level of procedure experience was closely associated with the outcome of colonoscopic polypectomy. Meticulous attention is critical to ensure the completeness of polypectomies performed by trainee endoscopists during the training program.
Disclosure of Interest: None declared

P0188 THE NICE, SANO AND WASP CLASSIFICATION IN SMALL COLONIC POLYPS EVALUATED WITH BLUE LASER IMAGING (BLI)

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Introduction: The accuracy in the differentiation of colonic polyps would allow a ''resect and discard'' strategy for small colonic lesions. Recently, the ESGE suggested ''that virtual chromoendoscopy can be used for real-time optical diagnosis of diminutive (< 5 mm) colorectal polyps to replace the histopathological diagnosis''. Blue Laser Imaging (BLI), is a new endoscopic system (Fujifilm-Japan) associated with magnification, which can potentially further improve the differentiation of polyps. The aim of this study was to measure the diagnostic accuracy of polyp assessment (adenomatous versus hyperplastic) in small (6-9mm) and very small polyps (≤5mm), to allow a ''resect and discard strategy'' predict using BLI and zoom magnification.
Aims & Methods: Colonic polyps < 10 mm were prospectively included in the study. Each polyp was evaluated with white-light, standard BLI, BLI-bright, with and without magnification (Zoom). Photos and video were performed for each polyp. Expert endoscopists reviewed all pictures and videos blindly, and classified polyps using size and the Paris, NICE, WASP and Sano classifications. Histological findings were correlated with clinical and endoscopic findings. Polyps were classified according the histopathological diagnosis between neoplastic lesions (adenoma n = 46, Sessile Serrated Adenoma SSA/Ps n = 4, and no invasive carcinoma) and non-neoplastic lesions (hyperplastic polyps n = 11 and polypoid expansion of normal colonic mucosa n = 15).
Results: A total of 76 lesions < 10mm (n = 33 of 6-9mm; n = 43 of ≤5mm) were detected in 29 patients, and their median size was 5mm (IQR 3-7). Morphologies of the lesions were: 19 polypoid (0-I) and 57 slightly elevated (0-IIa). No slightly depressed without ulcer lesion (0-IIc) was observed. Pathological type of the polyp was predicted and polyp management decided upon for all 76 detected lesions. Polyps' location was splenic flexure to cecum (proximal colon) and rectum to descending colon (distal colon) in 56% and 44% respectively. The overall sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy of BLI with magnification for the endoscopic diagnostic of neoplastic polyps were 0.88 (95% CI = 0.76-0.95), 0.58 (95% CI = 0.37-0.77), 0.80, 0.71 and 88%, respectively. Diagnostic accuracy of in vivo polyp assessment in 6-9mm and ≤5mm polyps were 92% and 83% respectively. Considering the adenoma detection, the accuracy of the NICE, Sano and WASP classifications was 64%, 64% and 92% (p = 0.0013) respectively.
Conclusion: At the era of BLI and zoom magnification, small polyps identification using NICE and Sano classifications was not sufficient to allow a ''resect and discard'' strategy. The 90% agreement in assignment of post-polypectomy surveillance intervals recommended by the ESGE was not reached with NICE and SANO classifications. The diagnostic accuracy using the WASP classification is a promising technique to pass the 90% cut-off identified by the ESGE.
Disclosure of Interest: None declared

P0189 OPTICAL DIAGNOSIS OF COLONIC POLYPS: WHICH CLASSIFICATION SHALL WE USE AT THE EDGE OF THE BLUE LASER IMAGING (BLI) TECHNIQUE? THE WASP AND THE SANO CLASSIFICATION' ACCURACY

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Introduction: Accurate endoscopic differentiation of colonic polyps would allow resect and discard strategy for small colonic lesions. Blue Laser Imaging (BLI), a new endoscopic system has been validated to detect adenoma. The accurate endoscopy differentiation remained a challenge and new classifications have been developed to better identify adenoma from hyperplastic polyps. Recently, a classification system based on narrow band imaging (NBI) was validated for endoscopic differentiation of small and diminutive adenomas, hyperplastic polyps and Sessile Serrated Adenoma/polyps (SSA/Ps): the Workgroup serrAted polypS and Polyposis (WASP) classification. In addition, the SANO classification was validated in the same conditions using the pit pattern and the vascularization of the lesion. We herein stressed the WASP and the SANO classifications in optical diagnosis polyps using BLI and magnification.
Aims & Methods: 117 colonic polyps were studied in 45 patients in real-life colonoscopy, and prospectively included in the study. Each polyp was evaluated with white-light, standard BLI, BLI-bright, with and without magnification (Zoom). Experts endoscopists reviewed all pictures and videos blindly using WASP and Sano classifications. Polyps were classified according the histopathological diagnosis between adenoma (n = 72), hyperplastic polyps (n = 13), SSA/Ps (n = 14), polypoid expansion of normal colonic mucosa (n = 15) or invasive lesion (n = 3). Histological findings were correlated with clinical and endoscopic findings. The diagnosis accuracy was evaluated considering histology, size, WASP and SANO classifications. A discrepancy between SANO and WASP classification was considered as the most advanced type of lesions.
Results: 117 polyps were resected by endoscopic submucosal resection (EMR) with a mean size of 12.8mm (1–60mm). Polyps location was splenic flexure to cecum (proximal colon) and rectum to descending colon (distal colon) in 57% and 43% respectively. The overall sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy of BLI with magnification using WASP classification for the endoscopic diagnostic of colorectal adenomas were 0.76 (95% CI = 0.66-0.85), 0.42 (95% CI = 0.25-0.63), 0.80, 0.36 and 76%, respectively. The overall sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy of BLI with magnification using SANO classification for optical diagnosis of advanced polyps were 0.91 (95% CI = 0.84-0.96), 0.67 (95% CI = 0.51-0.81), 0.86, 0.78 and 90%, respectively. The diagnostic accuracy of SANO and WASP classifications to predict SSA/Ps were 79% and 85%, respectively. Neither SANO nor WASP classifications were superior to detect SSA/Ps from adenoma (p = 0.82).
Conclusion: BLI and magnification are advanced endoscopic images that challenges optical diagnosis. SANO classification permits better endoscopic differentiation of small adenomas and non-neoplastic lesions than WASP classification. We observe a trend to better optical diagnosis of SSA/Ps by WASP classification. Acquisition of basic knowledge in BLI and magnification endoscopy could permit to improve endoscopic optical diagnosis of SSA/Ps using the new WASP classification.
Disclosure of Interest: None declared

P0190 CONSTIPATION; TO SCOPE OR NOT TO SCOPE? THAT IS THE QUESTION: A LARGE DISTRICT GENERAL HOSPITAL STUDY

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Introduction: The European Society of Gastrointestinal Endoscopy and the British Society of Gastroenterology offer no specific guidelines on performing colonoscopy for constipation. The American guidelines advise to colonoscope those with constipation if new onset and over 50 years of age without prior bowel screening or in those with other alarm features (1). In Two US-Based Population retrospective case control studies, one suggested constipation had an increase Odds Ratio of 2.36 for colorectal cancer in those with bowel opening less than 3 times a week (2). The other study suggesting an increase Odds Ratio of 2.0 if needed laxatives 12-51 times in a year to 4.4 if laxative use was greater than 52 times in a year (3). A meta analysis of 8866 patients found that constipation as a primary indication was associated with colorectal cancer in 5.2% of patients which had a lower odds ratio of 0.56 when compared with other indications (4).
Aims & Methods: To determine if performing endoscopy in patients with constipation could detect cancers. All colonoscopies and flexible sigmoidoscopies performed for '' constipation'' between January 2012 and December 2014 at the East and North Hertfordshire NHS trust were looked at using an endoscopy database. Cancer pick-up rate in this cohort was assessed with histology followed up following the procedure for confirmation of cancers. Cancer detection rates were then compared with the 4 most common other indications for colonoscopy at the NHS trust. Two tailed T tests were used to compare cancer detection rates with p value set at (< 0.05).
Results: There were 298 endoscopies performed (165 Colonoscopies, 133 Flexible Sigmoidoscopies). There were 5 new cancers found on colonoscopy (3%) and 6 cancers found on flexible sigmoidoscopy (4.5%). When compared to the other top 4 indications for undergoing a colonoscopy there was no significant differences in cancer detection rate at (p < 0.05). ''Diarrhoea'' had a cancer detection rate of 0.8% which was significantly lower than for constipation detection rates. 3 New cancers were found with constipation as the primary indication with 5 cancers found for constipation with an abnormal CT scan.
Conclusion: As an indication for endoscopy, the indication ''Constipation'' remains a contentious issue without clear guidelines of when it is appropriate to scope. Our study has highligted that constipation as an only indication can still yield cancers as a rate similar to other important indications. This study has also highlighted the importance of imaging in those that are constipated. In those presenting with constipation a non invasive test first such as a CT scan to help rule out significant pathology.

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P0191 STARTING ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN CLINICAL PRACTICE: A MODEL TO PREDICT THE NEED FOR A P-EMR

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Introduction: To improve the quality of ESD outcomes with the initial cases, it is crucial that factors predicting the need to end the procedure with a piecemeal endoscopic mucosal resection (pEMR) are evaluated.

Aims & Methods: The aim of our study was to prospectively assess what factors were associated with changing the initially planned ESD to pEMR and to develop a predictive model to anticipate the need for a piecemeal resection. We prospectively enrolled the first 122 cases referred for an ESD from September 2008 to April 2015.

Results: Endoscopic treatment was aborted in five cases. Finally, 117 lesions were included in the *intention-to-treat* analysis (95.9%). A pEMR was necessary in 40 (34.2%). Factors significantly associated with the need for a pEMR were: experience $\leq$ 40 ESDs (OR: 4.01; IC 95%: 1.77 – 9.06; $p =$ 0.001), location out of the stomach (OR: 3.93; CI 95%: 1.55 – 9.63; $p =$ 0.003), procedure time- $>$ 180 minutes (OR: 2.62; CI 95%: 1.16 – 5.92; $p =$ 0.03) and size $>$ 3 cm (OR: 5.15; CI 95%: 2.24 – 11.82; $p <$ 0.0001). In the logistic regression model, the factors independently associated with changing technique to a pEMR were: size of the lesion $>$ 30 mm (OR: 4.80; CI 95%: 1.81 – 12.72; $p =$ 0.002) and experience $\leq$ 40 ESDs (OR: 5.98; CI 95%: 2.18 – 16.42; $p =$ 0.001). The value of the area under the ROC curve of the predictive model for a pEMR [logodds = 1.87 x (size $>$ 3 cm) + 1.66 x (first 40 cases) + 1.07 x location out of the stomach – 2.90] was 0.81 (CI 95%: 0.73 – 0.89). A cut-off point of $\geq$ 0.34 for predicting pEMR showed the following diagnostic performance: sensitivity: 82.5% (CI 95%: 81.2 – 83.8); specificity: 70.1% (CI 95%: 69.4 – 70.8).

Age (mean ± SD)	**69.8** ± 11.9
Male / Female n;%	**67 / 50** (57.3 / 42.7)
Tumor location n; %	
Esophagus	**1** (0.85)
Stomach	**42** (35.9)
Rectum	**45** (38.4)
Colon	**29** (24.8)
Mean tumor size, mm (mean ± SD)	**31.6** ± 16.1
En bloc resections (n; %)	**77** (65.8)
Piecemeal resections (n; %)	**40** (34.2)
Histopathology (n; %)	
Mucosal low grade neoplasia	**31** (26.5)
Mucosal high grade neoplasia	**71** (60.7)
Curative submucosal invasion	**3** (2.5)
Non-curative submucosal invasion	**7** (0.6)
Other (subepithelial tumors, carcinoids...)	**5** (4.3)
Procedure time (mean ± SD)	**190** ± 82
Delayed bleeding (n;%)	**12** (10.3)
Perforations (n;%)	**17** (14.5)

Conclusion: A scoring system combining the size and location of the lesion and the experience in ESD provided good diagnostic performance to predict the need for a p-EMR.

Disclosure of Interest: None declared

P0192 EFFECTIVENESS OF A SOFTWARE APPLICATION IN IMPROVING APPROPRIATENESS OF COLONOSCOPY PRESCRIPTION

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Introduction: There is evidence that a significant proportion of colonoscopies performed worldwide do not comply with clinical guidelines. This inadequacy on the medical prescription has important consequences on its diagnostic performance, the patients safety and costs. Results of educational interventions have been inconsistent in previous studies. The development of software tools, incorporated in the electronic medical record, might have a role in improving prescriptions' appropriateness.

Aims & Methods

Aims: To evaluate the effectiveness of a software application, integrated in the colonoscopy electronic request form of an university hospital and designed as prescription aid, to decrease colonoscopy prescription inadequacy.

Methods: Observational prospective study. An electronic colonoscopy request form has been designed including the algorithms and the recommendations for follow up on its most relevant indications and providing real time information on the procedures appropriateness on each clinical context. Six hundred colonoscopy prescriptions were evaluated before (PRE period) and after (POST period) software implementation. The colonoscopy was considered "appropriate" if it met the recommendations of any of the following guidelines with a six month difference or less: Spanish Gastroenterological Association Colorectal Cancer Prevention Guideline, European Guidelines for Quality Assurance in Colorectal Cancer Screening and Diagnosis or European Panel on the Appropriateness of Gastrointestinal Endoscopy (EPAGE II) categories "appropriate and necessary", "appropriate" or "uncertain".

Results: 1084 prescriptions were included in the analysis, 519 PRE / 565 POST, (average age 59.5 +- 14.6 y.o., 49.32% females). There is a significant reduction in the inapropriateness rate after the implementation of the software: PRE 21.19% VS POST 9.20% ($p < 0.001$). This improvement is statistically significant in the follow-up after surgical treatment of colorectal cancer and endoscopic resection of early colorrectal neoplasia (table).

TABLE: INAPPROPRIATENESS in PRE (n = 519) and POST (n = 565) PERIODS, disaggregated by indication. Data are shown as n(%).

Indication	PRE	POST	p
Anemia	1 (2.70)	0 (0)	0.21
Hematochezia	1 (3.23)	2 (3.03)	0.96
Constipation	1 (5.56)	2 (7.41)	0.81
Abdominal pain	2 (11.76)	3 (37.50)	0.13
Diarrhea	3 (8.11)	0 (0)	0.01*
Inflammatory bowel disease	4 (5.71)	1 (2.17)	0.36
Surveillance after endoscopic resection	59 (49.17)	26 (33.33)	0.03*
Surveillance after surgical resection of cancer	21 (35.00)	7 (15.22)	0.02*
Screening (high risk population)	6 (13.04)	5 (10.64)	0.72
FOBT +	0 (0.00)	1 (2.94)	0.48
Others	12 (18.18)	5 (6.42)	0.03*

Conclusion: The implementation of a decision-making aid software tool improves appropriateness of colonoscopy prescription.

Disclosure of Interest: None declared

P0193 IMPACT OF BOWEL PREPARATION QUALITY ON ADENOMA IDENTIFICATION DURING COLONOSCOPY AND OPTIMAL TIMING OF SURVEILLANCE

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Introduction: Present guidelines stating the surveillance interval after index colonoscopy are all based on optimal bowel preparation. However, in the case of poor bowel preparation, appropriate timing of repeat colonoscopy is not clear.

Aims & Methods: We compared adenoma detection rate and missing rate according to the status of bowel preparation in order to determine the appropriate timing of repeating colonoscopy in cases of poor bowel preparation. The medical records of patients who underwent colonoscopy in the last 5 years were retrospectively analyzed. Index colonoscopy was defined as the first colonoscopy in patients who received at least twice during the study period. Adenoma miss rate (AMR) was calculated by dividing the number of patients where at least one adenoma was detected during repeated colonoscopy by the total number of patients who received repeated colonoscopy. Bowl preparation quality was defined as optimal, fair, and poor.

Results: The overall adenoma detection rate (ADR) was 39.1% (95% confidence interval [CI], 38.0–40.1). However, the detection rate was significantly different based on bowel preparation status (optimal; 46.8%, fair; 25.6%, poor; 21.6%, $P < 0.001$). AMR was also significantly increased with poor bowel preparation (optimal; 27.3%, fair; 48.1%, poor; 69.6%, $P < 0.001$). We compared the AMR of optimal bowel preparation group with fair and poor bowel preparation groups on the basis of the repeat colonoscopy interval. When compared with the optimal bowel preparation group, AMR was significantly increased in both the poor and fair bowel preparation group for repeated colonoscopy within 2 years (poor group: OR 6.25; 95% CI, 3.76–11.83, fair group: OR 3.67; 95% CI, 2.19–6.16); however, there was no difference after 2 years.

Conclusion: Bowel preparation quality significantly affects AMR. Repeated colonoscopy should be performed within 2 years in patients who have received colonoscopy under suboptimal bowel preparation conditions.

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P0194 ENDOSCOPIC MUCOSAL RESECTION OF COLORECTAL LESIONS LARGER THAN 2 CM: THE EXPERIENCE IN A DISTRICT HOSPITAL

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Introduction: Endoscopic mucosal resection (EMR) has been shown to be useful in the removal of large lesions of the gastrointestinal tract. The aim of this study was to evaluate the experience of our hospital on the efficiency and safety of EMR in colorectal lesions, using inject and cut technique.

Aims & Methods: We did a retrospective study based on the EMR performed between June 2009 and June 2013. Resected lesions ≥20 mm in diameter were selected. The histological characteristics, complications, follow up and surgical needs were evaluated.

Results: During the study period, we performed 266 EMRs; 114 EMRs were performed in lesions ≥20 mm in diameter among 110 patients (64 men and 46 women) with an average age of 67.7 ± 11.8 years. The lesions average size was 30.9 mm, having 58% been located in the colon and 42% in the rectum. According to the Paris classification, the lesions were classified as: Is-77; IIa-33; IIb-3; IIa + IIc-1. Piecemeal resection was performed in 76% of cases. A complete endoscopic resection was achieved in 93% of the cases. Post-EMR argon plasma coagulation was applied in 18 lesions (16%). The histopathological results revealed: adenoma with high-grade dysplasia - 57; adenoma with low-grade dysplasia - 34; adenoma with focal adenocarcinoma - 13; invasive adenocarcinoma - 5; serrated adenoma - 6. Complications occurred in 4.4% of the procedures (1 intra-procedural bleeding; 2 delayed bleedings; 2 perforations). Until now, 226 follow up colonoscopies were performed in 94 patients. The average follow up time was 21.2 months, with endoscopic control ranging from 1 to 64 months post-EMR. Local recurrence occurred in 25 patients (22%), and the majority (88%) was managed with polypectomy or new EMR. Ten patients (8.8%) were referred for surgery, 50% because of histological evidence of invasive adenocarcinoma.

Conclusion: EMR is a safe and effective technique for colorectal lesions larger than 2 cm, with low risk of recurrence and complications. Local recurrences were successfully treated with endoscopic resection, avoiding the need for surgery in 88% of cases.

Disclosure of Interest: None declared

P0195 INCREASED INSULIN RESISTANCE IS AN INDEPENDENT RISK FACTOR FOR POST-ERCP PANCREATITIS

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Introduction: The relationship between insulin resistance and post-ERCP pancreatitis (PEP) was not known. We aimed to determine whether increased pre-ERCP insulin resistance is associated with an increased risk of PEP or not, and to evaluate the relationship of insulin resistance with well-established risk factors of PEP.

Aims & Methods: Consecutive patients who underwent ERCP with the diagnosis of choledocolithiasis between July and December 2013 were enrolled to this prospective study. Pre-procedural insulin resistance state and other risk factors were evaluated according to PEP development.

Results: Pancreatitis developed in 16 (11.3%) of 141 ERCP procedure. HOMA-IR (3.37 ± 0.8 vs 2.38 ± 1.4, $p < 0.001$) levels was found statistically significantly higher in patients who developed PEP than the ones who didn't. According to logistic regression analysis HOMA-IR ≥ 2.5 (OR:3.92), pancreatic duct cannulation (OR:4.09), procedure time (per minute OR:1.09), common bile duct diameter (per millimeter OR:0.80) and age (per year OR:1.05) were the important factors increasing PEP risk.

	PEP	Non-PEP	p value
Age	60 ± 15	58.8 ± 16.1	0.97
BMI kg/m^2	29.8 ± 3	27.9 ± 4.4	0.44
ALT (U/L)	99.6 ± 83	72.9 ± 71.7	**0.03**
MPV (fl)	8.9 ± 0.9	9.7 ± 1.2	**0.01**
Platelet Count (/mm^3)	237168 ± 68029	294259 ± 112605	**0.05**
Total Bilirubin (mg/dl)	1.5 ± 0.9	1.8 ± 1.8	0.69
HOMA IR	3.37 ± 0.8	2.38 ± 1.4	**<0.001**
Procedure time (min.)	33.5 ± 9	27.9 ± 7.2	**0.006**
CBD diameter (mm.)	10.1 ± 4	13.4 ± 4.5	**0.01**

Conclusion: According to our results, presence of insulin resistance is an independent risk factor for the development of PEP and increases the risk at least similar to the known risk factor of pancreatic canal cannulation.

Disclosure of Interest: None declared

P0196 COMPARATIVE STUDY ON THE SAFETY AND EFFICACY OF PROPOFOL INDUCED CONSCIOUS SEDATION DURING ERCP BETWEEN ANAESTHESIOLOGIST AND OTHER (NON - ANAESTHESIOLOGISTS) APPROPRIATELY TRAINED PHYSICIANS

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Introduction: During the last years, propofol has become the preferred short-acting sedation agent offering an alternative to the benzodiazepine midazolam anaesthetic induction agent during diagnostic and therapeutic endoscopic retrograde cholangiopancreatography (ERCP).

Aims & Methods: The aim of this retrospective study was to compare the safety and efficacy of propofol-induced conscious sedation in patients class I (normal healthy subjects), II (subjects with mild systemic disease) and III (subjects with non-incapacitating severe systemic disease,) according to the American Society of Anaesthesiologists ASA Physical Status Classification, undergoing ERCP administered either by anaesthesiologists or other (non-anaesthesiologists) appropriately trained physicians. Data from 2012-2014 were collected retrospectively by use of the Electronic Endoscopy Report Data Base at our center. A total of 195 patients (98 men, 69.61 ± 14.05 years and 97 women, 69.21 ± 13.78 years, respectively) were divided into propofol sedation group A under the supervision of the anaesthesiologist (N = 122, 62 men, 69.21 ± 13.78 years and 60 women, 69.73 ± 13.36 years, respectively) or into propofol sedation group B under the supervision of the non-anaesthesiologist appropriately trained endoscopist (N = 73, 36 men 70.77 ± 13.40 years and 37 women, 68.24 ± 14.51 years, respectively). Blood pressure, pulse, and oxygen saturation were measured. Propofol was administered either by the anaesthesiologist or by the endoscopist and titrated to the patients' response during ERCP to a maximum dose of 1-2 mg per kg.

Results: There was no significant statistical differences between two groups with respect to median age ($p = 0.618$), to sex ($p = 0.639$), to ASA classification ($p = 0.612$), to indication for ECP ($p = 0.451$), to serum bilirubin level ($p = 0.984$) and to endoscopist experience ($p = 0.538$). The mean required propofol during the procedure in the group A and B were 354.15 ± 210.74 mg and 217.5 ± 93.3 mg, respectively (t-difference: 7.342; $p > 0.05$). Furthermore, there was no statistical difference in selective cannulation of the common bile duct (86% versus 89%, $p = 0.597$) between the two groups. Only three patients (1/62 men and 2/60 women) developed sedation-related cardiorespiratory complications in group A and no patient in group B ($p = 0.14$).

Conclusion: Appropriately trained endoscopist-directed administration of propofol is totally safe and effective for providing propofol sedation in patients ASA Class I, II and III during ERCP.

Disclosure of Interest: None declared

P0197 PREDICTIVE FACTORS FOR POST-ERCP PANCREATITIS: ABOUT A LARGE MONOCENTRIC STUDY

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Introduction: Pancreatitis is the most common and serious complication of diagnostic and therapeutic endoscopic retrograde cholangiopancreatography (ERCP). Prevention strategies targeting risk factors could be important to reduce the rate of post-ERCP pancreatitis. However, the risk factors for post-ERCP pancreatitis (PEP) are still debated.

Aims & Methods

Aim: This systematic review ananalysis was performed to determine the prevalence of PEP and to identify its risk factors.

Methods: We conducted a retrospective study in a single center by reviewing all consecutive cases in which ERCP was performed between January 2010 and January 2015. The existence of pancreatitis before the procedure was an exclusion criteria. All patients remained in the hospital for at least 24 hours after the procedure to monitor them for clinical manifestations of pancreatitis. Serum amylase and lipase levels were measured at 4 and 24 hours (the next morning) after ERCP. We evaluated 8 variables, including patient-related factors and procedure related factors that could be analyzed in detail based on information in the patients' charts.

Results: A total of 1794 patients were included in our study.Therapeutic ERCP had been performed in all cases. 73% of cases were for common bile duct stones and in 27% of cases for biliary stent . Thirty five patients developed PEP with a prevalence of 1.95%. On univariate analysis, precut sphincterotomy ($p = 0.008$) and pancreatic duct cannulation ($p = 0.002$) were found to be significantly associated with PEP. On multivariate analysis, significant risk factors were: at least two pancreatic duct injections ($p = 0.05$) and age younger than 75 years ($p = 0.01$).
Conclusion: History of acute pancreatitis, precut sphincterotomy and pancreatic duct cannulation were all identified as independent risk factors for PEP.
Disclosure of Interest: None declared

P0198 PRECUT FISTULOTOMY: CANNULATION EFICIENCY AND RISK OF POST ERCP COMPLICATIONS IN A NOVEL TERTIARY HOSPITAL IN LIMA PERU

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Introduction: Precut sphincterotomy (PS) has controversial data about its performance and complications that are not fully elucidated. There are different types os PS. Precut Fistulotomy (PF) is a type of PS that employs a needle knife to create an incision at the level of the intraduodenal segment of the common biliary duct avoiding papillary orifice. Recent data show low risk of PEP for this technique in expert hands.
Aims & Methods
Aims: To evaluate success and safety of Precut Fistulotomy(PF), and the risk of complications, specially post ERCP pancreatits (PEP).
Methods: Between June 2012 and November 2013 a single-center prospective cohort study with retrospective analysis on 167 consecutive patients with native papillas referred for ERCP was conducted. Patients elegible were those referred for first ERCP at hospital over 18 years old. All patients were hospitalized 48h before and at least 48h after procedure. The major Indication for ERCP were choledocolithiasis suspected (88%). We intent a selective wire guided cannulation (WGC) in all patients. After 15 minutes of unsuccessfully cannulation or 2 unintentional guidewire advance into pancreatic duct (PD) the endoscopist realize PF by protocol. Success in cannulation was defined as deep placement of a catheter into the common bile duct. A diagnosis and severity of complication was made according to Cottońs classification. 4 endoscopists were involved in study (more than 200 ERCP each one 50 ERCP per year) but less than 5 year of experience. Complications were retrospectively evaluated.
Results: We collect 167 patients in the study time with a median age of 49.18 + 18.27. Female patients were 118 (72.39%).The main diagnosis post ERCP were: choledocolithiasis 114 (69.93%) oddities 22(13.50%) stone migration (6.13%) benign biliary stricture or bile leak 11 (6.75%) biliary malignancy (1.78%). WGC was successful in 119 patients (71.25%). Success cannulation with PF was reach in 163 patiens (97.6%). The overall incidence of PEP for PF patients was 20.5% vs 3.5% in those without PF ($p = 0.001$ RR 6.03). Unintentional pancreatic cannulation was the other significant factor for PEP (40.8% vs 4% $p < 0.001$ RR 8.40). These factors maintain its relation with PEP in de logistic regression model. There is no difference about bleeding rate between patients with PF or not (2.33% vs 2.52% $p = 0.59$).
Conclusion: Precut Fistulotomy is a useful technique that importantly improve successful cannulation. PF does not increase bleeding risk in our cohort but in this novel center we found a slightly increased risk of PEP. Future trials must evaluate if PF could be a risk factor for PEP in centers with low-volume ERCP biliary endoscopists.

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Disclosure of Interest: None declared

P0199 EFFICACY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PANCREATIC FISTULAS

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Introduction: Pancreatic fistulas (PF) may result from surgical resection, pancreatic trauma or chronic pancreatitis. Endoscopic retrograde cholangiopancreatography (ERCP) allows a faster resolution of PF, by performing pancreatic sphincterotomy (S) and/or placement of pancreatic stents (PS) with 5/7Fr.
Aims & Methods: Assess the role of ERCP in the treatment of PF. Cross-sectional study of patients referred for ERCP due to PF.
Results: Fifteen patients (10 males) had PF in pancreatogram, 5 in the cephalic portion, 1 in the neck, 6 in the body and 3 in the tail. Ten patients (66.7%) had undergone previous surgery, with the remaining being secondary to pancreatitis ($n = 3$; 20%) or traumatic transection ($n = 2$; 13.3%). Six of the operated patients had splenectomy. Median time to ERCP was 23 days. Fourteen patients (93.3%) placed PS and 8 (53.3%) performed S. Eleven patients (73.3%) resolved PF endoscopically, 24 days (8 – 401) after ERCP; 1 patient repeated ERCP, with the 3 remaining requiring surgery. Splenectomy was associated with endoscopic failure (50% *vs* 0%, $p = 0.048$). PS > 5cm and/or 7Fr were associated with a trend towards higher endoscopic resolution, respectively, 87.5% *vs* 66.7% ($p = 0.348$) and 100% *vs* 72.7% ($p = 0.198$). Time till endoscopic resolution was tend shorter when surgical fistulas (28 days *vs* 34 days, $p = 0.270$), when PS with 7Fr (22 days *vs* 28 days, $p = 0.203$) or > 5cm (14 days *vs* 34 days, $p = 0.301$).
Conclusion: ERCP with PS and S is effective in 75% of patients with PF. PS > 5cm or 7Fr may be more effective. Associated splenectomy is associated with endoscopic resolution failure.
Disclosure of Interest: None declared

P0200 LIMITATIONS OF PLASTIC STENTS IN MALIGNANT BILIARY DRAINAGE OF BILIARY OBSTRUCTION CAUSED BY PANCREATIC ADENOCARCINOMA

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Introduction: Plastic stents (PS) are cheaper, however, have lower patency than metal stents in pancreatic adenocarcinoma (PA).
Aims & Methods: Assess patency of different stents in biliary drainage of biliary obstruction condition by PA. Cross-sectional study of patients referred for endoscopic retrograde cholangiopancreatography (ERCP) for biliary drainage of biliary obstruction conditioned by PA.
Results: Seventy-nine patients underwent biliary drainage. Adjuvant therapy was performed in 49%, carried out prior to drainage in 41% of cases. PS were placed in 57% of patients, of which, 82% were 10Fr/11.5Fr and 22% were > 7cm. ERCP was repeated in 29% of the patients. In patients with survival longer than 30 days, ERPC was repeated when adjuvant therapy was performed after ERCP (45% *vs* 7%, $p = 0.009$, OR 10.8) and when PS were placed (49% *vs* 10%, $p = 0.001$, OR 8.3). There was a tendency to repeat ERCP when stents had a smaller caliber (83% *vs* 43%, $p = 0.067$). In the multivariate analysis, ERCP repetition was higher in PS (OR 9.5, $p = 0.002$). Stents patency was 76 days (IQR: 42 – 164), being lower in PS ($p = 0.001$) and in these, when smaller caliber (42 days *vs* 133 days, $p = 0.017$) or bigger dimensions (59 days *vs* 133 days, $p = 0.024$). Number of hospital admissions and ERCP repetition due to stent dysfunction was higher in PS (respectively, 49% *vs* 12%, $p < 0.001$, OR 7.2 and 42% *vs* 6%, $p < 0.001$, OR 11.6).
Conclusion: ERCP repetition is more common in PS. Patency is lower in PS, and in these, when smaller caliber or bigger dimensions.
Disclosure of Interest: None declared

P0201 IS PLASTIC BILIARY STENTING IN CHOLEDOCHOLITHIASIS A LONG TIME SAFETY PROCEDURE? A RETROSPECTIVE MULTICENTRIC STUDY

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Introduction: Plastic biliary stenting in patients with choledocholithiasis is suitable until a second ERCP or surgery. This option has demonstrated the fragmentation and dissapearence of large size bile duct stones. Also, it is a simple and safe method for high-risk surgical patients.
Aims & Methods
Objective: To study the effectiveness of plastic biliary stenting in patients with incomplete choledocholothiasis removal, as final technique or as a bridge for additional endoscopic or surgical intervention.
Materials and Methods: Retrospective and multicentric study based on a review of ERCP performed between October 2005 and January 2015.
Results: 72 ERCP were enrolled (52 patients), 26 male and 26 female (50%). The therapeutic indications were: incomplete removal (n43, 82.69%), intradiverticular papilla (n4, 7.7%) and others (n5, 9.6%). In most cases, they had

anaesthetic risk (n36, 69.23%) and the endoscopic procedure was suspended due to severe oxygen desaturation in 3 patients.
The size of plastic biliary stent usually used was 7 or 10 cm and 8,5Fr or 10Fr. In general, patients with 10Fr stent showed less complications than patients with 8,5Fr stent (38.8% vs 62.5%)
We established three groups of patients:
1. Plastic biliary stenting as definitive technique (n15, 28.8%) with an average age of 82.07 ± 12.38. 33.3% of patients delivered biliary disease (4 cholangitis, 1 biliary colic) in an average time of 15.6 months, without migration of stent. In these cases, we changed the stent in 3 patients and stone clearance with removal the stent in 2. After this, these patients were asymptomatic. Five patients died of causes not related and carried the stent during an average time of 10.6 months.
2. Plastic biliary stenting as a brigde for surgical intervention (n9, 17.3%). 33.3% of patients showed biliary disease (1 cholecystitis 6 months after initial placement, 1 pancreatitis 1 month after placement and 1 biliary colic, 18 months after). These patients underwent elective cholecystectomy. Surgical intervention was carried out in an average time of 2.75 months.
3. Patients with additional ERCP (n28, 53.8%). 22 patients (78.2%) needed 2 ERCP getting stone fragmentation and/or removal in most cases (n17, 77.2%). 6 patients (21.5%) needed more than 2 ERCP to successfully resolve the bile duct obstruction in 83.3% (n5). Only 3 patients (10.7%) required a surgical intervention for the resolution of choledocholithiasis.
Conclusion: According to these results, the effectiveness of plastic biliary stenting are directly related with placement time. Plastic stent as a final option needs to be replaced annually. As a bridge for surgical intervention, this procedure should be carried out before 3 months. In patients with additional ERCP, it is an effective measure. However further studies are required to confirm this data.

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Disclosure of Interest: None declared

P0202 POST-ERCP PANCREATITIS (PEP) – DOES ROUTINE USE OF RECTAL INDOMETHACIN AFFECT OUTCOMES? A HIGH-VOLUME SINGLE-CENTRE EXPERIENCE FROM THE UK

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Introduction: Post-ERCP pancreatitis (PEP) is a common but potentially life-threatening complication of ERCP with an incidence of up to 10% in unselected patients in large international series[1]. A number of prospective trials have shown that administration of rectal indomethacin is beneficial in reducing the incidence of PEP in high-risk patients[2]. We aimed to compare the rate and severity of PEP in an unselected group during the pre and post-indomethacin era at our hospital, which has one of the largest ERCP practices in the UK.
Aims & Methods: A retrospective analysis of a prospectively-collected ERCP database in all adult patients undergoing ERCP from January 2011 to December 2014. In 2011 no rectal indomethacin was given, whilst in 2014 all patients recieved it. In 2012-13 only high-risk patients recieved indomethacin. Therefore, the unselected patient cohorts from 2011 (pre group) and 2014 (post group) were compared. PEP was diagnosed and categorised into mild, moderate and severe according to Cotton's 1991 consensus guidelines[3].
Results: 1432 patients were included. Of 717 patients in the pre group, 27 (3.7%) developed pancreatitis, 11 (1.5%) mild, 10 (1.4%) moderate and 6 (0.8%) severe with 4 deaths. Of 715 patients in the post group, 21 (2.9%) developed PEP; 15 (2%) mild, 4 (0.6%) moderate and 2 (0.3%) severe with 1 death. There was no difference in the overall incidence of pancreatitis between the post and pre groups [OR 0.77; p = 0.38], but the combined incidence of moderate and severe PEP was significantly lower in the post group [OR 0.37; p = 0.03]. There was no difference in haemorrhage rates in post 7 (0.9%) vs pre group 5 (0.7%)[OR 1.45; p = 0.56].
Conclusion: We observed that in our cohort of patients the unselected use of rectal indomethacin did not significantly reduce the incidence of PEP, however there was a significant reduction in moderate to severe PEP. This study therefore suggests a beneficial effect of the routine use of rectal indomethacin in unselected patients, consistent with current European Society of Gastrointestinal Endoscopy (ESGE) recommendations.

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P0203 COMPARISON OF CONVENTIONAL DUODENOSCOPE AND SINGLE-BALLOON ENTEROSCOPE TO PERFORM ERCP IN PATIENTS WITH BILLROTH II GASTRECTOMY

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Introduction: Billroth II partial gastrectomy precludes conventional endoscopic retrograde cholangiopancreatography (ERCP) because of altered anatomy. It renders ERCP more difficult because of the intubation of the afferent limb and the orientation of the intact papilla.
Aims & Methods: Comparison of ERCP procedures performed with the conventional duodenoscope and the single-balloon enteroscope (SBE) in Billroth II patients in 2 university endoscopy units. 34 Billroth II patients underwent 64 ERCP procedures between 2006 and 2014. Technical aspects, therapeutic success and complications were recorded.
Results: Male/female ratio was 20/14 (59/41%) with a mean age of 72 ± 1 (48-91) years. The initial choice of endoscope type was at the endoscopist's discretion. 29 (45%) ERCPs were started using a duodenoscope of whom 25 (86%) were successful and 3 were completed using SBE. 21 (33%) ERCPs were started using SBE of whom 16 (76%) were successful and 2 were completed using a pediatric colonoscope. 5 (8%) ERCPs were started using a pediatric colonoscope of whom 4 were completed with a duodenoscope and 2 with the SBE. In total 9 (14%) procedures needed a change of endoscope type in order to complete the procedure. Overall therapeutic success rate using a duodenoscope was 87% vs 81% using SBE ($P > 0.05$; Chis-square), whereas success rate using a pediatric colonoscope was only 43% ($P < 0.05$; Chi-square). Complication rate using a duodenoscope was 7% (pancreatitis; embolism) vs 14% (pancreatitis; biliary leak) using SBE ($P > 0.05$; Chi-square), without mortality. The use of a duodenoscope allowed complete sphincterotomy and both plastic and metallic stent placement, whereas the use of SBE often needed to combine sphincterotomy with additional sphincteroplasty (8-15 mm) and only 7 Fr plastic stent placement was possible due to the 2.8 mm working channel diameter. However, SBE allowed easy access to the papilla in the afferent limb and sphincteroplasty often allowed direct cholangioscopy using SBE. Indications were bile duct stones (55%), chronic pancreatitis (26%), cholangitis (16%), livertransplantation (3%).
Conclusion: Therapeutic ERCP success rate is high in patients with Billroth II gastrectomy using either a conventional duodenoscope or the SBE, with an acceptable and comparable complication rate. The choice of endoscope may depend on the endoscopist's experience, postoperative anatomy (gastrojejunostomy and length of afferent limb) and therapeutic indication (metallic stent placement and direct cholangioscopy).
Disclosure of Interest: None declared

P0204 BALLOON CATHETER VERSUS BASKET CATHETER FOR ENDOSCOPIC BILE DUCT STONE EXTRACTION: A MULTICENTRE, PROSPECTIVE RANDOMISED CONTROLLED TRIAL

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Introduction: Endoscopic bile duct stone (BDS) removal using the basket or balloon catheter is a well-established treatment. However, the choice of extraction devices depends on the operator's preference because there has been no study comparing outcomes with the two catheters.
Aims & Methods: We conducted a non-inferiority trial to investigate the performance of individual catheter for stone extraction. Patients with a BDS diameter ≤10 mm and common bile duct diameter ≤15 mm were enrolled in this study. The participants were randomly assigned to groups that were treated with the basket or the balloon catheter at 12 hospitals from October 2013 through September 2014. After stone extraction with the assigned catheter was completed, balloon occlusion cholangiography was performed in both groups to confirm the clearance of the duct. Primary endpoint was the rate of complete clearance of the duct by the assigned catheter. Secondary endpoints were the rate and time of complete clearance in one endoscopic session.
Results: We initially enrolled 172 consecutive patients, but 14 patients were excluded after randomisation. The total number of patients available for analysis was 158. The rates of complete clearance by the assigned catheter were 92.3% (72/78) in the balloon group and 80.0% (64/80) in the basket group. The difference of the rates between the two groups was -12.3%, indicating failure of non-inferiority of the basket catheter (non-inferiority limit 10%; $p = 0.17$ for non-inferiority). However, the results revealed superiority of the balloon over the basket catheter ($p = 0.037$). There were no significant differences in secondary endpoints.
Conclusion: The balloon catheter is recommended for a first-line device of endoscopic BDS removal. This study was registered on the UMIN Clinical Trial Registry (UMIN000011887).
Disclosure of Interest: None declared

P0205 A NOVEL MODIFIED APPROACH TO SINGLE-BALLOON ENTEROSCOPY FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY

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Introduction: Although increasing evidence of the usefulness of single-balloon enteroscopy (SBE) for endoscopic retrograde cholangiopancreatography (ERCP) has been reported in postoperative patients with altered gastrointestinal anatomy, no short-type SBE has been made available in the market. Thereafter, the technical limitations or parameters of SBE (working length, 200 cm; working channel diameter, 2.8 mm; SIF-Q260, Olympus Medical Systems Corp., Tokyo, Japan) necessitate the use of prototype endoscopic instrumentation or the replacement of SIF-Q260 with another endoscope through the overtube.

Aims & Methods: We evaluated the efficacy of a novel SBE approach by using PCF-PQ260L (with passive bending and high-force transmission; working length, 168 cm; working channel diameter, 2.8 mm; Olympus Medical Systems Corp.) in patients with an altered gastrointestinal anatomy, without the use of special or prototype instrumentation or an enteroscope replacement. Between February 2012 and March 2015, 38 modified SBE-assisted ERCP procedures were performed in 24 postoperative patients (15 men and 9 women; mean age, 64.7 years [range, 25–93 years]) with altered gastrointestinal anatomy (Roux-en-Y hepaticojejunostomy, 16 procedures in 6 patients; Roux-en-Y gastrectomy, 9 procedures in 7 patients; Billroth-II gastrectomy, 7 procedures in 5 patients; pancreatoduodenectomy, 4 procedures in 4 patients; and gastrojejunostomy, 2 procedures in 2 patients). In all of the cases, a side hole was made 110 cm from the distal end of the overtube. ERCP was performed by inserting a PCF-PQ260L through the side hole of the overtube and then into the gastrointestinal tract. We retrospectively evaluated the success rate of reaching the blind end, the mean time required to reach the blind end, the diagnostic success rate, the therapeutic success rate, the mean procedure time, and the complications.

Results: Endoscopic therapeutic procedures were performed as follows: plastic biliary stent (ERBD) insertion, 15 times in 10 patients, including endoscopic sphincterotomy (EST) performed 4 times; balloon dilatation for stenosis of hepaticojejunal anastomosis, 5 times in 2 patients; choledocholithiasis extraction, 5 times in 5 patients, including EST performed 4 times; removal of ERBD, 3 times in 2 patients; endoscopic nasobiliary drainage, once; and removal of debris from the bile duct, once. In the remaining 4 patients, brush cytology of the pancreatic duct and cholangiography were performed. The success rate of reaching the blind end was 97.4% (37/38 patients). The mean time required to reach the blind end was 28.3 ± 24.0 min. The diagnostic success rate was 92.1% (35/38 patients). The mean procedure time was 59.4 ± 39.5 min. The success rate of the overall modified SBE-assisted ERC was 89.5% (34/38 patients). The complication rate was 23.7% (hyperamylasemia in 9 patients).

Conclusion: Diagnostic and therapeutic ERCP using our novel approach of modifying SBE without the use of a special or prototype instrumentation, or an enteroscope replacement is sufficiently safe and effective. It may potentially serve as an alternative to the SBE-assisted ERCP with SIF-Q260.

Disclosure of Interest: None declared

P0206 DICLOPHENAC POTASSIUM VERSUS CEPHTAZIDIME FOR REDUCTION OF POST ERCP PANCREATITIS IN AVERAGE RISK PATIENTS-RANDOMISED DOUBLE BLIND CONTROLLED TRIAL

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Introduction: Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) is the most common major complication of ERCP. Its incidence has substantial variations ranging from 5.1% to more than 25% of all ERCP procedures. In some cases pancreatitis is followed by severe course with pancreatic necrosis and multiorgan failure. Diclophenac sodium together with indometacine is currently standard treatment in prevention of PEP while ceftazidime is possible alternative treatment for patients with contraindication for nonsteroidal anti-inflammatory drugs (NSAID).

Aims & Methods: The primary aim of this study was to determine whether prophylactic, parenteraly administered ceftazidime reduces the frequency of PEP compared to rectally applied diclofenac sodium. All eligible patients who underwent ERCP in tertiary care center during a 20-month period (June 2013 to February 2015) were enrolled in this study. Estimating the prevalence of PEP of 10% and reduction of incidence of 50% ($\alpha = 0.02$, beta $= 0.95$) calculated total sample size was 248. In a double-blinded randomized controlled trial, patients received a suppository containing a 100 mg of diclofenac sodium rectally and placebo intravenously (group A) or 1g of ceftazidime intravenously and placebo rectally (group B) immediately before the procedure. PEP was diagnosed according to the standardized criteria (Cotton criteria). The study was registered at Clinical Trial.gov (NCT01784445)

Results: We included 272 patients, mean age of 71.9 years ($SD \pm 12.2$), female 128 (47%). There were 129 (47.4%) patients in the diclofenac sodium group and 143 (52.6%) in the ceftazidime group. The occurrence of post-ERCP pancreatitis (PEP) in complete sample was 11.8% (32/272). There was no statistical difference in occurrence of PEP between diclofenac and ceftazidime group (RR = 1.72; 95%CI = 0.86-3.43, P = 0.17). PEP incidence in females was similar in booth groups 7(11.7%) in diclophenac sodium and 11(16.2%) in ceftazidime group (RR = 0.7212; 95%CI 0.29 to 1.74, P = 0.46).

Conclusion: There are no statistically significant difference in incidence of PEP among patients who received ceftazidime or diclophenac potassium. Ceftazidime may be used as alternative treatment for prevening PEP in patients with contraincidations for NSAID.

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Disclosure of Interest: None declared

P0207 FULLY COVERED SELF-EXPANDABLE METAL STENTS TO DILATE PANCREATIC DUCT STRICTURES DUE TO CHRONIC PANCRERATITIS: A PILOT STUDY

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Introduction: Main pancreatic duct (MPD) strictures due to chronic pancreatitis (CP) may be treated endoscopically by insertion of single or multiple plastic stents. MPD stricture resolution after plastic stents removal occurs in near 60% of the cases.

Aims & Methods: We evaluate the use of removable fully covered, self expandable metal stents (FC-SEMS) to dilate MPD strictures secondary to CP. Patients with CP and symptomatic MPD strictures in the head of the pancreas that persisted >3 months after placement of a single plastic stent, were enrolled into a prospective single arm trial. The protocol was approved from the Ethic Committee of our University. A Nitinol FC-SEMS (Bumpy stent, Taewoong) was inserted and removed after 6 months. FC-SEMS diameter (6 or 8 mm) and length (3, 4, 5 cm) were chosen according to stricture anatomy and MPD diameter above the stricture. Stricture resolution was defined as a satisfactory pancreatico-duodenal contrast medium outflow and absence of pain during continuous flushing with saline (1000ml/day) for 24 hours through a 6 french naso-pancreatic drain. Primary objective was FC-SEMS removability. Secondary objectives were MPD stricture resolution rate and complications. Follow-up was planned every 6 months during a 2 year. Pancreatic pain episodes and recurrence of pancreatitis were recorded.

Results: Between Dec 2012 and Oct 2014, 15 patients (10M, mean age 60 y) were enrolled. Pancreatic calcifications were present in 6(40%) and ESWL was performed in 4. Four patients (27%) had a history of alcohol abuse. In 10 cases the FC-SEMS was inserted through the major papilla (7 had a previous biliary sphincterotomy, 2 had pancreatic sphincterotomy alone, 1 had choledochoduodenostomy), while 5 patients (3 pancreas divisum, 2 dominant dorsal duct) received the FC-SEMS through the minor papilla. One patient developed cholangitis after 24 hours due to occlusion of the biliary sphincterotomy from the FC-SEMS; cholangitis resolved after insertion of a plastic biliary stent. During stenting period 13 patients (87%) were asymptomatic while 2 had recurrent pancreatitis after 4 and 5 months; the FC-SEMS had migrated and the persistent MPD stricture was treated with a plastic stent. FC-SEMS completely migrated in 7 patients and could be removed endoscopically in the remaining 8 cases. Four patients (27%) developed a tight stricture induced by FC-SEMS at the level of its proximal end; in one case the stricture was overcome only after EUS-guided pancreatic rendez-vous. Follow-up is ongoing. Results are summarized in the table.

	N	%	Follow-up,mean months (range)
Patients	15	-	-
FC-SEMS removability	8/8	100	-
Complete FC-SEMS distal migration	7/15	47	-
FC-SEMS proximal migration	1/8	12	
MPD stricture resolution	10/15	67	-
SEMS ''induced'' MPD stricture	4/15	27	-
Asymptomatic	8/14*	57	12 (5-18)

*One patient excluded from follow-up (pancreatic cancer diagnosed 6 months after stent removal).

Conclusion: FC-SEMS removability from the MPD in chronic pancreatitis was feasible in all cases. After 1-year follow-up 57% of the patients were asymptomatic; this figure is similar to those obtained with plastic stents. Occurrence of FC-SEMS induced pancreatic strictures is a major issue and deserves further assessment. According to our experience the use of FC-SEMS in the MPD needs careful evaluation in the setting of clinical trials.

Abstract number: P0209

Biliary condition	n	CBD deep cannulation	Biliary sphincterotomy	Balloon dilation	Stent insertion	Successful biliary drainage	mortality
1.Papillary stenosis, migrated CBD stones	30	28 (93.33%)	28 (100%)	0	10/10 (100%)	28 (93.33%)	0
2.Stones < 10mm	90	87 (96.66%)	79/79 (100%)	EPBD up to 10 mm 28/28 (100%)	15/15 (100%)	87 (96.66%)	0
3.Malignant extrahepatic strictures	83	80 (96.38%)	72/72 (100%)	0	78/80 (97.5%)	73 (88%)	2/83 (2.4%)
4.Benign extrahepatic strictures	37	35 (94.59%)	35/35 (100%)	0	35/35 (100%)	35 (94.59%)	0
5.Biliary leaks	12	11 (91.66%)	11/11 (100%)	0	11/11 (100%)	11 (91.66%)	0
6.Stones > 10mm	51	50 (98%)	50/50 (100%)	Large EPBD27/31 (87%)	19/19 (100%)	49 (98%)	0
7.Hilar strictures	32	29 (90%)	29/29 (100%)	10/10 (100%)	28/29 (96%)	27 (84%)	1/32 (3%)
8.Billroth II anatomy	28	26 (93%)	0	16/16 (100%)	12/12 (100%)	26 (93%)	0
TOTAL	363	346 (95.3%)	254 (100%)	81(95%)	222 (98%)	336 (94%)	3/363 (0.8%)

CBD = Common Bile Duct. EPBD = endoscopic papillary balloon dilation. For small CBD stone extraction it was employed up to 10 mm. For larger CBD stones, 12-18 mm balloon diameter was used. In Billroth II balloon dilation and stent insertion were always performed after inserting a plastic stent in the Main Pancreatic Duct without previous sphincterotomy.

Disclosure of Interest: A. Tringali Lecture fee(s): Boston Scientific, P. Familiari: None declared, F. Barbaro: None declared, I. Boskoški Consultancy: Cook Endoscopy, G. Gigante: None declared, V. Perri: None declared, G. Costamagna Consultancy: Cook endoscopy, Olympus, Boston Scientific

P0208 FEASIBILITY AND PRELIMINARY SAFETY STUDY OF A NEW NITINOL "SOFT" FULLY COVERED SELF-EXPANDING PANCREATIC METAL STENT IN CHRONIC PANCREATITIS

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Introduction: Multiple plastic stents are used for calibrating distal stricture in severe chronic pancreatitis. A single metal stent which does not require exchanges would be useful in this setting.

Aims & Methods: Document feasibility and preliminary safety in ongoing pancreatic endotherapy in patients (pts) with painful chronic pancreatitis (CP) of Cremer Type IV using a new Nitinol "Soft" fully covered (6 mm diameter) self-expanding metal stent (Panc SEMS) (Pancreatic WallFlex, Boston Scientific Corporation, Marlborough, USA). Ten (10) patients enrolled. Intended Panc SEMS indwell 3 mo in 5 pts and 6 mo in 5 pts. Follow-up to 24 mo ongoing. Interim results reported on ITT basis.

Results: 10 pts (mean age 48, 60% male). CP etiology 60% alcoholic, 10% hereditary, 30% unknown. Calcific CP in 70% of pts. All pts had prior plastic stent placement(s) during a mean of 3 yrs (range 4 mo to 6 yrs). No pts had a prior Panc SEMS. At time of interim analysis, all pts were stent free with mean time on study 262 d (range 218-326 d) and mean stent-free period of 95 d (range 22-193 d). In total 14 stents were placed, with 2 pts having immediate removal and replacement of the initial stent due to deployment in unsatisfactory position and 2 pts needing a second stent placement after premature complete distal migration. Stent migration without symptoms, thought to be a reflection of adequate calibration of the benign stricture, occurred in 6 stent placements, not requiring restenting. Clinically meaningful complete distal migration (CDM) with symptoms occurred in 21% (3/14) stent placements. There were no proximal stent migrations. Endoscopic stent removal was performed per-protocol easily in one pt after 3 mo indwell and in 2 pts after 6 mo indwell without stent removal-related adverse events (AEs). To date 80% (8/10) pts remain stent free and follow-up is ongoing. One pt had premature CDM followed by placement of plastic stents. One pt had no pain relief after SEMS placement and had subsequent pancreatic diversion surgery which did not provide pain relief either. Mean Izbicki pain scores were 59 (range 15-86) at baseline, 42 (range 0-88) at time of SEMS removal or observation of complete distal migration, and 44 range (0-90) at last visit. AEs occurred in 50% (5/10) of pts, with 7 AEs (2 pain associated with premature CDM, and at time of SEMS placement 3 transient pain, 1 bacterial infection, and 1 mild acute pancreatitis). No SEMS needed to be removed due to intolerable pain after SEMS placement. There were no stent-induced ductal changes.

Conclusion: Feasibility of FC SEMS implantation and removal in pts undergoing pancreatic endotherapy was confirmed. Preliminary safety was acceptable with only mild adverse events, represented mainly by anticipated pain after implantation. SEMS removability was achieved without adverse events in all patients, either per protocol or by spontaneous complete distal migration. No stent induced ductal changes were observed at the time of removal. Further study to assess effectiveness of pancreatic endotherapy

Disclosure of Interest: None declared

P0209 ERCP QUALITY EVALUATION THROUGH SELF-ASSESSMENT AND OUTCOMES

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Introduction: ERCP is one the most difficult gastrointestinal endoscopic procedures, therefore monitoring and enhancing the quality of this interventionn is of paramount importance.

Aims & Methods: All ERCPs performed in our center from January 2009 to September 2014 were prospectively included in a specific ERCP database. Procedures were analyzed retrospectively with a modification of the Rotterdam Assessment Form for ERCP (RAF-E) [1] that has proven to provide insight into the quality of individual ERCP performance and can be used to assess and set standards for quality control in ERCP. Only naïve papillae were considered as it is well known that after biliary sphincterotomy, cannulation and ERCP completion is usually easier. MRCP was routinely performed before ERCP.

Results: A total number of 363 ERCPs with naïve papilla were performed in this period of time by a single endoscopist. Results according to the retrospective appraisal using the modified RAF-E are shown in the table.

According to degrees of difficulty based on Schutz's classification [2], ERCP indications 1-5 correspond to level 1, 6-7 to level 2 and 8 to level 3. Diagnostic cholangiography or pancreatic procedures were never performed. For CBD cannulation a sphincterotom loaded with a guidewire was used.

Conclusion: Self-assessment is a valuable method to gain insight in ERCP performance. Outcomes can be compared with those obtained in centers of excellence to promote improvement. It appears that CBD deep cannulation can be considered as a surrogate for successful biliary drainage because it was accomplished in 97% of occasions after cannulation in the eight biliary scenarios reported in this study.

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Disclosure of Interest: None declared

P0210 ESTIMATED INCIDENCE OF MULTI-DRUG RESISTANT ORGANISMS AMONG DUODENOSCOPE TRANSMITTED INFECTION: RESULTS FROM A NATIONAL SPANISH SURVEY

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Introduction: Transmission of Multi-Drug Resistent Organisms (MDROs) has recently been linked to duodenoscopes. The epidemiology of this potentially serious problem is poorly understood. Variability across Units in endoscope cleaning and disinfection methods has received limited attention to date.

Aims & Methods: To survey the incidence of duodenoscope-transmitted infection overall and of MDRO in particular in Spain. Members of the Sociedad Española de Endosocopia Digestiva (SEED) registered at institutions offering ERCP were sent a questionnaire about disinfection standards and instances of duodenoscope transmitted infection in their Units. Self-reported recall data were pooled for analysis.

Results: Seventy one hospitals from across Spain participated in the study. The total estimated procedure volume covered by respondents was 70,000 ERCPs

over a 5-yr period. 3/71 (4.2%) centres performed manual cleaning of the duodenoscopes. No infection transmission was reported from any of these hospitals. 68/71 (95.8%) units had automatic washing methods for cleaning. Thirteen infectious outbreaks linked to duodenoscopes were reported from 13 different centres. Only four of these outbreaks were related to MDRO. Three MDRO outbreaks involved multiple patients (Klebsiella Carbapenemase in two centers and Escherichia Coli producing extended-spectrum beta-lactamases in another) and a single patient in another (MDR Klebsiella). Microbiological genotyping revealed a common MDRO in patients referred from different hospitals to a single referral Unit. Clinical course ranged from fever to severe sepsis requiring ICU admission. MDRO was judged a potentially contributing factor in two postoperative deaths. A single patient was infected in the remaining 9 outbreaks. Isolated microorganisms were: Klebsiella species (4), Escherichia Coli (1), Enteroccocus (1), Pseudomonas (1), Serratia (1), Candida (1). No patient died. Routine microbiologic assessment of disinfections practices had only been performed in 2/13 centers with outbreaks. Corrective measures were implemented in all cases with MDRO
Conclusion: Duodenoscope transmitted infection was observed in 13 out of 71 centers (18.3%), with MDRO identified in 30% of outbreaks, typically involving multiple cases. Despite the limitations of this survey, it provides further evidence of duodenoscope-transmitted MDRO as an emerging problem. There is a need to address critical cleaning steps in the chain-of-transmission, pending future improvements in scope design.
Disclosure of Interest: None declared

P0211 SMALL PAPILLA OF VATER AS A RISK FACTOR FOR POST-ERCP PANCREATITIS

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Introduction: The pathogenesis of Post-ERCP pancreatitis (PEP) is multifactorial; mechanical injury, hydrostatic injury, chemical and thermal injury, have been postulated as factors for PEP development. Uchino et al. [1] suggested that a small papilla can also be considered as a risk factor for PEP. A small papilla makes the pancreatic orifice susceptible to trauma, which ultimately leads to pancreatitis.
Aims & Methods: A small papilla of Vater was defined as having less than 3 mm in size and/or the absence of a caudal fold (plica papillae). These criteria were applied retrospectively to a series of ERCP with naïve papilla with detailed reports. Common Bile Duct (CBD) drainage was the purpose of all ERCPs. CBD cannulation was always attempted with a sphincterotome loaded with a guidewire
Results: Main results are shown in the table.

Table: Pancreatitis rate according to papilla of Vater size

	n	PostERCP pancreatitis rate	Mortality
Normal papilla	94	8 (8.5%)	0
Small papilla	18	4 (22%)	1/18 (5.5)

Both groups were matched in terms of age, gender, ERCP indication, easy or difficult cannulation, precut use and stent insertion without biliary sphincterotomy.
Both pancreatitis and mortality rate showed a $p < 0.05$ between normal and small size papillas. The patient who died was an 80-yr old woman who had a very easy procedure. A 10 french biliary stent was inserted without sphincterotomy for CBD drainage. Biliary sphincterotomy to remove CBD stones was not attempted because of a small papilla of Vater with no clear landmarks for cutting. The patient suffered from a severe pancreatitis and died 72 hours later.
Conclusion: In this small series study, it appears that a small size papilla is a risk factor for PEP. Pancreatitis severity appears to be also greater when biliary sphincterotomy is not performed [2]. Further studies are warranted to confirm these results.

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Disclosure of Interest: None declared

P0212 PARTIALLY COVERED VERSUS UNCOVERED SELF-EXPANDABLE NITINOL STENTS WITH ANTI-MIGRATION PROPERTIES FOR THE PALLIATION OF MALIGNANT DISTAL BILIARY OBSTRUCTION: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Covered self-expandable metal stents (SEMSs) are increasingly used as alternatives to uncovered SEMSs for the palliation of inoperable malignant distal biliary obstruction to counteract tumor ingrowth.
Aims & Methods: The aims of this study were to compare the outcomes of partially covered and uncovered SEMSs with identical mesh structures and anti-migration properties, such as low axial force and flared ends. One hundred and three patients who were diagnosed with inoperable malignant distal biliary obstruction between January 2006 and August 2013 at a single tertiary center were randomly assigned to either the partially covered (n = 51) or uncovered (n = 52) SEMS group.
Results: There were no significant differences in the cumulative stent patency, overall patient survival, stent dysfunction-free survival, and overall adverse events, including pancreatitis and cholecystitis, between the two groups. Compared to the uncovered group, stent migration (5.9% vs. 0%, $P = 0.118$) and tumor overgrowth (7.8% vs. 1.9%, $P = 0.205$) were non-significantly more frequent in the partially covered group, whereas tumor ingrowth showed a significantly higher incidence in the uncovered group (5.9% vs. 19.2%, $P = 0.041$). Stent migration in the partially covered group occurred only in patients with short stenosis of the utmost distal bile duct (two in ampullary cancer, one in bile duct cancer), and did not occur in any patients with pancreatic cancer.
Conclusion: For the palliation of malignant distal biliary obstruction, endoscopic placement of partially covered SEMSs with anti-migration designs and identical mesh structures to uncovered SEMSs failed to prolong cumulative stent patency or reduce stent migration.
Disclosure of Interest: None declared

P0213 PROSPECTIVE, COMPARATIVE TRIAL EVALUATING FREE HAND INSERTION OF A SCOPE INTO THE BILE DUCT WITH MULTIBENDING VERSUS CONVENTIONAL ULTRASLIM ENDOSCOPE FOR DIRECT PERORAL CHOLANGIOSCOPY

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Introduction: Direct peroral cholangioscopy (DPOC) using an ultraslim endoscope has been increasingly applied for diagnosis and treatment of diverse biliary diseases. However, the usefulness of DPOC is limited by low, inconsistent success rates. The success rate can be increased by assistance of several accessories, but it's technically demanded and cumbersome. In addition, maintenance of desired scope position during interventional procedure is difficult.
Aims & Methods: The aim of this study was to evaluate the success rate of free-hand direct insertion into the bile duct using a newly developed multibending ultraslim endoscope as for a dedicated cholangioscope for DPOC. A total of 52 patients with biliary disease were prospectively enrolled. Each patient was performed two trials of DPOCs using a multibending ultraslim endoscope (Olympus Co., Tokyo, Japan) after a conventional ultraslim scope (GIF-XP290N, Olympus) without assistance of accessories. If a DPOC using multibending ultraslim endoscope without accessory failed, an intraductal balloon-guided DPOC was performed. The success was defined as successful advancement of the endoscope into the bifurcation or the obstructed segment of the biliary tree within 15 minute without accessory.
Results: The success rate of a DPOC using multibending endoscope without accessory was significantly higher than a DPOC using a conventional endoscope (90.4% vs. 28.8%; $p < 0.001$). The 5 patients failed in DPOC using multibending endoscope without accessory were all success with an intraductal balloon-guided DPOC using multibending endoscope. The success of interventional procedures was achieved with 36 of 37 (97.8%) trials including 11 intraductal biopsies, 9 intraductal lithotripsy. Adverse event was observed in one patient of mild hemobilia.
Conclusion: A high success rate of free hand direct insertion of a scope into the bile duct was achieved with newly developed multibending ultraslim endoscope with experienced endoscopist. DPOC without assistance of accessories can be possible with further development.
Disclosure of Interest: None declared

P0214 SAFETY OF ENDOSCOPIC PANCREATIC SPHINCTEROTOMY IN EXPERT HANDS

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Introduction: Endoscopic biliary sphincterotomy has been commonly used for biliary and pancreatic duct diseases, in cases of difficult biliary duct canulation, various methods like precut and endoscopic pancreatic sphincterotomy (EPDS) has been used. Various studies have reported variable rate of complications

after doing EPDS. Thus, we examined the indications and rate of complications in one of the largest center for endoscopic retrograde cholangiopancreatograph.
Aims & Methods: Among patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) between January 2012 and December 2014, 40 patients who underwent endoscopic pancreatic duct sphincterotomy (EPDS) were included in this retrospective study. We examined the indications, complications and safety of procedure.
Results: Out of 40 patients 52.5% were female and 47.5% were male. Diagnostic and therapeutic indications for ERCP were recurrent pancreatitis (10 cases), pancreatic pseudocyst (2 cases), and mass at porta hepatis (1 cases) pancreatic duct leakage (2 cases), cbd stone (3 cases), biliary stricture with obstructive jaundice (12 cases). The success rate of EPDS was 100% (40/40). Acute complications of EPDS included three cases (7.5%) of mild pancreatitis and no other complication was noted.
Conclusion: EPDS showed a very low incidence of complications and a high rate of treatment success; thus, EPDS is a relatively safe procedure when performed by an expert endoscopist

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Disclosure of Interest: None declared

P0215 AN OBJECTIVE APPROACH TO QUANTIFY TISSUE OBTAINED FROM ENDOSCOPIC ULTRASOUND GUIDED FINE NEEDLE BIOPSY (EUS-FNB): A POTENTIALLY IMPORTANT TOOL FOR FUTURE EUS-GUIDED BIOPSY TRIALS

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Introduction: Endoscopic ultrasound (EUS) guided tissue acquisition, with a fine needle, allows cytologic and/or histologic diagnosis of lesions within or adjacent to the gastrointestinal tract (GIT). Given most needles used so far are fine needle aspiration (FNA), the ''traditional'' primary outcome has been a cytological diagnosis. The recent development of core-like needles aims to increase the amount of tissue acquired for ''histological'' assessment. Apart from the conventional ''tissue diagnosis'', there has been no method or criteria to objectively quantify the tissue obtained from different EUS FNA needles. This may explain for the indifferences in trials that compared FNA versus FNB needles.
Aims & Methods: The aim was to evaluate an objective method to quantify the tissue acquired by EUS-guided biopsy using core needles.
Methods: Tissue acquired from biopsy of pancreatic mass by EUS-FNA technique was prospectively obtained from 18 subjects with suspected pancreatic malignancy. In each case, all material from two needle passes of either 22G or 25G Procore needle were flushed into a 5ml-bottle of formalin for direct histological processing, which involved extracting the material from the bottle (without spinning) for routine paraffin processing and generating slides as if the specimen was a ''histological specimen''. One of every 3 slides will be reviewed for presence of diagnostic material by a dedicated cyto-pathologist. In order to objectively quantify the tissue acquired from the needle, the slides will be scanned using the NanoZoomer (Hamamatsu Phototonic, Japan) and high definition images will be stored electronically. Using the associated software (NDP.view2, Phototonic, Japan), the characteristics of the diagnostic tissue will be further quantified by objectively assessing the length, width, presence of tissue-core (defined as tissue showing preserved architectural integrity, in which the length of the core is at least twice of the nominal inner diameter of the used needle), and the total surface area of diagnostic tissue.
Results: This approach was used to examine EUS guided biopsied specimens from 18 subjects with pancreatic mass, using 22-G Procore needle ($n = 10$) and 25-G Procore ($n = 8$). The final pathological diagnoses were achieved in all cases, with 16 invasive adenocarcinomas and 2 neuroendocrine tumour with Ki67 determination. When compared the tissue characteristics between the 22G and 25G Procore needle, both needles were able to acquired tissue-cores, but the cores were larger (376 ± 9.72 vs.262 ± 16.01 μm; $P < 0.0001$) and longer (1.93 ± 0.22 mm vs. 0.96 ± 0.18 mm; $P < 0.02$) with the 22G than the 25G Procore needle. Most importantly, the 22G Procore needle able to acquire more diagnostic material than the 25G needle, as quantified by the total surface area of diagnostic tissue (1.67 ± 0.51 mm^2 vs. 0.52 ± 0.14 mm^2; $P = 0.05$).
Conclusion: The characteristic and amount of tissue acquired from EUS guided biopsy can be objectively quantified by using the direct histological processing and NanoZoomer assessment. This method has great potential for research use, especially in the evaluation the outcome of different types of needles in practice of EUS guided biopsy.
Disclosure of Interest: None declared

P0216 SINGLE SESSION EUS-RENDEZVOUS ERCP VERSUS PERCUTANEOUS BILIARY DRAINAGE IN PATIENTS WITH FAILED COMMON BILE DUCT ACCESS AFTER ERCP

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Introduction: Common bile duct access (CBD) may fail in less than 5% of the patients undergoing ERCP. Traditionally, these patients will require percutaneous biliary drainage. However, the advent of EUS-biliary drainage provides another endoscopic means of achieving CBD access at the same session of failed ERCP. However, how single session EUS-rendezvous ERCP (ERV) compares to percutaneous biliary drainage is not known.
Aims & Methods: This was a multicentre study (3 Asian hospitals, 2 university affiliated) of all patients that underwent single session EUS-rendezvous ERCP after failed CBD access by ERCP, performed between January 2012 and October 2014. The outcomes of these patients were retrospectively compared to those that received percutaneous-rendezvous ERCP or antegrade stenting (PTBD) prior to the introduction of the EUS technique. These procedures were believed to be comparable as the goal of the procedures was to achieve transpapillary CBD access for subsequent interventions. The main outcome parameters included the success rate in gaining CBD access, adverse event rates, the number of sessions of interventions required in each patient to obtain CBD access and luminal drainage.
Results: A total of 128 patients were included (ERV:PTBD = 64:64). There were no differenced in background demographics (table 1). A high success rate in obtaining CBD access (92.2% vs 100%, $P = 0.056$) and achieving luminal drainage (93.8% vs 85.9%, $P = 0.241$) was observed in both groups. This was possible in a single session in all patients within the ERV group. Whilst, the median (range) number of sessions required to obtain CBD access in the PTBD arm was 2 (1-2), $P < 0.0001$. Similarly, significantly more interventions were required in the PTBD group to achieve transluminal drainage (3 [2-9] sessions, $P = 0.032$). The adverse events rates were comparable between the 2 groups (17.2% vs 23.4%, $P = 0.510$). The most common adverse events were cholangitis (6.2%) in the ERV arm and tube dislodgement (9.4%) in the PTBD group.
Conclusion: Single-session EUS-rendezvous ERCP may replace PTBD as the procedure of choice in patients with failed ERCP. The procedure allows same session CBD access and luminal drainage with avoidance tube related adverse events.

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Disclosure of Interest: None declared

P0217 ADVERSE EVENTS OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION OF PANCREATIC CYSTIC LESIONS USING THE LEXICON PROPOSED IN AN ASGE WORKSHOP: A PROSPECTIVE STUDY

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Introduction: There is concern about the safety of endoscopic ultrasound-guided fine needle aspiration of pancreatic cystic lesions. The aim of this study is to assess the incidence of adverse events of the technique in this setting using the lexicon recommended by ASGE.
Aims & Methods: Patients with pancreatic cystic lesions undergoing an endoscopic ultrasound-guided fine needle aspiration were prospectively included. A 22 gauge-needle was used in all patients. The procedure was performed under conscious sedation. A complete cystic fluid evacuation with a single needle pass was attempted in all cases. Patients received ciprofloxacin during the procedure and 3 days after. Adverse events were defined and graded following the lexicon recommended by ASGE. Patients were followed at 48 hours, one week and day 30 after the procedure. Potential predictive factors for adverse events were analyzed.
Results: A total of 132 patients were included and 7 adverse events (5.3%) were recorded: fever ($n = 3$, 2.3%); acute pancreatitis ($n = 3$, 2.3%) and cholangitis ($n = 1$, 0.75%). All adverse events had an early presentation (before 48 hours post-procedure) and resolved with medical therapy. All the episodes of pancreatitis were observed in patients with chronic pancreatitis or with a previous episode of acute pancreatitis ($p < 0.05$). We did not find any other variable related with the development of adverse events.

Conclusion: Endoscopic ultrasound-guided fine needle aspiration of pancreatic cystic lesions has a rate of adverse events slightly higher than that of solid masses, but small enough to consider this procedure a secure way to guide management of these patients.
Disclosure of Interest: None declared

P0218 THE ROLE OF ENDOSCOPIC ULTRASOUND IN THE EVALUATION AND MANAGEMENT OF GASTROINTESTINAL STROMAL TUMORS

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Introduction: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal gastrointestinal tumors (MTs), corresponding in most *post-mortem* studies, to less than 3% of gastrointestinal malignancies. Although its relatively indolent course, all GISTs are considered as potentially malignant, and so, its essential to stratify the tumors according to the relative risk of progression.
Aims & Methods: (1) Descriptive analysis of the experience of our center in the diagnosis and monitoring of MTs with the main focus on GISTs; (2) to assess the role of endoscopic ultrasonography in the identification of high risk-stigmata, and the correlation between endosonographic features and histological predictors of malignancy.
Retrospective analysis of all new cases of MTs, in the period between 2010 and 2014. We recorded demographic, clinical, pathological and radiological data. Risk stratification was performed according to the TNM classification and the Miettinen criteria. Endosonography high-risk stigmata was defined as presence of heterogeneous echopattern, cystic spaces, irregular extra-luminal margin and large tumor ($\geq$ 4 cm). Histological malignancy was defined as $>$ 5 mitoses on a total area of 5mm^2
Results: We identified 54 patients with mesenchymal tumors, 37 with immunohistochemistry confirmation of being a GIST. There was equal distribution between genders, with a mean age of 68 years. At diagnosis, 5 patients had a synchronous tumor (3 colorectal cancer). The mean size was 5.7 cm, being the spindle cell (81%) the most common subtype. Stomach was the most frequent localization (70%), followed by the small bowel. Concerning clinical presentation, in 50% it was an incidentaloma, gastrointestinal bleeding happened in 20% and in 10%, the diagnosis was established during the management of acute abdomen.
According to TNM classification, 83% were classified as localized disease and 24% as having high-risk of progression.
Endoscopic ultrasound was performed in 25 patients. At the first endosonography examination, 8 presented endosonographic high-risk stigmata, and were refer to surgery. In all cases, their histological analysis revealed a low mitotic index ($\leq$ 5 mitoses on a total area of 5mm^2). During the ecoendoscopic follow-up, none of the patients in the low-risk group, developed high-risk features or metastatic disease.
The mean follow-up was 24 months and the median overall survival at 2 years was 81% (localized disease: 82%; advanced disease: 63%).
Conclusion: Endoscopic ultrasound was a good method for following lesions with less potential for malignancy, avoiding the morbidities associated with an aggressive strategy. The presence of high-risk features in endoscopic ultrasound, did not correlate with the presence of histological malignancy (increased mitotic index). We identified a high prevalence of synchronous tumors.
Our data outlines the need of new prospective studies to create and validate new ecoendoscopic features for predicting histological malignancy.
Disclosure of Interest: None declared

P0219 CLINICAL IMPACT OF EUS ELASTOGRAPHY USING MEAN STRAIN HISTOGRAM VALUE: A SINGLE-CENTER EXPERIENCE

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Introduction: Endoscopic ultrasound (EUS) elastography is a recent ultrasound method used for the real-time visualization and evaluation of tissue elasticity. Qualitative and quantitative methods have been used, in particular in evaluation of pancreatic diseases and malignant lymph nodes, with interesting results regarding the accuracy and the differential diagnosis between malignant and benign masses. No consensus has been reached with regard to the superiority of different quantitative methods, but strain ratio and strain histogram (SH) remain the most used. SH corresponds to a graphical representation of the color distribution in a region of interest (ROI), and mean SH (mSH) value is a SH-derived quantitative measure of the global hardness in the evaluated ROI.
Aims & Methods: The aim of the present study was to describe the different elastographic patterns of solid pancreatic masses and malignant lymph nodes using the mSH value. This is a prospective, observational, monocentric study. One experienced EUS examiner performed the endoscopic procedure and elastographic measures. SH was calculated automatically by machine integrated software in a ROI manually selected by the operator. Four parameters were calculated using the histogram to quantify the elasticity of the pancreas: the mSH, the standard deviation of the histogram, the kurtosis and the skewness. Three different measures were performed by the same operator and the mean value of the previous described values was evaluated. After the elastographic measure a FNA was performed when a lesion was observed. We used the histology obtained by FNA or surgical specimens or the global assessment of cytology and imaging as reference standard for the diagnosis, except in case of normal examinations.
Results: A total of 42 patients were included (23 F/19M): 8 normals, 22 pancreatic adenocarcinoma, 4 neuroendocrine tumors (NET), 6 malignant lymph nodes and 2 benign lymph nodes. Compared with normal patients, we found a statistically significant difference in mSH value in both patients with pancreatic adenocarcinoma (111.13 vs. 29.9, $p < 0.05$) and malignant lymph nodes (111.13 vs. 63.52, $p < 0.05$), but not in NET lesions (111.3 vs 72.9, $p = 0.07$). A statistically significant difference was found in mSH between pancreatic adenocarcinoma and NET (29.9 vs. 72.9, $p < 0.05$), suggesting that mSH value could help in differential diagnosis between malignant pancreatic masses. Similarly, malignant and benign lymph nodes presented a statistically significant difference in mSH (63.52 vs 4.9, $p < 0.05$).
Conclusion: Mean strain histogram value seems an interesting quantitative tool to differentiate between different malignant pancreatic masses and between benign and malignant lymph nodes. A larger number of patients is needed to confirm our data.
Disclosure of Interest: None declared

P0220 DIFFERENTIAL DIAGNOSTIC EFFICACY OF ENDOSCOPIC ULTRASOUND ELASTOGRAPHY FOR CHRONIC PANCREATITIS AND PANCREATIC CANCER

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Introduction: Endoscopic ultrasound (EUS) elastography represents a new imaging procedure that allows quantification of tissue stiffness, with a high degree of accuracy for the differential diagnosis of pancreatic disease.
Aims & Methods: The aim of this study was to evaluate the efficiency of quantitative EUS elastography for the differentiation of chronic pancreatitis (CP) and pancreatic cancer (PC). Between August 2014 and April 2015, 54 patients with PC, 39 patients with CP who underwent EUS were prospectively enrolled. EUS elastography was performed using linear Pentax EUS and Hitachi HI VISION Preirus. The quotient B/A (strain ratio; SR) is considered as the measure of the elastographic evaluation. Area A is representative of the pancreatic lesion strain. Area B refers to a soft peripancreatic tissue strain. The SR results were measured at the head and body, respectively.
Results: A total of 93 patients (mean age 60.2 years, 58 male) were included. The mean SR was 8.96 ± 6.05 for CP, 22.04 ± 13.57 for PC. The SR was different significantly in two groups respectively (CP vs. PC; $p < 0.001$). The area under the curve (AUC) of EUS elastography for diagnosing CP was 0.811 (95% confidence interval (CI) 0.746-0.858), the sensitivity and specificity was 71.8% and 80.2% (cut off SR of 5.81). The AUC of EUS elastography for PC was 0.983 (95% CI 0.971-0.995), the sensitivity and specificity was 94.4% and 97.4% (cut off SR of 9.15).
Conclusion: In our study, we provided the reference range of SR value of normal pancreas, CP, and PC respectively as well as good parameters of the AUC analysis. Also, EUS elastography is a promising useful method for differentiating CP and PC. Further prospective and multicenter research in this method is needed.
Disclosure of Interest: None declared

P0221 A DOUBLE APPROACH FOR ULTRASOUND-GUIDED TISSUE ACQUISITION OF PANCREATIC SOLID TUMORS IN THE ERA OF TARGET THERAPY: IS CYTOLOGY SUITABLE FOR MOLECULAR PROFILING ?

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Introduction: Endoscopic Ultrasound-Guided Fine Needle Aspiration (EUS-FNA) is the procedure of choice to differentiate pancreatic tumors. EUS-FNA has a good diagnostic yield particularly when procedure is performed with on-site pathologist. However, cytology alone may be not sufficient to perform immunohistochemical studies and therefore to individualized the therapy.
Aims & Methods: We evaluated the diagnostic yield of EUS-FNA on pancreatic masses using both cytological and histological approach. To do that, we retrospectively identified 122 consecutive patients (67 males, mean age 64 ± 13.7 years) who underwent EUS-FNA for solid pancreatic masses from August 2012 to January 2015. In forty-five subjects synchronous or metachronous malignancies other than pancreatic cancer were present at the time of endoscopic procedure. In most cases (115/129, 89.1%) a 22 G standard needle was used with a mean number of passes of 2.1. Obtained material was recovered in cytolit by flushing the needle with saline. There was no pathologist present in the endoscopy room. Fragments of tissue, when present, were embedded in paraffin and processed for mini-histology, whereas residual material was cytospinned and processed for cytology. Whenever collected material was adequate for that, molecular profiling was studied mainly using immunohistochemical staining.
Results: A total of 129 procedures were performed and the material collected was judged adequate for diagnosis in 112 cases. In 5 subjects with no evidence

of cancer on FNA, diagnosis was supported by negative follow-up in 4 cases and by definitive histology in 1 resected lesion. A metastatic pancreatic lesion was detected in 10 out of 107 patients. Resective surgery was performed in 32 patients and initial diagnosis was confirmed in all of them but one in whom an acinar cell carcinoma resulted a mixed type tumor (endocrine and acinar). In 7 cases the procedure was repeated two times and in all of them definitive diagnosis was obtained at the second exam (overall diagnostic accuracy: 112/122, 91.8%). Cytology was judged adequate for diagnosis in 74 out of 112 cases, whereas mini-histology in 102 out of 112 cases. Adequate material for immunostaining was obtained in 84 (9 cytological and 75 mini-histological, $p < 0.001$) samples. In 49 patients molecular profiling was considered to be essential for a definitive diagnosis: 32 patients with other malignancies, 11 primary neuroendocrine tumors, 2 pseudopapillary solid tumors, 1 adenosquamous carcinoma, 2 acinar cell carcinoma and in one case of mixed-type carcinoma.
Conclusion: Trying to collect material for both cytology and mini-histology helps to increase the diagnostic yield of EUS-FNA, especially when on-site pathologist is not available. In our experience immunostaining is feasible in a consistent number of FNA specimens. Mini-histology is more suitable than cytology for tissue profiling and the former should be preferred when a firm diagnosis is required to target the therapy.
Disclosure of Interest: None declared

P0222 A NOVEL PIG MODEL OF BILE AND PANCREATIC DUCT DILATATION FOR EUS TRAINING

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Introduction: It is known that obtaining skills of endoscopic ultrasonography is difficult, especially in the field of pancreatic and biliary disease. However, there are few animal models suitable for training in diagnostic and interventional EUS of the pancreaticobiliary field. It is not ethically acceptable that endoscopists perform practical training in patients in order to learn EUS procedure. EUS training model could help alleviate these problems.
Aims & Methods: The purpose is to develop the pig model for the training of diagnostic and interventional EUS. Abdominal operation was performed on a pig (n = 8) under endotracheal general anesthesia. The external catheters were introduced into orifice of bile and pancreatic duct. The EUS model of both biliary dilatation and pancreatic duct dilatation was established. We evaluated feasibility of the model of the pancreaticobiliary disease for EUS imaging and intervention.
Results: In all pig models, EUS image showed the dilation of bile duct and pancreatic duct at 3 days after surgical procedure. Moreover, using this model, the puncture for the biliary duct and the pancreatic duct were performed under EUS and fluoroscopic guidance (n = 8 success rate 100%). After puncture, a displacement of the duct diameter could be adjusted by control amount of injecting water to external catheters. Ducts were able to be dilated, and diameter of CBD and MPD were able to be controlled 10mm and 6mm respectively. In this way, our pig model was available more than ten times for puncture of these ducts. It is possible for 10 beginner endoscopists to confirm the bile and pancreatic duct, and then to perform the puncture for the bile and pancreatic duct.
Conclusion: We developed successfully the innovative model which has variable-sized ducts and repeatability of interventional EUS procedure in pancreaticobiliary field. The unconventional novel model will be very valuable for EUS training, and will surely contribute to development of interventional EUS-guided technology.

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Disclosure of Interest: None declared

P0223 DIAGNOSTIC ACCURACY OF 22/25-GAUZE CORE NEEDLE IN ENDOSCOPIC ULTRASOUND-GUIDED SAMPLING OF SOLID PANCREATIC LESIONS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: It is uncertain if novel core needle increases the diagnostic accuracy by obtaining sufficient amount of tissue. The aim of this study was to use systematic review and meta-analysis to define the diagnostic accuracy of EUS-guided core needle aspiration.
Aims & Methods: Studies were identified by searching medical databases for reports published between 1994 and 2015, using a reproducible search strategy comprised of relevant terms. Studies using 22/25G core needles, irrespective of comparison with standard fine needles, that used surgical histology or at least 6 months clinical follow-up. Pooled sensitivity, specificity, diagnostic odds ratio (DOR) and summary receiver operating characteristic (SROC) curves for the diagnosis of pancreatic malignancy were used to estimate the overall diagnostic efficiency.
Results: Eleven studies involving 929 subjects met the defined inclusion criteria. Of the 929 patients, 583 were in the core group and 346 were in the standard needle (both needles were used in 242 patients). The pooled sensitivity, specificity and diagnostic odds ratio (DOR) of the core needle were 0.88 (95%CI 0.85–0.91), 0.99 (95%CI 0.96–1) and 167.68 (64.53-435.77) respectively. The pooled sensitivity, specificity and diagnostic odds ratio (DOR) of the standard needle were 0.84 (95%CI 0.78–0.88), 1 (95%CI 0.97–1) and 129.77 (34.00-495.35) respectively. The core and standard needles were comparable in the sensitivity and specificity. In addition, the area under the curve (AUC) of core needle and standard needle in the diagnosis of pancreatic malignancy were 0.9748 and 0.9555, respectively. There were no significant differences in accuracy (RR 0.98, 95% CI 0.92, 1.04) and technical failure (RR 5.07, 95%CI 0.68-37.64). There was lower procurement of histologic core in core needle (RR 0.81, 95% CI 0.72-0.92).
Conclusion: The core and standard needles were comparable in terms of diagnostic accuracy, technical performance and safety profile. However, there was lower procurement of histologic core in the core needle group.
Disclosure of Interest: None declared

P0224 ENDOSCOPIC ULTRASOUND-GUIDED CUTTING BIOPSY FROM UPPER GASTROINTESTINAL SUBEPITHELIAL LESION USING FORWARD-VIEWING ECHOENDOSCOPE

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Introduction: Endoscopic ultrasound (EUS)-guided fine needle aspiration has become an accurate technique for obtaining tissue acquisition from upper gastrointestinal (GI) subepithelial lesions. However, the diagnostic yields for small lesions were relatively low. To increase the diagnostic yield, we developed EUS-guided cutting biopsy (EUS-CB) using a forward-viewing echoendoscope.
Aims & Methods: We evaluated the feasibility of EUS-CB for tissue acquisition from upper GI subepithelial lesions. This study was a prospective case series and approved by the institutional review board of the Nagoya University. Between January 2015 and April 2015, ten patients with upper gastrointestinal subepithelial lesions underwent EUS-CB by using a hot biopsy forceps. After mucosal cuts, several specimens were taken within the lesion using this forceps under real-time EUS visualization. Finally, the incision site was closed using hemoclips. The following points were assessed; (1) diagnostic yield, (2) number of samples, (3) procedure time, and (4) adverse events.
Results: Ten patients (median lesion size 16mm, range 15-44 mm) were enrolled. The overall rate of histological diagnosis of EUS-CB was 100% (10/10). The median number of samples within tumor was 4.5. The procedure times for EUS-CB and complete closure were 28.5 and 4.5 minutes. Adverse events did not occur.
Conclusion: This newly developed EUS-CB is feasible and allowed forceps biopsy from upper GI subepithelial lesions under EUS visualization.

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Disclosure of Interest: None declared

P0225 EUS-GUIDED BILIARY DRAINAGE VERSUS PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE AFTER FAILED ERCP IN MALIGNANT BILIARY OBSTRUCTION

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Introduction: Percutaneous transhepatic biliary drainage (PTBD) is the method of choice for the palliative relief of malignant biliary obstruction in cases where ERCP is not feasible. EUS-guided biliary drainage (EUSBD) is purported to be an alternative to PTBD in this setting. However, evidence to back this claim is still limited.
Aims & Methods
Aim: To compare safety and efficacy of EUSBD and PTBD.
Methods: Records from 40 consecutive patients with unresectable malignant biliary obstruction undergoing PTBD after failed ERCP over a 5-year period at one tertiary hospital and from 40 age and sex matched controls undergoing EUSBD for the same indication at another tertiary center in the same city were reviewed. Baseline bilirubin values, days from admission until drainage, number of sessions required, technical success rate (drain/stent placement), internal biliary drainage rate, type of stent, clinical success (80% decrease in serum bilirubin values from baseline), adverse events, procedure-related deaths, stent dysfunction, need for reinterventions, hospital stay, stent patency and overall survival were compared between the two groups. Chi-squared and Fisher's test were used where appropriate.

Results: EUSBD: age, mean (range)= 68.12 (40-92) years; 60% male. Pancreatic cancer, 40%; Metastasis, 22.5%; Cholangiocarcinoma, 22.5%; Other, 15%. Hilar biliary obstruction in 37.5%. PTBD: age, mean (range)=72.6 (50-93); 55% male. Pancreatic cancer, 30%; Cholangiocarcinoma, 32.5%; Metastasis, 15%. Hilar biliary obstruction in 32.5%. No statistically significant differences in baseline features, including serum bilirubin, days from admission to drainage were noted between the two groups. Regarding treatment outcomes, rates of technical success, type of stent, clinical success, adverse events, stent dysfunction, stent patency, reinterventions, hospital stay, overall survival and procedure-related deaths were no different between the two groups (Table). The rate of internal biliary drainage was significantly higher in EUSBD (39 versus 32, p=0.029) and the number of sessions to obtain it was significantly lower (1.32 in EUSBD versus 2.2 in PTBD; $p < 0.001$).

	DBUSE	CTPH	p
Baseline Bilirubin (mg/dL)	10.65	13.64	0.077
Time from Admission to Drainage (days)	8.95	9.28	0.816
Treatment sessions (n)	**1.35**	**2.2**	**0.000**
Technical Success (n)	39	40	1.000
Internal biliary drainage (n)	**39**	**32**	**0.029**
Metal Stent (n)	32	32	0.610
Clinical Success (n)	27	25	0.750
Adverse Events (n)	6	10	0.586
Procedure-realted deaths (n)	1	2	0.215
Stent dysfunction (n)	10	7	0.586
Reinterventions (n)	22	11	0.738
Hospital Stay (days)	11.63	9.53	0.397
Stent patency (days)	89.45	111.83	0.477
Survival (days)	212	149	0.265

Conclusion: The safety and efficacy of EUSBD is comparable to that of PTBD in patients with unresectable malignant biliary obstruction and failed ERCP. The number of treatment sessions is lower with EUSBD, and the rate of internal biliary drainage higher than that of PTBD.
Disclosure of Interest: None declared

P0226 FACTORS PREDICTIVE OF CLINICAL OUTCOME FOLLOWING BILIARY DRAINAGE IN PATIENTS WITH UNRESECTABLE MALIGNANT BILIARY OBSTRUCTION AND FAILED ERCP

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Introduction: Unresectable malignant biliary obstruction (MBO) carries a poor prognosis. Biliary stent insertion achieves adequate palliation. Predictive factors of clinical success, procedural complications and long-term survival require further elucidation, specifically in the setting of novel procedural approaches to drainage.
Aims & Methods
Aims: To identify predictive factors of clinical outcome after technically successful biliary drainage following either percutaneous transhepatic (PTBD) or endoscopic ultrasound-guided (EUSBD) access in patients with unresectable MBO and failed ERCP.
Methods: Baseline features and clinical course of 80 patients with unresectable MBO drained by PTBD or EUSBD at two tertiary centers were retrospectively analyzed. Binary uni- and multivariate logistic regression analysis was carried out for the following dependent variables: technical success, clinical success, complications, in-hospital death, stent dysfunction, 3 and 6-month survival. Uni- and multivariate Cox proportional hazard model was performed. Independent variables analyzed were: age, sex, tumor etiology, level of obstruction, baseline bilirubin, reason for failed ERCP, days from onset of jaundice to drainage, days from failed ERCP to drainage, number of attempts, stent type, rate of internal biliary drainage, postprocedure chemotherapy. $P < 0.05$ was considered significant.
Results: Demographics: 57.5% male; mean (SD) age, 72.8 (13.9) years; 76.2% primary MBO vs 23.8% metastatic; 35% hilar vs 65% distal MBO. Mean survival was 161 days. Failed access to the papilla as a reason for failed ERCP was an independent predictive factor of decreased postprocedure complication risk (OR 0.178, IC 95% 0.045-0.700, p=0.014). Time from failed ERCP to final drainage procedure was an independente predictive factor of increased in-hospital death risk (OR 1.121, IC 95% 1.005-1.250, p=0.040). Hilar location was an independent predictive factor of decreased 3 and 6-month survival (OR 0.155, IC 95% 0.029-0.819, p=0.028, and OR 0.155, IC95% 0.029-0.821, p=0.028). Reintervention because of sent dysfunction was a predictor for increased 6-month survival (OR 5.839, IC 95% 1.296-26.312, p=0.022). Hilar location and reintervention for stent dysfunction were independent predictors of mortality over time (HR 1.969, IC 95% 1.037-3.737, p=0.038 y HR 0.476, IC 95% 0.254-0.890, p=0.020). PTBD versus EUSBD were not predictors for any of the dependent variables at uni- or multivariate analysis.
Conclusion: Hilar location, reason for failed ERCP, days between failed ERCP and final drainage procedure, and reintervention caused by stent dysfuncion are predictors of clinical outcome in the subset of patients with MBO and failed ERCP. These data warrant confirmation, as they are potentially relevant to improve current practice patterns.
Disclosure of Interest: None declared

P0227 THE DIAGNOSTIC YIELD OF ENDOSCOPIC ULTRASONOGRAPHY IN PATIENTS WITH SUSPECTED CHOLEDOCHOLITHIASIS

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Introduction: Choledocholithiasis is the most common cause of biliary obstruction, which occurs in 10-20% of patients with cholelithiasis. Management of suspected choledocholithiasis requires confirmation of stones in the common bile duct (CBD). The diagnosis is based on clinical signs and symptoms, laboratory- and imaging examination findings. Likelihood of CBD stones can be prognosticated by the presence of various clinical predictors, however the sensitivity and specificity of these factors is moderate. Endoscopic ultrasonography (EUS) has been shown to be a non-invasive precise test for the detection of CBD stones.
Aims & Methods: Our aim was to assess the diagnostic yield of EUS in patients with suspected choledocholithiasis in a high-volume center during the period of one-month. Prospective study of patients with cholelithiasis and clinical symptoms or abnormal liver function tests who underwent transabdominal ultrasonography (USG) that could not detect CBD stones (except in one case) were categorized and divided into an intermediate- and high likelihood groups according to the clinical predictors (i.e. serum bilirubin, age, CBD diameter) defined by the American Society of Gastrointestinal Endoscopy (ASGE) guidelines and referred for radial EUS.
Results: Total of 26 patients, 14 females and 12 males (average age of 40.8 ± 17.3 and 51.1 ± 14.9, respectively) were assessed. CBD stones were detected by EUS overall in 17 (65.4%) patients: 61.5% of patients (8/13) in the intermediate likelihood- and 69.2% of patients (9/13) in the high likelihood group. The size and the number of detected CBD stones in all patients were confirmed by the followed therapeutic endoscopic retrograde cholangio-pancreatography (ERCP) except in one case where a preampullary calcific stenosis was described as a calculus during the EUS. Two-month follow up of those patients with no CBD stones detected on EUS revealed no clinical findings suspicious for biliary obstruction.
Conclusion: EUS is a highly sensitive and accurate diagnostic tool for the detection and evaluation of CBD stones also in patients with previous normal USG findings. Further study is needed to assess the potential correlation of clinical data with EUS findings in the detection of suspected choledocholithiasis.
Disclosure of Interest: None declared

P0228 MULTICENTRE RANDOMIZED TRIAL COMPARING EUS GUIDED FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) WITH FINE NEEDLE ASPIRATION BIOPSY (FNAB) IN SAMPLING SOLID PANCREATIC MASS LESIONS: PRELIMINARY RESULTS FROM THE PROCORE TRIAL

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Introduction: EUS-guided FNA is the standard of care for tissue sampling of pancreatic lesions. It has some limitations such as lack of proper histology sample, low sensitivity for malignancy in the presence of chronic pancreatitis, low diagnostic accuracy in the absence of on-site cytopathologist and false-positive rates up to 5-7%. The new Echo Tip ProCore biopsy needle (Cook Medical) was developed to obtain core tissue specimens improving the diagnostic yield and potentially obviating the need for onsite cytopathologist.
Aims & Methods: To compare the standard Echo tip ultra FNAC needle with the new Echo Tip Ultra ProCore FNAB needle in the sampling of solid pancreatic lesions. Sampling time, number of passes and sample adequacy were compared. Randomized multicenter trial in a tertiary university hospitals setting approved by the National Research Ethics Service (NRES). All patients referred for EUS guided tissue sampling of a solid pancreatic mass were invited to participate. Informed consent form was obtained from every participant. Linear EUS (Aloka-Olympus, Hitachi-Pentax) was performed and patients were randomised to either FNAC or FNAB. Due to the nature of the study the endoscopist could not be blinded. A 22G needle was used when sampling from the stomach and a 25G from the duodenum. A maximum of 5 passes[o] were allowed. Sampling time from first insertion of the needle into the lesion to the time the last sample is transferred into the histology pot, number of passes and adequacy for diagnosis reported by the pathologist were recorded and

included for analysis. Immediate and delayed complications between days 8-30 post procedure were also recorded.
Results: 266 patients were recruited (median age 67 years, 52% men); 142 were randomized to FNAC and 124 to FNAB. Two were excluded after randomization; no mass lesion was seen in 1 patient randomized to FNAC and the needle failed in 1 patient in the FNAB group and FNAC was performed. A total of 264 patients were analyzed, FNAC = 141 (22G = 83 and 25G = 58. Median lesion size 34 mm, range 10-87 mm) and FNAB = 123 (22G = 53 and 25G = 71. Median lesion size 33 mm, range 8-85 mm). There was no statistical significant difference in number of passes (median 4, range 1-5 in the FNAC group vs. median 3, range 1-5 in the FNAB group, p = 0.126), required time to obtain adequate samples (median 13 min, range 1-32 min vs. median 13 min, range 2-42 min, p = 0.636) and adequacy of the specimen for diagnosis (90.8% vs. 87%, p = 0.33). Three technical failures were observed in the FNAB cohort, 2 different needles had to be used in two patients as first was faulty and in 1 patient the needle did not come out from the scope (excluded for analysis). No technical failures noted in the FNAC cohort (1.6% vs. 0%, p = 0.998). No immediate or delay complications reported in either group.
Conclusion: FNAC and FNAB needles were comparable in terms of sampling time, number of passes, sample adequacy for diagnosis and safety. Technical failure was higher in the FNAB arm but not statistically significant.
Disclosure of Interest: J. Ortiz: None declared, M. Wireko: None declared, K. Ragunath Financial support for research: Olympus-Keymed, Cook Medical and Covidien, Lecture fee(s): Olympus-Keymed, Cook Medical and Covidien, Consultancy: Olympus-Keymed, Cook Medical and Covidien, M. James: None declared, P. Kaye: None declared, K. Oppong: None declared, M. Nayar: None declared, A. Darne: None declared, B. Mahon: None declared, C. Forde: None declared, P. Taniere: None declared, G. Aithal: None declared

P0229 DIAGNOSTIC YIELD AND THERAPEUTIC IMPACT OF EMERGENCY CAPSULE ENTEROSCOPY IN ACTIVE-OVERT OBSCURE GASTROINTESTINAL BLEEDING

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Introduction: Capsule enteroscopy (CE) allows the evaluation of the entire small bowel, representing an important tool in the management of obscure gastrointestinal bleeding (OGIB).[1,2,3] Nevertheless, the real impact of CE in the management of active overt OGIB (OOGIB) lacks evidence.[1] The aim of this study was to evaluate the diagnostic yield of CE and its therapeutic impact in patients with active OOGIB.
Aims & Methods: Between April 2005 and January 2015, all patients with active OOGIB who underwent emergency CE in the first 48 hours after a negative esophagogastroduodenoscopy and ileocolonoscopy were included. Severe active OOGIB was classified as persistency of melena or hematochezia despite an initial negative endoscopic assessment, resulting in hemodynamic instability (systemic arterial pressure < 100 mmHg and pulse > 100 beats/min) and/or the need for ≥2 units of packed red blood cells (PRBC). Patients with active OOGIB not fulfilling the preceding criteria were classified as mild-to-moderate. Descriptive analysis was performed.
Results: 42 patients underwent emergency CE, 50% were men with a mean age of 61.7 years. The mean hemoglobin at admission was 9.0+/-2.9 g/dL and 59.5% (n = 25) required PRBC transfusion, with a mean number of 1.4 units. OOGIB manifested with melena in 59.5% (n = 25) of patients and with hematochezia in 40.5% (n = 17) and was classified as severe in 59.5% (n = 25) and as mild-to-moderate in 40.5% (n = 17). CE identified a lesion in 52.4% (n = 22) patients with active OOGIB (n = 14 severe; n = 8 mild-to-moderate) and identified the location of bleeding in 38.1% (n = 16) of active OOGIB (n = 9 severe; n = 7 mild-to-moderate), totaling a diagnostic yield of 90.5% in active OOGIB (92% in severe; 88.3% in mild-to-moderate). Findings included active bleeding (n = 15); ulcers/erosions (n = 7); angiodysplasias (n = 6); tumors (n = 4); Meckel's diverticulum (n = 2); polyps (n = 2); signs of recent bleeding (n = 1); varices (n = 1). Further diagnostic and therapeutic procedures were performed in 73.8% patients, including endoscopy in 38.1%, surgery in 19%, endoscopy/surgery in 7.1%, endoscopy/radiology in 4.8%; radiology/surgery in 2.4% and radiology in 2.4%.
Conclusion: The diagnostic yield of emergency CE was 90.5%, establishing the diagnosis in 52.4% of the patients and identifying the location of bleeding in more 38.1%, resulting in a specific management in 73.8% of cases. This study highlights the importance of emergency CE in the diagnostic approach and subsequent therapeutic management in active OOGIB.

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Disclosure of Interest: None declared

P0230 ROLE OF ENDOSCOPIC CAPSULE IN PATIENTS WITH CHRONIC DIARRHEA AND ABDOMINAL PAIN OF UNKNOWN ORIGIN

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Introduction: Capsule endoscopy (CE) is a diagnostic method that enables visualization of intraluminal bowel, diagnosing disorders not diagnosed effectively.
Aims & Methods
Aim: To demonstrate the utility and diagnostic effectiveness of CE in patients with diarrhea and initially diagnosed and treated as irritable bowel syndrome and abdominal pain.
Methods: Retrospective study (03-2012 / 03-2014) in patients who underwent CE for abdominal pain and / or diarrhea, normal studies: gastroscopy, colonoscopy and laboratory; patients without improvement, previously treated as IBS according to Rome III criteria. We used 2 type of capsules: Mirocam (Intromedic) and SB2 (Given-Imaging).Readings were performed by a single physician who is blinded for the study.
Results: 216 CE were reveiwed. 65 (30%) subjects met the criteria. (35/65) or 53.8% were women. Median age was 50 years. Diarrhea was present in 33.8% (22/65) and abdominal pain in 66.1% (43/65). CE with diarrhea subjects showed: atrophy of the villi in 18.1% (4/22), and ulcers compatible with inflammatory bowel disease (IBD) 36.3% (n = 8/22), normal study in 45.4% (n = 10/22). CE in -abdominal pain subjects detected: ascaridiasis 2.3% (n = 1/43), atrophy of villi in 23.2% (n = 10/43), IBD in 25.5% (n = 11/43), gastroparesis in 6.9% (n = 3/43), submucosal tumor 2.3% (n = 1/43), nonspecific erythema 4.65% (n = 2). In total, the CE detected 48% more lesions that had a clinical impact of 100%.
Conclusion: The CE showed an important role in managing IBS patients with no response to treatment.
Disclosure of Interest: None declared

P0231 PREDICTING INFLAMMATORY PATHOLOGY AT CAPSULE ENTEROSCOPY: WHAT IS THE UTILITY OF A RAISED FAECAL CALPROTECTIN?

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Introduction: Faecal Calprotectin (FCP) is a widely used biomarker of gastrointestinal (GI) mucosal inflammation. Many capsule enteroscopy (CE) services are receiving increased referrals of patients with abdominal symptoms combined with an elevated FCP (> 50μg/g) but normal gastroscopy, colonoscopy or radiology. There is little data on using FCP levels as a screening tool for selecting patients in whom CE will lead to a definitive diagnosis. Elevated FCP levels may indiscriminately drive investigations in endoscopy and imaging-negative patients who subsequently have normal findings at CE. We aimed to determine the incidence of inflammatory pathology on CE in patients with a raised FCP, and if a suitable concentration of the biomarker could be identified as a screening tool to avoid unnecessary CE.
Aims & Methods: A single centre retrospective review of The Newcastle upon Tyne Hospitals CE database was conducted (Feb 2012-Feb 2015). Patients with GI symptoms (abdominal pain, diarrhoea, bloating, vomiting, weight loss) and a raised FCP (> 50μg/g) were identified. Findings at CE considered to be inflammatory were: erythema, ulceration, erosions and fissuring.
Results: 35 patients were identified with elevated FCP and GI symptoms. 45.7% (n = 16) had inflammation identified by CE and in 54.3% (n = 19) no inflammatory pathology was identified. The mean (+/-SE) FCP was higher in patients with evidence of inflammation at CE in comparison to those with no inflammation: 452.1(95.8)μg/g vs. 206(20.8)μg/g; p = 0.01. Stratifying patients according to FCP revealed that only 8.3% of patients (n = 1/12) with a FCP of 50-200μg/g had inflammatory findings at CE. This rose to 58.3% of patients (n = 7/12) with a FCP of 201-300μg/g, and 72.7% of patients (n = 8/11) with a FCP > 300μg/g. A threshold of 200μg/g FCP revealed a sensitivity of 94.1% to predict inflammation at CE, with a specificity of 55.6%. This FCP threshold had a negative predictive value of 90.9%, and positive predictive value of 66.7% for CE inflammation.
Conclusion: In this small retrospective analysis of a sub-group of patients referred for CE with a FCP of > 50μg/g the likelihood of identifying inflammatory pathology at CE increased with rising FCP concentrations above 200μg/g. A threshold of 200μg/g provided a high negative predictive value for CE inflammation and may be a useful screening tool to reduce the requirement for CE in select patient groups. This retrospective analysis should be confirmed in a larger prospective cohort.
Disclosure of Interest: None declared

P0232 ROLE OF SECOND-GENERATION COLON CAPSULE ENDOSCOPY FOR WHOLE GUT EVALUATION

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Introduction: Although colon capsule endoscopy (CCE) was developed for evaluation of the colon, it can be used to assess the entire GI tract since it offers excellent images also of the esophagus and the small bowel (SB), with the exception of the stomach that remains poorly evaluated. Usually, after the firsts 3 min of running, CCE slows down the frame rate to 14 images/min. When SB is detected CCE automatically restarts using the Adaptive Frame Rate (AFR) technology. Nevertheless, CCE can be also "activated" to the AFR mode prior to the ingestion allowing the whole gut evaluation at a high frame rate acquisition.

Aims & Methods: Aim of this preliminary, feasibility study was to evaluate the ability of CCE to evaluate esophagus, small bowel and colon if patients take CCE after early, manual activation. Methods: 19 pts (8F, mean age 58 yrs, R 31-78 yrs) were enrolled. All pts underwent second-generation CCE. Pts were invited to follow the standard regimen of preparation for CCE. It consists of the regimen recommended by the ESGE guidelines with the inclusion of Gastrografin in adjunct to sodium phosphate booster. The day of the procedure all CCE were manually activated to AFR before the ingestion. Pts were asked to swallow CCE following the recommended procedure for ESO capsule. They remained in hospital until CCE transit into the SB was confirmed. They were, then, invited to drink the first booster and leave the hospital. Esophageal, SB and colonic transit times (TT) were evaluated. Esophagoscopy was defined complete when Z line was visualized. Completeness and cleansing level of SB and colon were evaluated. Significant findings were defined as findings that could explain the reason for referral and/or that had any effect on the medical decision making.

Results: Indication for CE was: incomplete colonoscopy (n = 7), OGIB (6), colonoscopy refusal (4), iron deficiency anemia (2). A total evaluation of the entire GI tract was possible in 14 out of 19 pts (74%): Z line was not visualized in 4 pts and colonoscopy was incomplete in 1. Overall the Z line was visualized in 15/19 (79%) pts. Mean esophageal capsule TT was 69 sec (R 5-497). 1 (5%) pt had esophagitis. Complete capsule enteroscopy and SB adequate cleansing level was achieved in all pts. Mean SBTT was 106 min (R38-231). Significant SB findings were diagnosed in 3 (16%) pts and included diverticula (1), ulcerations (1) and large bleeding polyp (1). Colon TT was 104 min (R 10 734). CCE was complete and cleansing level was adequate in 18/19 (95%) pts. Significant findings were diagnosed in 6 (31%) pts: ≥6mm/≥3 polyps (5) and caecal angiodysplasia (1).

Conclusion: Second-generation CCE is feasible for whole GI evaluation and it has a relevant impact on medical decision making. The indications for a pan-endoscopy, however, need to be clarified and the procedure should be validated.

Disclosure of Interest: None declared

P0233 UPPER AND LOWER GASTROINTESTINAL LESIONS OVERLOOKED AT CONVENTIONAL ENDOSCOPY AND FURTHER DIAGNOSED WITH SMALL BOWEL CAPSULE ENDOSCOPY: THE CRUCIAL ROLE OF ENDOSCOPIC EXPERIENCE IN PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING

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Introduction: The role of small bowel capsule endoscopy (CE) in the investigation of obscure gastrointestinal bleeding (OGIB) is well established, with a mean diagnostic yield of 60%. However, in up to 20% of patients the cause of OGIB is located within the reach of upper and lower endoscopy. No data are available regarding the impact of endoscopic experience on the rate of lesions missed by previous esophagogastroduodenoscopy (EGDS) or ileocolonoscopy (ICS) and further found with CE. The aim of this series is to clarify if the experience of the endoscopy units could influence the rate of overlooked lesions.

Aims & Methods: We retrospectively reviewed the charts of 584 patients who underwent CE at Endoscopy Unit between October 2008 and March 2015 for OGIB. The CE-derived data are recorded and analyzed in terms of non-small-bowel CE findings (gastric, duodenal and colonic lesions) overlooked at previous upper and lower endoscopy. The type of endoscopic units who performed the conventional endoscopy (tertiary referral centres or primary level centres) and the respective lesions miss rate was recorded. The Given M2A video capsule system (Pillcam; Given Imaging Ltd, Yoqneam, Israel) was used. The day before the exam bowel preparation with 2L of polyethylene glycol solution was administered. Capsule ingestion was performed in the morning after a overnight fast. All the patients gave their written informed consent.

Results: 547 patients were enrolled for the final investigation (41 cases were excluded from further analysis because of the capsule did not reach the colon). In 35 patients (6.4%) one or more lesions previously missed by conventional endoscopy were diagnosed at CE. 20 of these 35 cases were males. The mean age was 72.8 years (range 51-89). 77.1% of lesions were overlooked at primary level endoscopy units; 22.9% at tertiary level units ($p < 0.01$). The overlooked lesions are reported in the table according to the type of endoscopic centre. The most frequently missed lesions were located in stomach and duodenum (66.6%); primary centres missed lesions mostly during EGDS (71.4%); tertiary centres miss lesions during EGDS and ICS equally. Both types of centres can miss neoplasias (66.6% at primary centres): tertiary centre overlooked a gastric GIST (gastrointestinal stromal tumor); primary centres overlooked a non invasive intraepithelial gastric haemorrhagic neoplasia and an ascending colon adenocarcinoma.

Conclusion: Our results suggest that endoscopic experience, in terms of number of referral patients, can significantly reduce the miss rate of lesions located in upper or lower gastrointestinal tract, avoiding unhelpful CE.

Disclosure of Interest: None declared

P0234 COLON CAPSULE TRANSIT TIMES AND IMAGE QUALITY IN PATIENTS PREPARED WITH POLYETHYLENE GLYCOL + ASCORBATE (PEG + A) AND BOOSTER OF EITHER PEG + A OR GASTROGRAFIN AND LOW DOSE SODIUM PHOSPHATE (NAP)

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Introduction: Successful colon capsule endoscopy (CCE) requires high capsule excretion rates and high-quality bowel cleansing. Most cleansing regimens are based on polyethylene glycol (PEG) supplemented with a booster of NaP to accelerate transit time. Because of potential renal toxicity associated with NaP, we have piloted two novel CCE cleansing regimens.

Aims & Methods: *Prep1* was designed as a NaP free regimen comprising 2L PEG + Ascorbate (PEG + A) administered as a split dose, with an additional 1L booster after capsule ingestion. *Prep2* comprised identical split dose 2L PEG + A, but the post capsule ingestion booster was low dose NaP (30-45ml) and gastrografin (50-100ml), a contrast medium known to accelerate bowel transit. 34 CCEs were reviewed, 17 from each group. Oro-caecal, caeco-rectal transit times and capsule excretion rates were measured. Quality of bowel cleansing was assessed by two independent observers, using a modified small bowel cleansing scale grading from the first caecal image and every 15 minutes until the end of the study. At each time point the assessors graded each of the two static images recorded by the CCE cameras. The proportion of visualised mucosa was graded as M3 (>75% of mucosal surface visualised), M2 (50-75%), M1 (25-49%) and M0 (<25%). Obscuration was graded as O3 (<5% of the image obscured by bubbles, debris or unclear fluids), O2 (5-24%), O1 (25-50%) and O0 (>50%). If capsule remained stationary more than 15 minutes, the time was extended to the frame 15 minutes following onward movement of capsule.

Results: In 6 of the 17 CCEs (35.29%) assessed in *prep1* group, the capsule camera was excreted, providing a complete assessment of the colonic mucosa. The excreted capsule cameras for the *prep2* group were 15 of 17 (88.23%) ($p = 0.001$).

Three hundred seventy five frames were assessed and graded from the group that received *prep 1*. Three hundred sixty six frames were assessed and graded from the group that received *prep 2*.

In total 55.4% of frames in *prep1* group scored M2/M3 for mucosal visualisation (equivalent to good/excellent bowel preparation as described by standard CCE grading scores), whilst in *prep2* group 82.23% of frames scored M2/M3 ($p < 0.001$).

In *prep1* group 24.53% of frames scored O3 for obscuration (equivalent to insignificant obscuration with standard CCE scores), whilst in *prep2* group 40.71% of total frames scored O3 ($p < 0.001$).

Conclusion: *Prep1* assessed whether a PEG + A booster could produce a "tsunami" prokinetic cleansing effect and *Prep2* examined boosting with a combination of gastrografin and low-dose NaP. Failure of capsule excretion occurred in almost two thirds *of Prep1* patients, whilst with *Prep2* the 88.2% completion rate was similar to that expected in standard colonoscopy. In *Prep1* group 55% of frames examined scored M2/M3 for mucosal visualisation and 43% O2/O3 for obscuration, whilst in *Prep2* group 82% of frames scored M2/M3 and 72% O2/O3.

PEG + A is an ineffective booster and fails to achieve adequate cleansing whilst the booster combination of gastrografin and low dose NaP appears to offer both excellent excretion rates and enhanced bowel cleansing.

Disclosure of Interest: None declared

Abstract number: P0233

	Gastric angioectasia	Gastrojejunal anastomosis haemorrhagic erosions	GAVE	Gastric neoplasia	Erosive haemorrhagic gastritis	Gastric ulcer	Gastric Dielafoy's lesion	Duodenal angioectasia	Duodenal Dielafoy's lesion	Duodenal varix	Erosive haemorrhagic duodenitis	Colonic Angioectasia	Colonic polyp	Colonic neoplasia
Primary Endoscopy	1	2	2	1	1	1	1	7	2	1	1	6	1	1
Tertiary Endoscopy	1	-	-	1	1	-	-	1	-	-	-	4	-	-

P0235 COLON CAPSULE ENDOSCOPY FOR THE PATIENTS WHO REFUSED STANDARD COLONOSCOPY

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Introduction: Colon capsule endoscopy (CCE) is an attractive alternative for the patients who refuse the standard colonoscopy.
Aims & Methods: To evaluate technical aspects and feasibility of CCE in the daily clinical practice. From I.2014 to XII.2014 we performed 57 CCE (PillCam Colon2) in 56 patients (m-26, f-30, mean age 51.4 ± 11.7 years, range 26-75). In 1 (2.7%) case the capsule retained in the stomach for 10 hours, so we repeated CCE once more. The main indication for colonoscopy was CRC screening – 37 (66.1%) patients; complaints of pain and constipation – 18 (32.1%); surveillance – 1 (1.8%) patient. The majority (96.4%) of patients refused to perform conventional, including sedated, colonoscopy. For the bowel preparation, we used regimen recommended by ESGE guidelines; for the evaluation of preparation – J.A.Leighton scale.
Results: Total CCE was performed in 52 (92.8%) patients. Slow capsule transit in sigmoid colon (until the battery exhausted) was observed in 3 (5.3%) patients, in transverse colon – in 1 (1.8%) patient. The mean transit time of the colon-capsule through the gastrointestinal tract was 7 hours 58 min ± 3 hours 33 min. The mean colon transit time was 6 hours 18 min ± 3 hours 04 min. Only 64.3% of the capsules were excreted in conditional 10 hours after ingestion. Colon preparation in 20 (35.7%) patients was excellent, in 25 (44.6%) - good, in 8(14.3%) – fair, in 3(5.4%) – poor. Colon abnormality was detected in 48 (85.7%) patients: polyps in 29 (60.4%), in 13 cases the size of polyps ranged from 1 to 6 mm, in 16 - was more than 6 mm; diverticulosis in 14 (29.1%) patients; erosions in 5 (10.4%); focal inflammation in 8 (16.6%); angioectasias in 6 (12.5%); melanosis in 1 (2.1%); aphtous ulcers in 7 (14.6%); anal fissure in 1 (2.1%) and hemorrhoids in 11 (22.9%) patients. No adverse events related to CCE were revealed. After CCE we recommended colonoscopy for 23 patients, but at the moment only 7 (30.4%) agreed. Results of CCE were completely confirmed in 3(42.8%) patients, partially – in 3(42.8%) and non-confirmed in 1(14.4%).
Conclusion: CCE was able to examine the whole large bowel in 92.8% of patients and to detect abnormalities in 85.7%, including polyps in 60.4% of patients. With reduced rates CCE could become the method of choice for CRC screening and incomplete colonoscopy.
Disclosure of Interest: None declared

P0236 MALE GENDER, PRESENCE OF ANGIODYSPLASIAS AND SMALL BOWEL POLYPS ARE RELATED WITH POORER BOWEL PREPARATION IN SMALL BOWEL ENDOSCOPY

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Introduction: Polyethylenoglucol has been widely used as bowel preparation before small bowel capsule endoscopy.
Aims & Methods
Aim: To determine risk factors those affect small bowel preparation with polyethilenoglycol.
Methods: 1030 patients undergone small bowel capsule endoscopy, gastroscopy and colonoscopy were evaluated. 165 with inflammatory bowel disease, 11 with celiac disease and 124 with underlined neoplasia were excluded from the analysis. 401 were evaluated for iron deficiency anemia, 149 for undefined gastrointestinal bleeding, 178 for diarrhea, 102 for other causes. Bowel preparation quality was defined as adequate (good, fair) or inadequate (poor). Stat: t-test, X2, logistic regression analysis.
Results: Bowel preparation was adequate in 533 (64.2%) patients. Mean age: adequate preparation: 63 ± 18 years, inadequate preparation: 63 ± 19 years ($p = 1.00$); Preparation was adequate in: Gastrointestinal bleeding: 93 (62.4%), anemia: 249 (62.1%), other indications for capsule endoscopy: 191 (68.2%, not statistical difference for capsule endoscopy indication); Male gender: 277 (59%, $p = 0.004$), active smoking: 119 (69%, $p = 0.20$), alcohol consumption: 46 (55%, $p = 0.08$); Small bowel polyps: 49.3%), small bowel ulcerative lesions: 142 (67.3%, $p = 0.28$), small bowel ulcers: 36 (59%, $p = 0.37$), angiodysplasias: 154 (57.5%, $p = 0.005$); Diabetes mellitus: 107 (55.7%, $p = 0.005$), motility disorders 12 (60%, $p = 0.69$), ischemic heart disease 150 (58.8%, $p = 0.03$), stroke 21 (60%, $p = 0.59$), hypothyroidism 74 (66.1%, $p = 0.66$), chronic renal failure 21 (48.8%, $p = 0.03$), use of antidepressants 42 (63.6%), use of tranquillizers: 78 (63.9%, $p = 0.005$). Moreover in patients excluded preparation was adequate in 7 (53.8%, $p = 0.44$) of patients with small bowel cancers. Small bowel transit time in patients with adequate preparation was 332 ± 142 min, while in those with inadequate preparation was 355 ± 137 min ($p = 0.02$). Capsule study completion was 78.2% in those with adequate preparation and 77.1% with those with inadequate ($p = 0.71$). In logistic regression analysis: male gender ($p = 0.009$), presence of angiodysplasias ($p = 0.048$) and presence of small bowel polyps ($p = 0.03$) predispose to inadequate bowel preparation.
Conclusion: Inadequate preparation is related with male gender, presence of angiodysplasias and small bowel polyps. The former possibly due to underline pathologies like diabetes or ischemic heart disease, while the latter two as they predispose to slower bowel transit. More thorough preparation is needed for those patient groups.
Disclosure of Interest: None declared

P0237 CAPSULE ENDOSCOPY IN PEDIATRIC PATIENTS WITH ESTABLISHED AND SUSPECTED CROHŃS DISEASE: SINGLE-CENTER EXPERIENCE OF 180 PROCEDURES

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Introduction: Capsule endoscopy is a non-invasive method that enables excellent visualization of the small-bowel mucosa. The method has been evaluated for detection of Crohn's lesions in the adult population but data about the method's clinical value for diagnosing Crohn's disease in a large pediatric clinical material is still scarce.
Aims & Methods: The aim of our study was to examine the impact and safety of capsule endoscopy performed in children and adolescents being investigated for established and suspected Crohńs disease (CD) at a tertiary academic hospital in Scandinavia.
A retrospective, single-center study included 180 capsule endoscopy examinations in 169 consecutive patients between October 2003 and December 2014. Patients had a median age of 13 years (range 3-17 years) and the indications for capsule endoscopy were clinically suspected (125 cases, 69%) and established (55 cases, 31%) CD. Capsule endoscopy was performed with PillCam™ SB (Given Imaging) capsule endoscopy system with 8-12 hours of registration without bowel preparation.
Results: 26 of 180 (14%) capsules were endoscopically placed in the duodenum. Patency capsule examinations were performed in 47 (26%) cases.
Capsule endoscopy detected findings consistent with CD in 71 (40%) examinations, 17 (9%) procedures showed minor changes but were not diagnostic for CD. 92 (51%) examinations displayed normal intestinal mucosa. In 30 of 180 (17%) procedures the capsule did not reach the colon during recording time and were defined as incomplete examinations.
A change in therapy was recommended in 53/180 (29%) patients based on capsule endoscopy results.
The most feared complication, capsule retention, occurred in only one (0.6%) patient with established CD.
Conclusion: Capsule endoscopy is a safe method in children with suspected and established CD. The result of capsule endoscopy often leads to a definitive diagnosis and have significant impact on the clinical management of pediatric patients with CD.
Disclosure of Interest: None declared

P0238 THE NEW 360° PANORAMIC-VIEWING CAPSULE ENDOSCOPY SYSTEM: RESULTS OF THE FIRST MULTICENTER, OBSERVATIONAL, STUDY

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Introduction: CapsoCam® SV1 (CapsoVision Inc, Saratoga, USA) is a new small bowel capsule (SBC) with "panoramic view", wire-free technology, and a long-lasting battery life. It is equipped with 4 high frame rate cameras (3-5 frames/second/camera), located at the side of the capsule, resulting in a very high number of acquired frames. Previous studies, comparing this device with frontal view SBCs, showed comparable operative and diagnostic performance [1-2].
Aims & Methods: Accordingly, we conducted a multicenter, observational study to assess the performance of CapsoCam® SV1 in real-life clinical setting. Between January 2014 and April 2015, all consecutive patients undergoing SBC with CapsoCam® SV1 in four Italian and two British Institutions were enrolled. All the identified findings were classified according to their bleeding probability and clinical significance, in line with Saurin classification [3], as **P0**: low probability; **P1**: intermediate probability; **P2**: high probability. Capsule endoscopy was defined as "positive" if at least one P2 finding was identified.
Results: Eighty-nine patients underwent SBC (49 men; median age ± SD: 66 ± 17 years, range: 15-86 years). 70/89 were referred for obscure GI bleeding (18 with overt and 52 with occult OGIB) and 19/89 for suspected (17) or established (2) Crohn's disease (CD). One technical failure occurred - due to short battery life (270min) - leading to incomplete enteroscopy. 88/89 patients excreted and retrieved the capsule. One capsule was retained due to a neoplastic stricture, no acute obstruction occurred and retrieval was done at time of surgery.
The overall diagnostic yield (rate of positive tests) was 42.5%, whereas it was 43.5% for OGIB (50% for overt bleeding) and 38.8% for CD. The ampulla of Vater was identified in 40% of patients and the capsule explored the entire small bowel in 91% of patients.
In a per-lesion analysis, overall 328 findings were detected (P0: 43, P1: 119, P2: 166). Most of the lesions were located in the small bowel (273/328: 83.2%) and 55% of them were classified as P2. Interestingly, 47/328 (14.3%) and 8/328 (2.4%) lesions were detected in the upper and in the lower GI tract, 22 and 6 of them were classified as P2 respectively.
Conclusion: Our data suggest that even when used in the everyday clinical practice, CapsoCam® SV1 has a detection rate and a safety profile comparable to other SBCs with frontal view.

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Disclosure of Interest: None declared

P0239 COLLAGE MODE IS A VALID TIME SAVING TOOL TO ASSESS COLON CAPSULE ENDOSCOPY

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Introduction: Colon capsule endoscopy (CCE) is a valid, non-invasive method to detect colon polyps. However, CCE is time consuming. We evaluated a software algorithm that might reduce investigation time.

Aims & Methods: 29 CCE videos (CCE-2, Covidien®) were analysed by blinded investigators using the "collage mode" (Rapid 8 software, Covidien®) by experienced (n = 3; two-day training course for detecting polyps in CCE and experience of at least 50 CCE investigations) and unexperienced investigators (n = 3, twenty minute briefing about morphology of polyps and technique of CCE). Gold standard was the finding of an experienced extern investigator (> 100 CCE) and results of subsequent flexible colonoscopy. Localisation of the entry to the colon and all detected polyps were marked. Videos were assessed under standardized conditions without interruption.

Results: Evaluation of CCE videos took 7.1 and 7.7 min for experienced and unexperienced investigators, respectively.

Sensitivity of experienced investigators was significantly higher than sensitivity of unexperienced investigators to detect at least one polyp, but specificity was similar in both groups see table 1.

Table 1: Sensitivity and specificity of using the collage mode for detecting at least one colonic polyp per patient.

n = 29	experienced investigators	unexperienced investigators
Sensitivity	88.1+/-8.25%	56.96+/-30.82%
Specificity	84.86+/-7.36%	86.67+/-11.54%
Investigation time per CCE video	424+/-198 sec.	458+/-229 sec.

Conclusion: The use of collage mode reduces the time to investigate colon capsule videos to less than eight minutes. Experienced investigators using this tool are able to achieve excellent sensitivity.

Disclosure of Interest: None declared

P0240 SINGLE-VISIT MEASURES OF GUT TRANSIT AND POSTPRANDIAL GASTRO-INTESTINAL MOTILITY USING MRI METHODOLOGY: A FEASIBILITY STUDY

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Introduction: Symptoms related to intestinal motility are common in irritable bowel syndrome and even inflammatory bowel disease. Patient symptoms of bloating and nausea are typically worse post-prandially but clinical investigations to date are carried out fasting or after aggressive and unpleasant bowel preparations likely to alter physiology. Moreover, different appointments necessitating multiple patient visits are usually needed to assess motility across different segments of the gastrointestinal (GI) tract.

Aims & Methods

Aims: We describe here a novel paradigm to assess fasting and postprandial motility in a single visit and assess its feasibility in healthy volunteers. The paradigm uses a validated soup meal[1], and MRI to measure gastric emptying[2], gall bladder contraction[3], small bowel motility[4], small bowel water content[5] and whole gut transit[6] in this cohort.

Methods: Ten healthy participants (5 male, age 32 (11) yrs) were recruited for this study MRI scanning was carried out on a 1.5T Philips Achieva scanner. The subjects were asked to swallow five MRI transit marker capsules (20 mm x 7 mm) at 09:00 am, 24 h before undergoing an MRI scan[6] and fasted from 2000 h the night before. On the day of the scan, a baseline fasting scan at 0900 hours was acquired. At 0925 hours, subjects were asked to consume a soup meal (Heinz cream of chicken 204 kcal, 11.8g fat or mushroom soup 214 kcal, 11.4g, 400g) within 20 min with the first immediate postprandial scan acquired at 0945 hours. Data collection time points were every 15 min for the first 60 min and every 30 min up to 270 min. At each time point scans were acquired to assess gastric volume, gall bladder volume, small bowel water content and small bowel motility, 2 additional scans were acquired at baseline to determine the position of the transit pills.

Results: Data is presented as mean (standard deviation (SD)). All participants completed the study. In the immediate postprandial state, the gastric volume was 416 (73) mL. The mean half-life of the meal in the stomach was 41 (20) min. The gall bladder maximum ejection fraction was 59 (19) % which occurred within the first 60 minutes postprandially. The fasted small bowel contained a total volume of 41 (27) mL of resting water. Postprandially this small bowel water content rose to a maximum value of 107 (46) mL. Across the 10 volunteers, a motility index based on the SD of signal intensity across the small bowel rose by 47 (30) % postprandially . The mean whole gut transit as measured through a weighted average position score[6] was 1.9 (1.5).

Conclusion: This novel paradigm is feasible and well tolerated by participants. The soup meal challenge was effective in inducing a change in multiple measured end-points, monitoring markers of GI motility in a single visit. This methodology may be applied to a variety of disease groups to understand alterations in GI physiology, allowing us to identify symptom biomarkers to target pharmacologically.

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P0241 NOVEL PROBE-BASED QUANTATIVE IMAGE OF MITOCHONDRIA IN LIVE COLON CANCER TISSUES BY MULTIPHOTON MICROSCOPY

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Introduction: Multiphoton endomicroscopy is the recentely updated technique for endoscopy and virtual image and optical sectioning. However optimized probe has not been established for multiphoton endomicroscopic image. Therefore we developed novel probe for mitochondria and applied for colon neoplasm tissues. In cancer cell, abnormally increased mitochondrial replication is related mitochondrial dysfunction and Warburg effect.[1]

Aims & Methods: We used newly developed multiphoton probe for micochondria imaging which are made using benzofuran derivative (BFP, maximal multiphoton fluorescence at 570 nm). Fresh mucosal tissues of colonic adenoma and adenocarcinoma were obtained from endoscopic biopsy. Multiphoton probe BFP for mitochondria was stained for tissues and imaging performed using multiphoton microscopy.

Results: BFP shows high enhancement factor upon binding mitochondria, good selectivity, cell permeability, and can readily detect mitochondria in human tissues by multiphoton microscopy. Mitochondria were detected in human colon mucosa tissues. Calculated mitochondria area were increased in adenocarcinoma tissues compared to normal mucosal tissues.

Conclusion: Newly developed multiphoton probe for mitochondria are usable to image human live colon tissues. Mitochondrias are increased in colon cancer tissues compared to normal colon mucosa tissues.

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Disclosure of Interest: None declared

P0242 COMPARISON OF COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING IN THE DISCRIMINATION OF INTRA- AND EXTRAPERITONEAL RECTAL CANCER: INITIAL EXPERIENCE ON 38 PATIENTS

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Introduction: Abdominal CT may have a role in the loco-regional evaluation of rectal cancer, besides systemic staging. The discrimination between intra- and extraperitoneal rectal cancer has important implications for both oncologic and surgical grounds. Indeed, based on intra- and extraperitoneal location the therapeutic approach may change because of the different risks of local recurrence and different prognosis.

Aims & Methods: Aim of the study was to compare the diagnostic performance of CT with that of MRI to determine the intra- or extraperitoneal location of rectal cancers, using surgical exploration as reference standard. We

Abstract number: P0243

Sensitivity	Specificity	Post-test probability for positive US result at prevalence 76.4%	Post-test probability for negative US result at prevalence 76.4%
69% (95% CI 59% to 78%)	81% (95% CI 73% to 88%)	92% (95% CI 88% to 95%)	55% (95% CI 46% to 63%)

retrospectively evaluated MRI and CT examinations of patients with rectal cancer defining the extra- or intraperitoneal location of tumor's inferior edge with respect to the anterior peritoneal reflection (APR). We assessed the quality of identification of the APR according to a 4-point confidence scale and we measured the distance from the inferior edge of tumors to the anal verge and from the APR to the anal verge.
Results: Thirty-eight patients were included: 24 men and 14 women with a mean age of 68.8 ± 9.4 years. The APR was appreciable in all MRI examinations and in 36/38 patients on CT images. Mean distances from the APR to the anal verge were 98.97 ± 18.8 mm at MR and 100.6 ± 12.9 mm at CT ($p = 0.6653$, t-test for independent samples). MR showed sensitivity of 100% (95% CI: 89.62-100.00%), specificity of 75% (95% CI: 20.34-95.88%), positive predictive value of 97.14% (95% CI: 85.03-99.52%), negative predictive value of 100% (95% CI: 30.48-100.00%). Diagnostic performance of CT was: sensitivity 100% (95% CI: 89.32-100.00%), specificity 60% (95% CI: 15.40-93.51%), positive predictive value 94.29% (95% CI: 80.81-99.13%), negative predictive value 100% (95% CI: 30.48-100.00%). The mean distance from the inferior edge of tumors to the anal verge was 62.3 ± 21.2 mm at MR and 62.5 ± 20.1 mm at CT ($p = 0.8181$ Mann-Whitney test for independent samples), with a strong correlation (Spearman's coefficient of rank correlation (rho): 0.995; $p < 0.0001$).
Conclusion: The results of our study confirm the great clinical value of MRI in determining the location of rectal cancers by direct visualization of APR in preoperative setting; CT demonstrated a potential supporting role in the evaluation of rectal cancer, showing a strong correlation with MRI in regarding measurements of the distance betweenthe tumor's inferior edge and the anal verge.
Disclosure of Interest: None declared

P0243 ABDOMINAL ULTRASOUND FOR DIAGNOSIS OF ACUTE APPENDICITIS: SYSTEMATIC REVIEW AND META-ANALYSIS OF DIAGNOSTIC ACCURACY STUDIES

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Introduction: Acute appendicitis (AA) is one of the most frequent causes of acute abdominal pain (1, 2). Clinical signs of AA have overall diagnostic accuracy for the disease of about 80% (3). Reported sensitivity and specificity of abdominal ultrasound (US) for diagnosis of AA is up to 92% and 96%, respectively (4, 5). The reported negative appendectomy rate is up to 34% (6, 7).
Aims & Methods: The aim of this systematic review was to determine diagnostic accuracy of US for diagnosis of AA. Medline, Embase, The Cochrane library and Science Citation Index Expanded from January 1994 to October 2014 were systematically searched. The reference standard for evaluation of final diagnosis was pathohistological report from the tissue obtained on appendectomy. Summary sensitivity, specificity and post-test probability of AA after positive and negative result of US with corresponding 95% confidence intervals (CI) were calculated. The pre-test probability was defined as the prevalence of AA in the population of included studies. Review Manager 5 (8) and METADAS macro for SAS were used for statistical analysis (9). Methodological quality of included studies was evaluated using Quality Assessment in Diagnostic Accuracy Studies 2 (QUADAS-2) tool (10).
Results: There were 3,306 references identified through electronic searches. Full-texts of 296 reports were assessed for inclusion, out of which 17 reports met the inclusion criteria. A total of 2,841 participants were included in the analysis. None of the included studies were of high methodological quality. The results of meta-analysis are presented in the Table. The result of sensitivity analysis did not significantly influence summary results of the main analysis.
Conclusion: Abdominal ultrasound does not seem to have a role in the diagnostic pathway for acute appendicitis. The sensitivity and specificity of US do not seem to exceed that of clinical examination. Patients with lower clinical probability of having AA that require additional diagnostic workup should be referred to more sensitive and specific diagnostic procedures, such as computed tomography.

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Disclosure of Interest: None declared

P0244 ENDOSCOPIC MANAGEMENT OF TEMPORARY PLACEMENT OF FULLY COVERED SELF-EXPANDABLE METAL STENTS IN BENIGN BILIARY STRICTURES

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Introduction
Background/Aims: Benign biliary strictures (BBSs) have been endoscopically managed with plastic stent placement. Fully covered self-expandable metal stents (FCSEMSs) are gaining acceptance for the treatment of BBSs. We performed a large prospective study to analyze the clinical outcomes; following endoscopic treatment data regarding fully covered self-expandable metal stents (FCSEMSs) in BBS patients remain scarce in Rio de Janeiro.
Aims & Methods: Methods: In a nonrandomized study a single center, 263 patients (145 men, 55%) with BBSs underwent FCSEMS placement between January 2012 and March 2015. Efficacy and safety were evaluated retrospectively. Patients were considered to have resolution if they showed evidence of stricture resolution on cholangiography and if an inflated retrieval balloon easily passed through the strictures at FCSEMS removal.
Results: The mean FCSEMS placement time was 6.2 (1.0-12.2) months. Patients were followed for a mean of 10.2 (1.0-36.0) months after FCSEMS removal. The BBS resolution rate was confirmed in 241 of 263 (92%) patients who underwent FCSEMS removal. After FCSEMS removal, 36 of 241 (15.8%) patients experienced symptomatic recurrent stricture and repeat stenting was performed. When a breakdown by etiology of stricture was performed, 17 of 20 (85%) patients with chronic pancreatitis, 53 of 53 (100%) with gall stone-related disease, 57 of 61 (93%) with surgical procedures, pancreatic collections 45 of 47 (93.3%), Endoscopic complications (perforation and bleeding) 14 of 14 (100%) and 55 of 68 (80%) with BBSs of other etiology had resolution at FCSEMS removal. Complications related to stent therapy occurred in 40 (15%) patients, including pain (n = 23), proximal migration (n = 10), cholecystitis (n = 1), distal migration (n = 2), and occlusion (n = 4).
Conclusion: Endoscopic treatment of temporary FCSEMS placement in BBS patients is safe and effective and can be considered a first-choice alternative to surgical and/or plastic stenting. The potential benefits and risks should be evaluated in further investigations.
Disclosure of Interest: None declared

P0245 USE OF PARTIALLY COVERED AND UNCOVERED METALLIC PROSTHESIS (GIOBOR STENT) FOR ENDOSCOPIC ULTRASOUND-GUIDED HEPATICOGASTROSTOMY: RESULTS OF A RETROSPECTIVE MONOCENTRIC STUDY

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Introduction: Endoscopic ultrasound-guided hepaticogastrostomy (EUS-HGS) represents an option to treat obstructive jaundice when endoscopic retrograde cholangio pancreatography (ERCP) fails, in alternative to surgery or percutaneous transhepatic biliary drainage (PTBD). The success rate of this technique has been shown to be very high, with resolution of jaundice in up to 98.5% of cases. Up to now plastic and covered or uncovered self-expandable metallic stents (SEMS) have been used, each of them presenting some limitations.
Aims & Methods: Aims of this study were to evaluate the technical and functional success of EUS-HGS using a dedicated biliary SEMS with a half covered part (GioBor stent- Taewoong Medical ®). We retrospectively reviewed data of patients who underwent EUS-HGS at our centre, with at least 6 months of follow up. Demographics, clinical and laboratory data were extracted from the patient's charts and electronic records. Technical success was defined as the passage of the GioBor stent across the stomach, along with the flow of contrast medium and/or bile through the stent, while functional success as the decrease of bilirubin value of at least 25% of the pre-treatment value within the first week. The rate of early (in the first month after EUS-HGS) and late (at 6 months follow up) complications was assessed.
Results: A total of 41 patients were included (21F/20M, mean age 66, range 45-65). Obstructive jaundice was due in most of patients (39/41, 95%) to a malignant disease. Reasons to EUS-HGS were failed biliary cannulation in 18 patients (44%) and failed bile duct decompression in 24 patients (56%). Technical success was obtained in 37/41 patients (90%), while functional success, measurable in only 29 patients, was obtained in 19/29 patients (65%). Thirteen patients (33%) presented an early complication, mostly represented by infectious complications. At six months follow up, 10/37 patients (27%) required a new biliary drainage and 11/37 (30%) died because of their disease.
Conclusion: EUS-HGS using GioBor stent is technically feasible, clinical effective, safe and may be an alternative to PTBD in case of ERCP failure for biliary decompression. Randomized controlled studies comparing GioBor prosthesis with "classical" SEMS are needed to confirm these preliminary results.
Disclosure of Interest: None declared

P0247 COVERED SELF-EXPANDABLE METALLIC STENT WITH LOW AXIAL FORCE FOR UNRESECTABLE MALIGNANT BILIARY OBSTRUCTION

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Introduction: Although covered self-expandable metallic stent (SEMS) has longer patency than uncovered SEMS in patients with unresectable malignant distal biliary obstruction, the complication rate of covered SEMS are quite different among the stents due to their mechanical properties. Niti-S SUPREMO (Tae Woong Medical) is a newly developed fully-covered SEMS with lower axial force than a standard Covered WallFlex (Boston Scientific) stent.
Aims & Methods: We retrospectively analyzed the outcome of both types of covered SEMS in patients with unresectable malignant distal biliary obstruction. Medical records were retrospectively reviewed for consecutive patients with unresectable malignant distal biliary obstruction who underwent placement of Covered WallFlex between April 2009 and March 2011 (group W) and Niti-S SUPREMO 10 between April 2011 and June 2014 (group S). Background characteristics, procedure-related complications and long-term stent dysfunction were compared between the groups.
Results: Seventy-one patients were analyzed (25 vs. 46 in group W vs. group S, respectively). There were no significant differences in patient characteristics; median age of 65 vs. 67, male gender in 52% vs. 52%, perfomance status of 0 in 64% vs. 67%, pancreatic cancer in 93% vs. 94%, and receiving chemotherapy in 78% vs. 93%. Procedure-related complications were significantly higher in group W; acute pancreatitis in 8% vs. 0% ($p = 0.04$) and acute cholecystitis in 12% vs. 0% ($p = 0.01$). Stent dysfunction were seen in 16% vs. 28% ($p = 0.27$) and median time to stent dysfunction by Kaplan-Meier method were 196 days vs. 150 days ($p = 0.50$ by log-rank test). The median overall survival time were 259 days vs. 244 days ($p = 0.84$).
Conclusion: Niti-S SUPREMO, a newly developed covered SEMS with lower axial force, decreased the risk of procedure related complications of acute pancreatitis and acute cholecystitis compared with covered WallFlex without significant differences in long-term outcomes.
Disclosure of Interest: None declared

P0248 EVALUATION OF ANTI-MIGRATION PROPERTIES OF BILIARY COVERED SELF-EXPANDABLE METAL STENTS

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Introduction: Endoscopic placement of self expandable metal stents (SEMSs) has been pivotal in providing relief from obstructive jaundice in patients with biliary stricture. Covered SEMSs tend to show a higher rate of stent migration than uncovered SEMSs, which is the most important issue to be resolved during deployment of the covered SEMSs for biliary stricture. Stent properties such as the stent framework, flare structure and radial force (RF) may prevent stent migration.
Aims & Methods: The purpose of the study was to measure the anti-migration potential of 6 different covered SEMSs including 5 braided types and one laser-cut type using a phantom model inducing migration of biliary SEMSs, and to evaluate whether RF and flare structure contribute to the anti-migration potential.
Anti-migration potential was measured using a phantom model for migration. The metal stents were fixed at a round hole of silicone walls of three types of hole diameter, 6, 8 and 10 mm. The distal end of the stent was fixed at a force gauge device. During experiments, the distal end of the stent with the force gauge device was retracted at a speed of 1mm/sec. using the retraction robot. The force of the resistance of the stent to the retraction (resistance force to migration; RFM) was measured from starting retraction of the stent to dislocating the distal end of the stent from the silicone wall.
The RF was measured by using a radial force measurement machine when the stent was compressed to 6, 8 and 10 mm in outer stent diameter.Three variables of stent flare structure including outer diameter of the flare (ODF), height of the flare (HF) and taper angle of the flare (TAF) were measured. The correlations between RF and RFM as well as between variables of the stent flare structure and RFM were analyzed.
Results: The smaller the compressed outer diameter of the stent (CODS), the higher the RFM and RF exhibited for all the 6 SEMSs. The laser-cut SEMS has higher RFM than any braided SEMSs whether the stent fully expands or not. A strong correlation between RF and RFM was observed when CODS was 6 mm ($r = 0.849$), but there was no strong correlation when the CODS was 8 or 10 mm. In addition, when the stent fully expanded (CODS was 10 mm), only TAF ($r = 0.837$) closely correlated with RFM in all the 6 SEMSs, and ODF ($r = 0.952$), HF ($r = 0.943$) and TAF ($r = 0.906$) closely correlated with RFM in 5 braided SEMSs. When the stent not fully expanded state (CODS was 6 or 8 mm), there was no strong correlation between three variables of stent flare structure and RFM.
Conclusion: The RF plays an important role in anti-migration when the covered SEMS not fully expanded state. In the fully expanded covered SEMS, the stent flare structure is strongly related to the anti-migration potential. The laser-cut stent potentially possesses extremely higher resistance force to migration whether the stent fully expands or not. The stent properties including radial force, flare structure and stent framework should be considered before selecting covered SEMS for biliary stricture.
Disclosure of Interest: None declared

P0249 EFFICIENCY AND SAFETY IN CASE OF TECHNICAL SUCCESS OF EUS-GUIDED TRANSHEPATIC ANTEGRADE BILIARY DRAINAGE. REPORT OF A MONOCENTRIC STUDY

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Introduction: EUS-guided biliary drainage like choledochoduodenostomy, hepaticogastrostomy, antegrade stenting and rendezvous are alternative procedures in case of obstructive jaundice and altered anatomy or failed endoscopic-retrograde-cholangiography (ERCP). Complications related to EUS-guided antegrade drainage (EUS-GAD) are still described as substantial in up to 10%. Combination of procedures is sometimes suggest to avoid adverse events like biliary leakage, even in case of primary successful EUS-GAD.
Aims & Methods: Aims of this study were to evaluate the efficiency and safety of EUS-GAD with transhepatic access in case of technical success. We retrospectively reviewed computer data collected between 2006 and 2015 of patients with malignant and non-malignant biliary obstructive lesions who underwent EUS-GAD in a single, tertiary care center.
Results: A total of 20 patients were included (9F/11M, mean age 68, range 40-90, mean ASA score 2). Obstructive jaundice was due in most case to a malignant disease (19/20 patients, 95%). Reasons for EUS-GAD was failed ERCP in 13/20 (65%), duodenal stenosis in 4/20 (20%), altered anatomy after surgical intervention in 3/20 (15%). Intrahepatic biliary duct puncture was done with a 19G EchoTip® Ultrasound Needle in 16/20 (80%), with an EchoTip® Ultrasound Access Needle in 7/20 (35%). The hepaticogastric tract was performed in 20/20 with a cystostoma 6 fr, without puncture site closure at the end of procedure. Stenosis dilatation was done in 3/20 (15%) and calibration with cystostoma 6 fr in 9/20 (45%). SEMS was transpapillary in 19/20 (95%) and non transpapillary in 1/20 (5%). Drainage was completed in intraoperative stage in 2/20 (10%), once by hepaticogastrostomy and once by percutaneous drainage of the right liver. Clinical success was 17/20 (85%). 1/20 (5%) patient presented a persistent obstructive infectious cholangitis treated by another SEMS via ERCP. 2/20 (10%) patients died of infectious complication and incomplete drainage in case of advanced cancerous disease. One of these 2 patients was treated by EUS-GAD and hepaticogastrostomy in same time. None patients developed bilioma or bile leakage. 2/20 patients were treated later by an endoscopic duodenal SEMS for a duodenal obstruction.
Conclusion: EUS-GAD by transhepatic way is clinical effective and a safety method to treat biliary obstructive disease, in case of technical success. Closure of the gastric puncture site is not mandatory if drainage is efficient. Complementary method for biliary decompression should be combined in case of incomplete drainage and not to prevent potential adverse events. Additional studies are needed to target the most appropriate patient's characteristics to undergo this type of intervention.
Disclosure of Interest: None declared

P0250 EUS-GUIDED ANTEGRADE BILIARY STENTING FOR UNRESECTABLE MALIGNANT BILIARY OBSTRUCTION IN PATIENTS WITH SURGICALLY ALTERED ANATOMY: A SINGLE CENTER PROSPECTIVE PILOT STUDY

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Introduction: Therapeutic ERCP for malignant biliary obstruction (MBO) in patients with surgically altered anatomy (SAA) is challenging even with application of enteroscopies. Percutaneous transhepatic biliary (PTB) or surgical approach is common alternatives for failed enteroscopy-based ERCP, but is associated with considerable complications.
Aims & Methods: The aim of this study was to evaluate the feasibility and safety of EUS-antegrade biliary stenting (EUS-ABS) for MBO in patients with SAA in prospective cohort.
EUS-ABS for unresectable MBO was attempted in 20 patients with SAA between 8/2012 and 2/2015. EUS-ABS was performed as follows: The left intra-hepatic bile duct (IHBD) was initially punctured from the intestine followed by cholangiography and antegrade guidewire manipulation. ABS with uncovered metallic stent was performed. A naso-biliary drainage tube (NBD) was placed if necesssary.
Results: SAAs were gastrectomy with Roux-en-Y reconstruction in 18, BillrothII reconstruction in 1, and hepatectomy with biliary reconstruction in 1. Biliary puncture was successful in 95% of the patients (19/20). In the patient with failed biliary puncture, inadequate biliary dilation did not allow EUS-guided puncture. The guidewire placement and subsequent ABS were successful in 19. Therefore, the overall technical success rate was 95% (19/20). NBD was placed in 3 and was removed in a median of 7 days. A median procedure time was 37 min (22-80). Adverse events were recognized in 20% of the patients (4/20) and were fever-up in 1 and mild pancreatitis in 3.
Conclusion: EUS-ABS for MBO in patients with SAA is feasible and can be an option as a safe and effective alternative. Further studies are warranted.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 09:00-17:00
SURGERY I - HALL 7

P0251 LONG-TERM OUTCOMES OF LAPAROSCOPIC SLEEVE GASTRECTOMY AND EFFECTS ON GERD SYMPTOMS

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Introduction: Laparoscopic Sleeve Gastrectomy (LSG) is a bariatric procedure with documented efficacy at short and midterm follow-up but there are only few data at long term follow-up.
Aims & Methods
Aim: To evaluate the long-term results of LSG describing the effect on GERD symptoms.
Methods: 105 obese patients eligible for bariatric surgery underwent LSG. According to the preoperative BMI obese patients were divided in two Groups: Group 1 (N = 61, patients with preoperative BMI $\leq$ 50 Kg/m^2) and Group 2 (N = 44, patients with preoperative BMI > 50 Kg/m^2). All underwent a preoperative assessment including evaluation of comorbidities, standardized GERD questionnaire, a double-contrast barium swallow, an upper-gastrointestinal endoscopy. At 5 years after LSG the following data were collected: BMI, GERD symptoms, modification of comorbidities, complications. The adopted criteria of surgical success were BMI $\leq$ 35 kg/m^{2}in patients of Group 1 and BMI $\leq$ 40 kg/m^{2}in patients of Group 2.
Results: Table 1 showed the demographic characteristics and prevalence of some comorbidities in the two groups of the study before LSG

	Group 1 N = 61/105 (58.1%)	Group 2 N = 44/105 (41.9%)	p
Weight, kg	**114.2 ± 19.0**	**161.70 ± 19.76**	**< 0.001**
BMI, kg/m^2	**41.2 ± 4.7**	**57.25 ± 5.60**	**< 0.001**
Age, yr	**39.9 ± 10.1**	**38.5 ± 11.5**	**0.51**
Women, n (%)	**44 (72,1)**	**23 (52,3)**	**0.04**
Hypertension	**19 (31.1%)**	**14 (31.8%)**	**0.88**
Hyperlipidemia	**20 (32.8%)**	**22 (50%)**	**0.11**
Type 2 diabetes	**11(18%)**	**9 (20%)**	**0.9**
Typical GERD symptoms	**19 (31%)**	**11 (25%)**	**0.6**

At 5 years of follow-up, the success rate (BMI < 35) was achieved in 85.5% of Group 1 and in 62.9% of Group 2 (p = 0.01). Among the patients of Group 1: 73.3% referred the resolution, 26.7% the persistence and 15% the new onset of GERD complaints. Among the patients of Group 2, 44.4% referred the resolution, 55.6% the persistence and 7.7% the new onset of GERD complaints. Patients of Group 1 that did not meet the criteria of surgical success (BMI < 35) at 5 years of follow-up showed a similar prevalence of postoperative GERD symptoms compared to patients who showed a surgical success according to the adopted success criteria (p = 0.52). On the other hand, the patients of Group 2 that did not meet the criteria of surgical success (BMI < 40) at follow-up reported an higher prevalence of GERD symptoms (p = 0.03).
Conclusion: LSG is an effective treatment and showed good weight loss outcome and resolution of comorbidities also on long term follow-up; although the success rate was significantly lower in pazients with preoperative BMI > 50. A good percentage of patients with resolution of GERD symptoms was observed. However in patients with preoperative BMI > 50 who failed to reach the success criteria, there was a high percentage of GERD persistence or new onset.
Disclosure of Interest: None declared

P0252 CLINICOPATHOLOGIC PROFILES AND CLINICAL OUTCOMES OF RECURRENCE AND MORTALITY OF PATIENTS WITH GASTROINTESTINAL STROMAL TUMORS AT THE PHILIPPINE GENERAL HOSPITAL

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Introduction: Gastrointestinal stromal tumors (GIST) occur in less than 1% of all digestive tumors, but are the most common mesenchymal neoplasms of the gastrointestinal tract. This is the first study that described the clinicopathologic profiles and clinical outcomes of recurrence and mortality of GIST patients at the Philippine General Hospital (PGH).
Aims & Methods: This was a retrospective, descriptive study including all biopsy-proven GIST cases in PGH from 2009 to 2014. Data from the review of hospital records were encoded and analyzed using Microsoft Excel.
Results: A total of 58 patients were included. Median age at diagnosis was 50 years, with female to male ratio of 1.3. Most common primary site was stomach (39.7%). Median duration of symptoms prior to first consult was 6 months. Most common presenting symptom was abdominal pain (37.9%). Mean size of primary tumor was 7.6 cm. Immunohistochemical staining result for CD 117 was positive in 63.8%. Five percent was noted to have unresectable metastatic disease at presentation. Liver was the site of metastasis for all these cases. Ninety-five percent underwent surgery and 100% of which was reported to have R0 resection. Majority were stratified as low risk (46.6%), followed by high risk (43.1%), then moderate risk (8.6%). After a median follow up of 32.5 months, 7.3% developed local recurrence and 5.1% was reported as mortality.
Conclusion: This hospital-based study showed that the clinicopathologic profile of GIST in PGH is comparable to other population-based studies. Survival was favorable in completely resected cases and in lower-risk groups.
Disclosure of Interest: None declared

P0253 NON-EXPOSURE ENDOSCOPIC FULL-THICKNESS RESECTION WITH SIMPLE SUTURE TECHNIQUE, A PRELIMINARY RANDOMIZED COMPARATIVE ANIMAL STUDY

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Introduction: Recently, endoscopic full-thickness resection (EFTR) with simple suture technique which did not expose gastric mucosa to peritoneum was developed. This new technique includes the steps of laparoscopic seromuscular suturing with a barbed suture thread (V-Loc), which results in inversion of the stomach wall; EFTR of the inverted stomach wall from inside the stomach; and finally, endoscopic mucosal suturing with endoloops and clips.
Aims & Methods: The aim of this study was to assess the outcome of EFTR using simple suture technique compared with that of laparoscopic wedge resection using linear stapler in animal model.
Preliminary analysis of prospective, randomized, controlled animal study. EFTR group (n = 4) use the method of EFTR with simple suture technique and linear stapler group (n = 4) use laparoscopic linear stapler for resection and suturing. Locations were cardia, upper body anterior side, upper body greater curvature, and antrum lessor curvature side of stomach. Successful complete resection (en-bloc resection with clear resection margin) rates and successful closure rates and complications of each group were evaluated.
Results: Complete resections rates were 100% of EFTR group and 50% of linear stapler group. Successful closure rates were 100% in both groups. Complications were developed in only linear stapler group (a leakage at cardia and a stenosis at antrum). The procedure time were significantly shorter in linear stapler group (mean ± SD; 29.5 ± 12.7 min) than EFTR group (112.3 ± 27.4 min, p = 0.002). The sizes of resected tissue were significantly larger in linear stapler group (mean ± SD; 7.4 ± 0.9 cm) than EFTR group (4.6 ± 0.7 cm, p = 0.002).
Conclusion: Outcome of non-exposure EFTR with simple suture technique was compatible with that of laparoscopic wedge resection using linear stapler in preliminary study. Completion of study is needed.
Disclosure of Interest: None declared

P0254 RISK FACTORS FOR MARGINAL ULCER AFTER GASTRIC BYPASS SURGERY FOR OBESITY

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Introduction: Marginal ulcer (MU) is a common and potentially serious complication of gastric bypass surgery (GBP) for obesity, but little is known about its etiology.
Aims & Methods: The study aimed to asses risk factors for MU. This population-based cohort study of GBP in Sweden in 2006-2011 evaluated MU in relation to exposure to diabetes, hyperlipidemia, hypertension, chronic obstructive pulmonary disease (COPD), ulcer history, and use of proton pump inhibitors (PPIs), aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), and selective serotonin re-uptake inhibitors (SSRIs). Multivariable Cox proportional hazard regression models estimated hazard ratios (HRs) and 95% confidence intervals (CIs), adjusted for confounding.
Results: Among 20,294 GBP patients 2006-2011, diabetes and peptic ulcer history entailed statistically significantly increased risk of MU (HR = 1.26, 95%CI 1.03-1.55 and HR = 2.70, 95%CI 1.81-4.03), while hyperlipidemia, hypertension and COPD did not. PPI users had an increased HR of MU (HR = 1.37, 95%CI 1.17-1.60). Aspirin and NSAID consumption $\leq$median entailed decreased HRs of MU (HR = 0.56, 95%CI 0.37-0.86 and HR = 0.30, 95%CI 0.24-0.38), while aspirin and NSAID users > median had an increased risk and no association with MU, respectively (HR = 1.90, 95%CI 1.41-2.58 and HR = 0.90, 95%CI 0.76-1.87). SSRI use $\leq$median had a decreased risk of MU (HR = 0.50, 95%CI 0.37-0.67), while use > median entailed increased HR (HR = 1.26, 95%CI 1.01-1.56).
Conclusion: Diabetes and peptic ulcer history seem to be risk factors for MU, but not hyperlipidemia, hypertension, or COPD. Limited doses of aspirin, NSAIDs and SSRIs might not increase the risk of MU, while higher doses of aspirin do. The association with PPI could be due to confounding by indication.
Disclosure of Interest: None declared

P0255 PREDICTING DIETARY INTAKE AFTER DISCHARGE FOLLOWING UPPER GASTROINTESTINAL SURGERY USING DIET DIARIES AND A GASTRIC ACCOMMODATION TEST PRIOR TO HOSPITAL DISCHARGE

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Introduction: Patients undergoing upper gastrointestinal surgery are often malnourished and following hospital discharge eat poorly despite dietetic input. The 'slow satiety' drinking test has been used to assess impaired gastric accommodation in functional dyspepsia. We examined if a drinking test done along with a 2 day diet diary could predict dietary intake post hospital discharge.

Aims & Methods: Prior to discharge, patients undergoing an oesophagectomy or total gastrectomy for cancer completed a 2-day dietary diary and underwent a gastric accommodation test. The accommodation test comprised of drinking 20ml/min of polymeric sip feed until they felt comfortably full. After hospital discharge patients completed 2 day dietary diaries at 3, 6 and 12 weeks. The diaries were analysed using Dietplan 6 and tabulated. We calculated energy intake as absolute intake (Kcal) and % of calculated requirement (using the Harris-Benedict formula). The accommodation test (volume of feed taken and time taken) were correlated (pearsons) with energy intake at hospital discharge. The accommodation test results and energy intake at hospital discharge were also correlated with energy intake at 3, 6 and 12 weeks post discharge.

Results: 28 patients (22 men), median age 66 (IQ range 60, 74) were recruited, oesophagectomy = 18 Gastrectomy 10.

There was no correlation between the accommodation test and actual energy intake or % of required energy intake at hospital discharge.

Accomodation test		Energy (Kcal) intake as % of calculated requirements			
Volume (ml)	Time (min)	Discharge	3 weeks	6 weeks	12 weeks
106 (72, 140)	389 (244, 534)	66 (58, 74)	78 (69, 87)	79 (71, 88)	90 (77, 102)
	Correlation coefficient		0.34	0.43	0.40
	P value		0.078	0.023	0.034

Dietary energy intake (Kcal) at hospital discharge did not correlate with post discharge energy intake, but when expressed as a % of calculated requirements there was a correlation at 6 and 12 weeks. The volume of feed consumed and time taken to drink the sip feed for the accommodation test did not correlate with post discharge dietary intake.

Conclusion: Energy intake at hospital discharge was modest and increased slowly to reach 90% of requirements at 12weeks. There was only a weak correlation between dietary records done just prior to hospital discharge and those done at 6 and 12 weeks. There was no correlation between the gastric accommodation test and post discharge dietary intake. Neither the gastric accommodation test or 2 day dietary records done just before hospital discharge after upper gastrointestinal surgery predicted post discharge dietary intake.

Disclosure of Interest: None declared

P0256 DISTRIBUTION OF LYMPH NODE METASTASES IN OESOPHAGEAL ADENOCARCINOMA; A PROSPECTIVE COHORT STUDY

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Introduction: The distribution of lymph node metastases in oesophageal adenocarcinoma is not well studied. LN status is an important prognostic factor in oesophageal carcinoma. Distribution of metastatic LN may be influenced by tumor location, invasion depth and neo-adjuvant chemoradiation therapy. For the extent of the radiation field, as well as the extent of the lymphadenectomy it is essential to elucidate the distribution pattern of lymph node metastases.

Aims & Methods: To describe the distribution pattern of lymph node metastases in oesophageal adenocarcinoma and to identify lymph node echelons with high risk of metastases, adjusted for primary tumor location.

Between April 2014 and April 2015, all patients with an oesophageal adenocarcinoma undergoing transthoracic oesophagectomy with a complete 2 field lymphadenectomy were reviewed. In all patients the lymph node stations according to the 7th edition of the AJCC classification were excised and separately sent for histopathological examination. Patients were excluded if they were diagnosed with an oesophageal squamous cell carcinoma, or when a salvage resection was performed.

Results: 43 patients (36 male, mean age 64 years) were included. An adenocarcinoma of the distal oesophagus was diagnosed in 40 patients, while 3 patients were diagnosed with an adenocarcinoma of the mid-oesophagus. 84% of patients were neo-adjuvantly treated with chemoradiation. A median of 36 (IQR 27-44) lymph nodes were resected.

Lymph node metastases were found in 22/43 (51%) patients, of which 2 patients (9%) were not treated with neo-adjuvant chemoradiation therapy. A median of 3 (IQR 1-10) tumour-positive lymph nodes were found.

Lymph node metastases were observed most frequently in the paracardial lymph node stations (9/22 patients, 41%: right vs. left = 4 vs. 5 patients), in lymph nodes around the left gastric artery (7/22, 32%), and in station 2R (paratracheal: 6/22, 27%). Ten out of 22 patients (45%) diagnosed with lymph node metastases, had tumour-positive lymph nodes above and below the diaphragm.

Conclusion: Oesophageal adenocarcinoma frequently metastasizes to both the mediastinal and abdominal lymph node stations. Paracardial lymph nodes, in close proximity to the primary tumor, have the highest risk of lymph node metastases.

Disclosure of Interest: None declared

P0257 SURVIVAL AFTER OESOPHAGECTOMY FOR CANCER PRE- AND POST- COMPUTED TOMOGRAPHY- POSITRON EMISSION TOMOGRAPHY (CT-PET) INCEPTION

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Introduction: CT-PET is indicated and funded in the UK for staging potentially curable oesophageal cancers in order to identify those patients with occult distant metastases. It has become an integral component of the staging pathway. The aim of this study is to analyse the effect of CT-PET use on overall survival and assess the patterns of recurrence before and after CT-PET inception.

Aims & Methods: Consecutive 424 oesophagectomies performed for cancer [median age 62 (24-80) yr; 337 male; 360 Adeno, 64 Squamous cell carcinoma; 254 neoadjuvant therapy] were recorded in a prospectively-maintained database. 169 were performed after the routine use of CT-PET began. Primary outcome measure was overall survival based on intention to treat.

Results: Overall 5-year survival pre-CT-PET was 37%, post-CT-PET was 49% (Chi^2 4.991, df 1, $p < 0.025$). On multivariable analysis, pT stage (HR 1.497 [95% CI 1.344-1.667], $p < 0.001$) and pre- or post- CT-PET (HR 0.509 [95% CI 0.352-0.735], $p < 0.001$) were independently associated with survival. There were 119 (46.7%) recurrences in pre-CT-PET patients: 24.4% local; 58.8% distant; 16.8% both. Post-CT-PET patients had 33 (19.5%) recurrences: 27.3% local; 57.6% distant; 15.1% both.

Conclusion: The use of staging CT-PET independently improves overall survival in patients undergoing oesophagectomy for oesophageal cancer, although the patterns of recurrence remain unchanged.

Disclosure of Interest: None declared

P0258 SENTINEL NODE MAPPING BY USING A FLUORESCENT DYE AND VISIBLE RAY DURING LAPAROSCOPIC GASTRECTOMY FOR EARLY GASTRIC CANCER: RESULTS OF A PROSPECTIVE CLINICAL STUDY IN A SINGLE INSTITUTE

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Introduction: Sentinel node is defined as the first draining lymph node from the primary tumor, and sentinel node navigation surgery (SNNS) is a procedure in which the extent of surgery will be planned according to the metastatic status of sentinel node. Recently, SNNS has been investigated to avoid unneccesary extensive lympg node dissection in surgery for early gastric cancer (EGC). Various dyes and detecting methods were evaluated to acquire the accuracy of detecting sentinel nodes in SNNS for EGC.

Aims & Methods: The aim of this study is to investigatethe safety and feasibility of sentinel node mapping with a fluorescent dye and visible rayin the patients with gastric cancer.

Nineteen patients with gastric cancer, in whom laparoscopic distal gastrectomy with standard lymphadenectomy, were enrolled in this study. Before lymphadenectomy, they underwent endoscopic peritumoral injection of Fluorescein solution. The sentinel basin was investigated through inspecting the laparoscopic fluorescent imaging under a blue ray (wave length of 440-490 nm) emitted from a LED curing light.The detection rateand lymph node status were analyzed in the enrolled patients. In addition, short-term clinical outcomes were also investigated.

Results: Sentinel nodes were detected in18of 19enrolled patients (94.7%). Metastatic lymph nodes were found in two enrolled cases. These lymph nodes belonged to sentinel basin of each patients. Meanwhile, a patient (5.3%) underwent postoperative complication that had little relation with the sentinel node mapping. In all enrolled cases, nomortality was recorded.

Conclusion: The sentinel node mapping with visible light fluorescence was safe and effective at visualization of sentinel node. In addition, this method is superior than other fluorescent imaging techniques in visualizing the concrete correlation of sentinel node and surrounded structures.

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Disclosure of Interest: None declared

P0259 WHAT IS THE BEST PROCEDURE FOR T1 TUMORS OF ESOPHAGO-GASTRIC JUNCTION ?

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Introduction: There is still no consensus of surgical strategy for early stage tumor at esophago-gastric junction (EGJ). It is urgent issues to establish which stations of lymph node (LN) should be resected and to discuss which reconstruction is adequate for such patients that postoperative QOL is considered for their promised long-term survival.
Aims & Methods: The aim of this study is firstly to analyze our experienced 36 cases of pT1 EGJ tumor clinicopathologically and discuss appropriate LN resection fields and adequate reconstruction. Second is to introduce our novel reconstruction after lower esophagectomy and proximal gastrectomy, which is hand-sewn valvuloplastic esophagogastrostomy using ''double flap technique''.
This study included 36 patients with pT1 tumor from total 131 patients with EGJ tumors. LN stations are reviewed by Japanese classification of esophageal cancer 2nd English edition (1).
Results: A total of 36 patients, consisting of 28 with adenocarcinoma (AC), 6 with squamous cell carcinoma (SCC) and 2 with other subtypes were enrolled in the study. Location of tumors was E: 21, EG: 4, E=G: 2, GE: 4 and G: 5 patients. pT1b was noted in 27 patients and LN metastasis was observed in 13.9% (5/36). Lower mediastinal LN metastasis (#110) was observed in only 1 patient, who had sm3 tumor and 3cm of esophageal invasion (EI). Abdominal station (#1, #3) was observed in other 4 patients. Only 2 patients both of who were of subtypes tumors were died of the illness. One was a patient of malignant melanoma, who had 5 LNs metastasis in #1, #3 and was died of liver metastasis. The other was a patient of basaloid, who had vascular invasion without any LN metastasis and was died of liver metastasis and mediastinal recurrence after 48 months. 32 patients (88.9%) survived without any recurrence.
As consideration, pT1a was noted in 9 patients, suggesting the difficulty of preoperative accurate diagnosis. For tumors located mainly in G, LN dissection should be performed in stations conformed to the guideline of proximal gastrectomy (Japanese gastric cancer treatment guideline ver. 4), but for tumors located mainly in E #110 station should be resected in addition. With regard to prognosis, AC or SCC groups showed radical cure and will be expected long-term prognosis. For reconstruction, we have adopted the hand-sewn morphological and functional valvuloplastic esophagogastrostomy with ''double flap technique'' since 2011, which showed excellent clinical outcome without any medication for reflux esophagitis even when anastomosis was located in lower mediastinum. So far, as our department policy proximal gastrectomy with D1+ is standard and if EI is more than 2cm we performed intently #110 dissection in addition. Reconstruction is the ''double flap technique'' for first choice regardless of the anastomosis site.
Conclusion: In conclusion, in cT1 tumors it is important to set the appropriate LN dissection stations. In addition, since there is expectation of long-term prognosis, there also need to be considered suitable reconstruction for long-term postoperative QOL.

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Disclosure of Interest: None declared

P0260 ENDOSCOPIC TREATMENT OF GASTRIC ANASTOMOTIC LEAKS AND FISTULAS SECONDARY TO BARIATRIC SURGERY: SINGLE-CENTER EXPERIENCE

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Introduction: One of most feared complications of modern bariatric surgery is gastric anastomotic leak (GL). First-line treatment of leaks is external drainage collection and antibiotics. Treatment of the GL used clips, tissucol, Self-Expanding Metal endoprothesis (SEMS) and later pigtails. Endpoint of treatment is absence of contrast agent leakage on RX or CT.
Aims & Methods: We reviewed retrospectively 1794 cases of bariatric surgery performed in our hospital between 2008 and 2015 (Sleeve gastrectomy and Roux-en-Y gastric bypass). 19 patients were referred to gastro-enterologists for GL. Following treatments were used: SEMS exclusively (n:12), SEMS plus pigtails (n:1), SEMS then pigtails (n:2),double pigtails (n:3), clip (n:1).
Results: In SEMS group, the fistulas disappeared in most patients (12/13, 92.7%). In one patient, endoclip needed to be placed after removing the stent.
In the pigtails group, all patients responded (4/4,100%) to treatment.
Median hospitalization stay was 3.5 weeks in the SEMS group (n:13, 0.6-7.1w) and 1.1w in the pigtail group (n: 5, 1.1-4.42w).
Nineteen prosthesis (Ultraflex 3, Endoflex 11, Taewoong Medical 4, Life Partners Megastent (Barthet) 1) were used. Two patients were lost for follow up. Early migration occurred in 6/13 (46.1%) patients with SEMS. Longstanding nausea, vomiting, retrosternal pain and gastro oesophageal reflux occurred in more than half of patients with SEMS (8/13, 61.5%) vs none in the pigtail group (0/4).
Conclusion: SEMS are effective in treatment of GL. Tolerance is usually bad, especially after Sleeve gastrectomy. More recently, endoscopic placement of double pigtails was introduced for treatment of GL. Early results in selected patients are promising in terms of fistulas closure and tolerance. Further studies are required to confirm these preliminary results.
Disclosure of Interest: None declared

P0261 EVALUATION OF THE CLINICAL EFFICIENCY OF THE INTESTINAL BLOOD FLOW QUANTIFICATION BY USING INDOCYANINE GREEN (ICG) AS A NEAR-INFRARED FLUORESCENT IMAGING SYSTEM

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Introduction: Anastomotic leakage (AL) is one of the frequent complications in colorectal surgery. Although a principal factor of AL is thought to be vascular compromise, there is currently no accepted method to assess blood flow. To prevent AL, surgeons had to rely on the color of the intestine and the pulse of the marginal artery.
Aims & Methods: The aim of this study was to evaluate the clinical efficiency of the intestinal blood flow quantification by using indocyanine green (ICG) as a near-infrared fluorescent imaging system (NIFI). From May 2013 to April 2015, we enrolled patients who underwent low anterior resection (LAR). After 1.0 ml of ICG solution (2.5mg/ml) was injected intravenously by the anesthetist just before formation of the anastomosis, the blood flow was visualized in real time by NIFI.
Results: The median (range) age of the patients was 70 (38-81) years. The median (range) BMI was 23.7 (15.4-30.6) kg/m^2. Forty-six percent of patients were female. In all cases, the evaluation of the blood flow distribution of intestinal wall was clearly achieved. After ICG injection, median (range) time to visualize the blood flow was 35 (22-105) seconds. The occurrence of delay in the blood flow distribution to the anastomotic site compared to the proximal side of intestine was observed in 3 cases. In 2 of the 3 cases, revision of the intestinal transection point was done before formation of the anastomosis. In the other 1 case, AL due to bowel ischemia occurred.
Conclusion: The intestinal blood flow can be evaluated by ICG fluorescence by NIFI. The occurrence of delay in the blood flow distribution may cause AL due to ischemia. By using ICG fluorescence, intestinal ischemia of the anastomotic site of LAR might be avoided.
Disclosure of Interest: None declared

P0262 PASIREOTIDE IN DUMPING SYNDROME – RESULTS FROM A PHASE 2, INTERNATIONAL, MULTICENTRE STUDY

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Introduction: Dumping syndrome is a prevalent complication of gastric bypass surgery, characterised by early (cardiovascular and gastrointestinal response, along with rise in haematocrit [Ht] and pulse rate [PR]) and late (hypoglycaemia due to excess insulin) postprandial symptoms. Only a subset of patients (pts)

responds to treatment based on dietary measures, off-label use of acarbose and somatostatin analogues (SSA). Pasireotide (PAS), a next-generation SSA with high affinity to 4 of the 5 somatostatin receptor subtypes (sst), being a potent inhibitor of incretin and insulin secretion (via sst_2 and sst_5), prevents postprandial hypoglycaemia.

Aims & Methods: This is a single-arm, open-label, multicentre, intra-patient dose escalation, phase 2 study to evaluate the preliminary efficacy, safety and pharmacokinetics of PAS subcutaneous (s.c.) and long-acting release (LAR) in pts with dumping syndrome. The 6-month (mo) core period included a 3-mo s.c. phase followed by a 3-mo LAR phase. Eligible pts started treatment with PAS s.c. 50μg tid (before meals); dose could be increased by increment of 50μg up to 200μg tid based on the presence of hypoglycaemia (plasma glucose <60mg/dL) during an oral glucose tolerance test (OGTT) in the s.c. phase. In the LAR phase, pts received a fixed dose of PAS LAR 10 or 20mg based on the dose at the end of s.c. phase. Primary endpoint was the proportion of pts with no hypoglycaemia during an OGTT (ie, response rate [RR]) at the end of s.c. phase (mo 3). A RR of ≥50% was considered to be clinically relevant. Secondary endpoints included RR at the end of LAR phase (mo 6). The Ht levels and PR were evaluated at all OGTT time points.

Results: Of the 43 pts enrolled, 33 and 31 pts completed the s.c. and LAR phase, respectively. Main reason for discontinuation was adverse events (AEs; 11.6% [n = 5]). The RR in terms of prevention of hypoglycaemia was 60.5% (26/43; 95% CI: 44.4% > 75.0%) and 36.4% (12/33; 95% CI: 20.4% > 54.9%) in the s.c. and LAR phases, respectively. Notably, plasma glucose levels during OGTT were higher at all time points with s.c. dose vs baseline and vs LAR dose. Fewer pts had an increase in PR of ≥10 beat/min and an increase in Ht level of ≥3% (from pre-OGTT to 30 min post-OGTT) at mo 3 than at the baseline (18.6% vs 60.5% and 16.3% vs 27.9%, respectively). Overall, the most frequent (>15% of pts [N = 43]) AEs were headache (32.6%); diarrhoea, hypoglycaemia (25.6% each); abdominal pain (18.6%); upper abdominal pain and nausea (16.3% each). Grade 3/4 AEs occurred in 32.6% pts; most frequent (≥2 pts) were hypoglycaemia (9.3%); diarrhoea, upper abdominal pain, dizziness and small intestinal obstruction (4.7% each).

Conclusion: These results suggest that PAS s.c. effectively controls postprandial hypoglycaemia and improves changes in PR and Ht in pts with dumping syndrome. PAS s.c. and LAR were well tolerated; no new safety signals were identified in this population. A phase 3 study is warranted to confirm the effects of PAS in dumping syndrome.

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P0263 TRICLOSAN-COATED SUTURES FOR PREVENTION OF SURGICAL SITE INFECTION AFTER COLORECTAL CANCER SURGERY: A PROPENSITY SCORE-MATCHED RETROSPECTIVE STUDY

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Introduction: Colorectal surgery continues to have the highest rate of surgical site infections (SSIs) of all surgical procedures, accounting for 5–45% of all SSIs. Triclosan-coated sutures were developed to prevent bacterial colonisation of the suture material, and consequently to impair the local mechanisms of wound decontamination. We aimed to assess the effectiveness of triclosan-coated sutures used for skin closure on the rate of SSIs in colorectal cancer surgery.

Aims & Methods: We aimed to assess the effectiveness of triclosan-coated sutures used for skin closure on the rate of SSIs in colorectal cancer surgery. Until August 2012, our centre (Department of Gastroenterological Surgery, Fukuoka University Faculty of Medicine) used conventional methods for skin closure in colorectal cancer surgery. We were therefore able to retrospectively collect surveillance data from a 1.5 year period, which formed the control group. From September 2012, we began to use triclosan-coated polydioxanone antimicrobial sutures (PDS plus) for skin closure. We collected data for the study group from September 2012 until August 2013. Using propensity score matching, the control and study group cases were matched based on the following variables: patient age, sex, body mass index (BMI), medication use, complications, lifestyle-related factors, American Society of Anesthesiologists (ASA) physical status score as determined by an anaesthesiologist, type of surgery, operation time, quantity of blood lost, quantity of blood transfused, surgical wound classification, and method of skin closure. The baseline differences and selection bias were adjusted using the propensity score-matching method.

Results: A total of 374 colorectal cancer surgery patients were included in this study (control group, 221 patients; study group, 153 patients). Of all cases, 76 pairs were matched using the propensity score-matching method. Baseline patient characteristics were similar in the propensity score-matched groups. The incidence of SSIs within 30 days of the index operation, before matching, was 14.0% (31/221) in the control group and 7.2% (11/153) in the study group; the difference was statistically significant (p = 0.030). After matching, the incidence of SSIs was 23.7% (18/76) in the control group and 5.3% (4/76) in the study group; the difference was statistically significant (p = 0.001). Multivariable logistic regression analysis revealed that type of surgery was an independent factor affecting the incidence of SSIs prior to propensity score matching (p = 0.032). Emergent surgery (p = 0.017) and PDS plus (p = 0.002) were independent factors affecting the incidence of SSIs following propensity score matching.

Conclusion: Use of triclosan-coated sutures was associated with a significant decrease in the risk of SSIs following colorectal surgery.

Disclosure of Interest: None declared

P0264 THE IMPORTANCE OF BEING HONEST. METICULOUS REGISTRATION OF FOLLOW-UP DATA IN QUALITY REGISTERS INCREASE DATA VALIDITY - A STUDY OF 94185 CHOLECYSTECTOMIES

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Introduction: The Swedish national registry of gallstone surgery and endoscopic retrograde cholangiopancreatography, GallRiks, was founded in May 2005 and by the end of 2014 includes 98677 cholecystectomy registrations. The cholecystectomies are registered online by the surgeons immediately after surgery and then there is a 30-day postoperative follow-up (1). However, the hospitals participating in GallRiks have different complete 30-day follow-up frequencies.

Aims & Methods

Aim: The aim of our study was to analyze if these differences affect the frequency of reported adverse events.

Methods: 98677 cholecystectomy registrations were included. A total of 4492 registrations were excluded due to being non-index procedures, the cholecystectomy being part of major surgery or registrations with missing data. A total of 94185 cholecystectomies were included in the analysis (2.8% with complete 30-day follow-up of ≤90 (Group A) and 97.2% with a complete 30-day follow-up of >90% (Group B).

Results: The frequency of complete 30-day follow-up (≤90%) has increased somewhat from 0.2% (2005) to 4.1% (2014). The patients in Group A were somewhat older, included more urgent operations and slightly more males. The reported 30-day postprocedural adverse event rate was significantly less in Group A (OR 0.82; 95% CI 0.75-0.89) as well as the pancreatitis rate (OR 0.55; 95% CI 0.38-0.78) (Table 1). However, the perforation rate was significantly higher (OR 2.29; 95% CI 1.55-3.30) compared to Group B.

	Adverse events ≤90% 30d follow up vs. >90% 30d follow-up			
	Univariate		Multivariate	
	OR	95%CI	OR	95%CI
Intraprocedural	0.96	(0.85-1.09)	0.95	(0.84-1.07)
Postprocedural	**0.86**	(0.79-0.93)	**0.82**	(0.75-0.89)
Pancreatitis	**0.58**	(0.39-0.82)	**0.55**	(0.38-0.78)
Cholangitis	1.01	(0.54-1.73)	0.95	(0.51-1.62)
Bleeding	1.04	(0.81-1.32)	1	(0.78-1.27)
Perforation	**2.28**	(1.54-3.28)	**2.29**	(1.55-3.30)
Infection	1.09	(0.91-1.30)	1.04	(0.87-1.24)

Conclusion: The lower frequency of postoperative adverse events and pancreatitis in Group A could indicate that a lower frequency of 30-day follow-up registrations risk to miss cholecystectomies with adverse events whereas serious complications like perforation of the gut are seldom missed. The importance of a meticulous registration in quality registers in order to get valid data cannot be overstated.

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Disclosure of Interest: None declared

P0265 LONG-TERM FUNCTIONAL OUTCOME AND QUALITY OF LIFE AFTER RESTORATIVE PROCTOCOLECTOMY AND ILEAL - POUCH ANAL ANASTOMOSIS IN ULCERATIVE COLITIS PATIENTS

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Introduction: Restorative proctocolectomy with ileal-pouch anal anastomosis (IPAA) has become the surgical procedure of choice in patients with UC.

Aims & Methods: The aim of the study was to assess the long-term functional results and quality of life in those UC (n = 138) patients, who underwent IPAA from 1993-2013 in two Czech referral centers. In 129 of patients had been perfomed three-stage procedure, using stapled anastomosis. Qualite of life (QoL) was evaluated by using the Medical Outcome 36 item Health Survey, and Wexner Continence Grading Scale.The outcome of SF-36 item questionnaire has been compared with the Oxford study for the European. Statistical significance in all tests set to p,0.05, a Cronbachs alpha reliability of psychometrics tests was from 0.737-0.917.

Results: A total of 114 out of 119 pts completely answered the questionnaires. 62% of whom were male, a median of age (interquartile range) at proctocolectomy was 34 (27-44) years. During a median (range) follow-up of 7.9 (2.1–20.7) years. In 28% of these patients developed septic and/or obstructive and perianal complications. In 8.7% resp. 10.2% of patients anastomotic stricturae and complete fistula have been detected. Pouch failure occured in 7.9% of the patients and in 5.5% of pts '' re-do'' puche was done and in 2 pts continent ileostomy was done. One female patient developed carcinoma in IPAA seventeen months after poctocolectomy.

24% of pts developed at least one episode acute pouchitis, 15.0% had recurrent pouchitis. In majority of patients (63%) the median of functional outcome was 2 (0-4), according to the Wexner continence score. The median range of bowel moments was 5 (1-8) during the day, and 1 (0-3) at night. 24% had episodes of soiling, 11% urgency defecation, in 2/1.7% was seen true faecal incontinence. Nevertheless, 50% of patients occasionally had to change daily activities, and up to 62% of patients were taking antidiarrheal medications.

In patients after IPAA were observed slightly but significantly lower mean of QoL overall, and in five of eight SF-36 health dimensions than general population.The HRQoL was mainly impaired in the psychological and social areas and to a lesser degree in physical area. Physical Component Summary (PCS) and Mental Component Summary (MCS) were 46.37 and 46.55 (both are 50 in general population), respectively ($p < 0.001$). Patients with a certain degree of defecation function damage with a median Wexner score 9 (6-17) had a significantly lower quality of life in majority of dimensions of SF-36 than patients with perfect continence ($p < 0.001$). Regarding pouchitis in female significantly was affected all dimensions of MCS (median score 37, $p < 0.028$). On the other hand pts with perfect continence had normal QoL in all dimensions.

Conclusion: The ileal – pouch anal anastomosis in patients with ulcerative colitis confers a good quality of life. The majority of patients are fully continent. Subjective assessment of QoL and overall satisfaction was very high (98.3%).

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Disclosure of Interest: None declared

P0266 RESULTS OF ENDOSCOPIC DILATION OF ESOPHAGOGASTRIC ANASTOMOTIC STENOSIS

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Introduction: Esophagogastric anastomotic stenosis is the most common cause of dysphagia after esophagectomy with esophagogastroplasty for esophageal cancer.

Aims & Methods: To evaluate the results of endoscopic dilation therapy for esophagogastric anastomotic stenosis.

Retrospective analysis of prospectively collected database of patients who underwent subtotal esophagectomy for cancer and developed dysphagia due stenosis of the esophagogastric anastomosis, at the Cancer Institute of the University of São Paulo.

Results: From May 2010 to May 2014, a total of 32 patients were included, with dysphagia and stenosis of the esophagogastric anastomosis, and a median of 3 months after surgery (ranging from 0.5 to 19 months). Mean age was 58 years (range: 40 – 72 years), with male predominance (78.1%). Eight (25%) patients had fistulas or anastomotic leakage in the postoperative period. A 9.8mm endoscope could not traverse the stricture in 18 cases (56%). For endoscopic dilation, guidewire-assisted bougies (Savary-Gilliard; Wilson-Cook Medical) were used in 17 cases (56%), guidewire-assisted bougies or hydrostatic balloons (CRE-TTS, Boston Scientific) in 14 cases (43%), and hydrostatic balloons alone in 1 case. The maximum diameter of 16 mm was achieved in 31 patients (96%), with a median of 5 sessions per patient (range: 1 – 25 sessions per patient). There were no major complications, such as perforation or massive bleeding. Triamcinolone injections were performed in 22 cases (69%), with a mean of 2.1 sessions per patient (range: 1 – 5 sessions per patient), removal of sutures in 7 (22%), incisional therapy using electrocautery in 2 (6%), and placement of self-expanding metallic stent in 1 case. Therapeutic success rate, defined as clinical improvement without further dilation for a period of at least 6 months, was obtained in 28 patients (87.5%).

Conclusion: When patients undergoing esophagectomy and esophagogastric anastomosis develop symptomatic stenosis, they usually present dysphagia in the first 3 months after the operation. The endoscopic dilation carried out with bougies or balloons, associated with corticosteroid injection, is successful in almost 90% of the patients with no life-threatening related complications.

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Disclosure of Interest: None declared

P0267 RISK OF NEW-ONSET DIABETES AFTER PANCREATODUODENECTOMY: A SYSTEMATIC REVIEW

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Introduction: Resection is the only curative treatment option for patients with pancreatic and periampullary cancer. After pancreatoduodenectomy (PD) patients are at risk of developing new-onset diabetes mellitus (NODM). The exact risk of NODM after PD is relevant when counseling patients, but it is currently unknown since systematic reviews are lacking. The aim of this study is to determine the risk of new-onset diabetes mellitus (NODM) after pancreatoduodenectomy (PD) performed for benign and malignant diseases.

Aims & Methods: A systematic literature search was performed up to October 1st 2014 in PubMed, Embase (Ovid) and the Cochrane Library in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. All studies reporting on the incidence of NODM following PD for benign or (pre)malignant pancreatic or periampullary tumors were included. Studies of patients undergoing PD for chronic pancreatitis were excluded. Primary outcome was incidence of NODM.

Results: Of the 1863 studies identified, 13 studies (715 patients) fulfilled the eligibility criteria. Patients underwent PD for cancer (n = 602), benign disease (n = 62), or neoplasm from unclear origin (n = 51). The weighted mean percentage of NODM was 11.6% (±11.2). Only 4 studies, comprising 34 patients with NODM, reported the incidence of insulin-dependent diabetes mellitus (IDDM). The weighted mean post-PD percentage of IDDM among these patients with NODM was 20.5% (±6.02).

Conclusion: Incidence of NODM following PD for pancreatic or periampullary tumors is 11.6%. Routine postoperative screening for NODM seems advisable. More research into the risk of IDDM following PD is needed.

Disclosure of Interest: None declared

P0268 PERITONEAL IRRIGATION DOES NOT REDUCE RATE OF POST-OPERATIVE FORMATION OF INTRA-ABDOMINAL ABSCESS AFTER PERFORATED APPENDECTOMY

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Introduction: Annually 16,000 appendectomies are performed in the Netherlands. Although the overall rate of post-operative intra-abdominal abscess (PIAA) formation is small, there is a potential significant effect on mortality, morbidity, duration of hospital-admission and costs. Largest risk in developing PIAA is after perforated appendicitis (20%). Peritoneal-irrigation during surgery is frequently used as preventive procedure, however literature is lacking supporting evidence. The only available prospective study describes an increase of abscess-formation in a pediatric study-group. Primary objective of our study was to determine the efficacy of peritoneal-irrigation in perforated appendicitis on PIAA in adults.

Aims & Methods: All patients undergoing appendectomy for acute appendicitis from January, 2008, until December, 2013, were included in a database. Exclusion-criteria were age < 18yrs, incidental and interval-appendectomy. PIAA is used as primary outcome measure.

Results: 1163 of 1467 appendectomies were included. PIAA was diagnosed in 61 patients (5.2%). There were 245 (22.1%) appendix-perforations during surgery in which 37 patients (15.1%) developed PIAA, versus 24 of 917 patients in the non-irrigation group (2.6%). Between the peritoneal-irrigation and non-irrigation group were no significant differences in patient-characteristics. In the irrigation-group a greater risk in developing PIAA is shown versus non-irrigation (18.6% vs. 6.8%, OR 3.6, BI 0.9–13, p = 0.082). Additionally, irrigation is

associated with a longer hospital-admission, on an average of 1.7 days (OR 1.1, BI 1.0-1.4, P = 0.004).
Conclusion: Peritoneal-Irrigation during surgery in perforated appendicitis does not significantly reduce the rate PIAA formation in this retrospective study and probably increases the rate of this complication. Furthermore, patients in the irrigation group were admitted significantly longer.
Disclosure of Interest: None declared

P0269 STAGE APPROACH TO MEDICAL MANAGEMENT OF INTRA-ABDOMINAL HYPERTENSION

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Introduction: Intra-abdominal hypertension (IAH) may lead to the development of abdominal compartment syndrome (ACS) – potentially lethal complication. The experts proposed IAH/ACS medical management algorithm which on our point of view is something general (1).
Aims & Methods: The purpose of this study was to detail the stage approach to the management of IAH/ACS in the patients with general surgical pathology. The monitoring of intra-abdominal pressure (IAP) was performed by transbladder technique. In 7 operated patients (group 1) the volume of abdominal cavity was decreased by the abdominal wall surgery (5 – abdominoplasty, 2 – ventral hernioplasty). In 25 other patients (group 2) IAH was caused by the increase of the volume of abdominal content (14 – acute pancreatitis, 5 – paralytic ileus secondary to diffuse purulent peritonitis and in 2 – because of uremia and 4 – cirrhosis with progressive ascites). Taking into account that the rise of IAP always is a result of the disproportion of the ratio of the abdominal content volume to the volume of the abdominal cavity, management was focused on the decrease of the former or enlargement of the latter one. The first stage measures in the group 1 were focused on the improving of the abdominal wall compliance. In all patients receiving mechanical ventilation we started from the adjustment of the ventilator settings (decrease of tidal volume and increase of the respiratory rate). In parallel the adequacy of sedation and analgesia were checked, constricting dressings and bandages were removed. The same management was hold at the 1 stage in all patients of the group 2 on mechanical ventilation. But the main efforts were directed to reduce the volume of abdominal content. Thus in 8 non-operated patients of the group 2 with severe abdominal accumulations primary stage included their percutaneous drainage under ultrasound control. The main cause of the increase of the abdominal content volume in 15 patients was paralytic ileus. Here the first stage was focused on the evacuation of the gastro-intestinal content. If it was not effective, on the second stage enteral nutrition was minimized or even discontinued and fluid administration was optimized. The 3 stage treatment for these patients was neuromuscular blockade.
Results: The adjustment of the ventilator setting sand removing of compressive garments permitted to decrease IAP in 16 patients (including all patients of group 1) on 18.8 ± 2.6 mm H_2O. Thus there was no necessity to go to the next stage. But if abdominal wall compliance cannot be improved, neuromuscular blockade should be considered. Drainage of severe abdominal accumulations permitted to decrease IAP to less than 200 mm H_2O in 6 of 8 patients. In remaining 2 patients therapy was escalated to the second stage.
Conclusion: In 68.8% of cases it was enough the first stage measures to stabilize and decrease IAP. Described approach permitted to escape the decompressive laparostomy in 93.8% of patients without redundant manipulations.

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Disclosure of Interest: None declared

P0271 RISK OF THROMBOEMBOLIC DISEASE IN INFLAMMATORY BOWEL DISEASE

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Introduction: Patients with inflammatory bowel disease (IBD) are thought to be associated with an increased risk of developing venous thromboembolic (VTE) disease and arterial thombi (AT). There is conflicting data on the prevalence of VTE disease and AT in IBD, varying between 1.2% and 6.7% in clinical studies, which rises to 39% in postmortem studies. Our aims were to evaluate the rate and risk factors of VTE and AT in a large cohort of IBD patients.
Aims & Methods: We performed a retrospective review between the years 1984 to 2014 of all patients with IBD. These patients were identified from the IBD database and cross-referenced with the online electronic reporting system, patient notes and clinic letters.
Results: There were a total of 1678 patients with IBD, with 47 found to have VTE and AT, giving a prevalence rate of 2.8%. Of these 47 patients, 8 (17%) patients had recurrent disease with 6 (12.8%)patients having 2 incidents and 2 (4.2%) patients having 3 incidents of VTE disease. The median age was 60.2 years old with a greater risk for males than females (55% versus 45%) and with ulcerative colitis than Crohn's disease (2.8% versus 0.87%). A total of 6 patients were inpatients, unrelated to their IBD, and a diagnosis of VTE/AT was confirmed within 5 days of admission.
36 (2.1%) patients were diagnosed with deep venous thrombosis (DVT) and 20 (1.2%) with pulmonary embolism (PE). The remaining four had portal vein thrombosis, common femoral artery occlusion, femoral artery embolus and superficial femoral artery occlusion. Three patients were diagnosed with both DVT and PE in the same admission. The average duration from time of IBD diagnosis to VTE confirmation was 7.4 years. 5 patients were identified with VTE prior to their IBD diagnosis.
At the time of their diagnosis, 3 (5.3%) patients were treated for malignancy in the previous six months and 4 (7%) had undergone surgery in the previous four weeks. 32 (56%) patients were being treated with 5-aminosalicylic acid (5ASA) drugs, 17 (30%) with azathioprine, 12 (21%) with oral steroids, 4 (7%) with intravenous (IV) steroids, 2 (4%) had infliximab and 1 (2%) had adalimumab. Blood tests at time of diagnosis showed a median CRP of 46 and platelet count of 345. The mortality rate was 10.6%, of which one death was directly related to their VTE. 10.5% underwent surgery, 63% were anticoagulated and 1.8% underwent failed tissue plasminogen activator (TPA) therapy. 3.5% were left with a disability secondary to their VTE disease.
Conclusion: Thromboembolic disease is an increasingly prevalent and preventable complication of IBD. Positive risk factors identified in our cohort were patients that were male, increasing age and diagnosis of ulcerative colitis. Considering almost one third of those diagnosed were receiving oral or IV steroid therapy and had an average raised CRP, this supports the view that a disease flare is an ongoing risk factor for developing VTE and AT.

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Disclosure of Interest: None declared

P0272 ORAL ADMINISTRATION OF LACTOBACILLUS PLANTARUM 06CC2 ATTENUATES THE SEVERITY OF DEXTRAN SULFATE SODIUM-INDUCED COLITIS IN MICE

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Introduction: The dysbiosis of enteric microbiota cause host mucosal immune responses that result in gastrointestinal diseases such as enterocolitis.
Aims & Methods: In this study, we investigated the beneficial effect of *Lactobacillus plantarum* (*LP*) 06CC2 in dextran sulfate sodium (DSS)-induced colitis in C57BL6 mice. Heat-killed lyophilized *LP* 06CC2 was suspended in PBS. Two mice groups that had received DSS were orally administered PBS only (control group) or *LP* 06CC2 (LP group) by gavage for 15 consecutive days. We assessed the severity of colitis using a disease activity index, measured the colon length and weight, and colon tissue was examined macroscopically and histopathologically. We also collected colonic lamina propria mononuclear cells (LPMCs). The gene expressions of inflammatory cytokines (IFN-γ, IL-6, IL-12, TNF-α and IL-10) in LPMCs were determined.
Results: The body weight reduction in the LP group was significantly suppressed relative to the control group. The LP group demonstrated significantly lower disease activity index (1.5 ± 0.8 vs. 0.2 ± 0.3, respectively; $p < 0.05$) and pathology score (6.3 ± 1.5 vs. 3.8 ± 1.3, respectively; $p < 0.05$) compared to the control group. The LP strain significantly prevented foreshortening of the large intestine: the average colon length was 80 ± 8 mm in the LP group and 94 ± 7 mm in the control group ($p < 0.01$). IL-10 expression in colonic LPMCs was significantly higher in the LP group than the control group, although there was no significant difference of IFN-γ, IL-6, IL-12 expressions in LPMCs between two groups.
Conclusion: The *LP* 06CC2 strain attenuated colon inflammation by induction of IL-10 production in the colonic LPMCs.
Disclosure of Interest: None declared

P0273 ACTIVATION OF THE GCN2/EIF2ALPHA/ATF4 SIGNALING PATHWAY TRIGGERS AUTOPHAGY RESPONSE TO INFECTION WITH CROHN'S DISEASE-ASSOCIATED ADHERENT-INVASIVE ESCHERICHIA COLI

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Introduction: A high prevalence of the adherent-invasive *E. coli* (AIEC) in the intestinal mucosa of Crohn's disease patients has been shown. We previously showed that upon AIEC infection, autophagy is induced in host cells to restrain AIEC intracellular replication. The mechanism underlying such autophagy induction, however, remains largely unknown.
Aims & Methods: Here, we investigated the role of the GCN2/eIF2α/ATF4 pathway in autophagy response to AIEC infection. Autophagic activity was assessed by Western blot and immunofluorescent labelling of LC3. Intracellular bacterial number was determined by bacterial invasion assay and confocal microscopy. Binding of ATF4 to autophagy gene promoters was assessed by Chromatin immunoprecipitation (ChIP) assay. Wild type (WT) and GCN2

knockout (KO) mice were infected with an AIEC reference strain LF82 by gavage.
Results: Infection of human intestinal epithelial T84 cells with the AIEC LF82 strain activated the GCN2/eIF2α/ATF4 pathway as shown by increased phospho-GCN2 and phospho-eIF2α levels, enhanced ATF4 protein expression, and upregulated mRNA expression levels of ATF4 target genes. To explore the role of this pathway in host responses to AIEC infection, we used GCN2-deficient mouse embryonic fibroblasts ($GCN2^{-/-}$ MEF). GCN2 depletion suppressed eIF2α activation and inhibited the increase in ATF4 protein level induced by LF82 infection. mRNA expression levels of the autophagy genes *p62*, *MAP1lc3*, *Beclin1*, *atg3* and *atg7* were significantly increased in WT MEF upon LF82 infection, and this was blocked in $GCN2^{-/-}$ MEF. ChIP assay showed that GCN2 depletion inhibited the LF82-induced binding of ATF4 to the promoters of these autophagy genes. Consequently, autophagy induction upon LF82 infection was suppressed in $GCN2^{-/-}$ MEF, leading to increased LF82 intracellular replication and elevated pro-inflammatory cytokine production, compared to WT MEF. *In vivo* study consistently showed that LF82 infection activated the GCN2/eIF2α/ATF4 pathway in enterocytes from WT mice, but not GCN2 KO mice. In response to AIEC infection, autophagy was induced in WT mouse-derived enterocytes, and this was not observed in KO mice. LF82 persistence in the gut was increased in KO mice, leading to aggravated intestinal inflammation, compared to that in WT mice. Depletion of GCN2 did not affect susceptibility of mice to DSS-induced colitis, indicating that the effects obtained were not a consequence of inflammation and were specific for AIEC infection.
Conclusion: The GCN2/eIF2α/ATF4 pathway is activated in host cells during AIEC infection, which is served as a defense mechanism to induce a functional autophagy to control AIEC intracellular replication.
Disclosure of Interest: None declared

P0274 EPIGENETIC MECHANISMS OF AIEC-RECEPTOR CEACAM6 REGULATION IN CROHN'S DISEASE: CHROMATIN REMODELLING AND MICRO-RNA SIGNATURES

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Introduction: Abnormal expression of CEACAM6 is observed at the apical surface of the ileal epithelium in Crohn's disease (CD) patients. This allows Adherent-Invasive *Escherichia coli* (AIEC) to colonize gut mucosa, leading to development of inflammation. Our aims were to understand the regulation of *CEACAM6* expression in CD ileal mucosa and to investigate epigenetic mechanisms involved in *CEACAM6* overexpression during AIEC infection.
Aims & Methods: HIF-1α and histone H3 Serine 10 phosphorylation (H3S10p) levels were measured in *CEACAM6* promoter region by chromatin immunoprecipitation (ChIP). MicroRNAs (miRNAs) that potentially target CEACAM6 were predicted by in silico algorithms. MiRNA levels in human intestinal epithelial T84 cells were measured using quantitative reverse-transcription polymerase chain reaction (qRT-PCR). Luciferase assays were used to assess binding of predictive miRNAs to the 3'-untranslated region (3'-UTR) of *CEACAM6* mRNA. Effect of transfection of predictive microRNA precursors on *CEACAM6* expression in T84 cells was analyzed by Western blot. Impact of AIEC infection on miRNA levels in T84 cells was analyzed by qRT-PCR.
Results: Higher expression of CEACAM6 was observed in T84 cells compared to Caco-2 cells. This was associated with high binding of HIF-1α on the *CEACAM6* gene promoter in an open chromatin state region characterized by increased H3S10 phosphorylation level. In contrast, Caco-2 cells expressed low levels of CEACAM6 due to a compact chromatin state in *CEACAM6* promoter (low level of H3S10p). AIEC infection led to an increase in CEACAM6 expression related to enhance HIF-1α binding to CEACAM6 promoter. Abnormal H3S10 phosphorylation in *CEACAM6* promoter following AIEC infection enhanced HIF-1α binding and subsequent *CEACAM6* expression. Moreover, *in silico* analysis predicted several miRNAs that are potentially able to regulate *CEACAM6* expression. Luciferase reporter assays showed that among the predictive miRNAs, 11 hsa-miRNAs (in particular 29a-3p, 424-3p and 489-3p) directly bound to the 3'-UTR of *CEACAM6* mRNA. Interestingly, expression of some of these miRNAs was altered after AIEC infection.
Conclusion: This study suggests that AIEC bacteria have the ability to modulate gene expression in the host cell for their own benefit by altering different epigenetic marks as miRNA expression profile and histones post-translational modifications enhancing CEACAM6 abnormal expression. Thus, epigenetic pathways could be new targets to prevent AIEC colonization and AIEC-induced inflammation in CD patients.
Disclosure of Interest: None declared

P0275 VITAMIN D POTENTIATES THE IMMUNOSUPPRESSIVE EFFECT OF ANTI-TNF INDUCED MACROPHAGES

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Introduction: We have previously shown that anti-TNF treatment of mixed lymphocyte reactions (MLR) results in the induction of macrophages with immunosuppressive and wound healing properties. In patients who respond to IFX treatment, the number of these macrophages increases significantly in the intestine. In contrast, no increase is seen in non-responders, indicating the clinical importance of this cell population. Because Vitamin D has an immunosuppressive effect on immune cells, we wanted to determine the role of vitamin D in anti-TNF induced macrophages. The aim of this study was to determine if the Vitamin D receptor pathway was activated in anti-TNF induced macrophages and if Vitamin D can potentiate immunosuppressive effect of these macrophages.
Aims & Methods: Peripheral blood mononuclear cells (PBMC) were isolated from peripheral blood of healthy donors. MLR were established by co-culturing PBMC of two healthy donors in a 1:1 ratio. Cultures were treated with anti-TNF to induce anti-TNF induced macrophages. IFN- γ induced macrophages were generated by culturing monocytes in the presence of IFN-γ. Gene expression of anti-TNF compared to IFN-γ induced macrophages was determined by microarray or by real-time PCR. Protein expression of the Vitamin D receptor (VDR) was determined by western blot.
To determine the effect of Vitamin D on IFN-γ and anti-TNF induced macrophages cell culture experiments were performed in the presence or absence of 1.25-dihydroxyvitamin D.
Anti-TNF induced macrophages were isolated with CD14 microbeads and co-cultured with activated T-cells from a third donor. Subsequently T-cell proliferation was measured by 3H thymidine incorporation.
Results: Anti-TNF induced macrophages displayed increased expression of a number of components of the vitamin D receptor pathway including the transcripts for VDR, Osteopontin and the Retenoid X receptor. In line with this, anti-TNF induced macrophages showed increased VDR protein expression compared to IFN-γ induced macrophages, confirming the results of the micro array. Furthermore anti-TNF induced macrophages showed increased expression of the VDR response gene cathelicidin antimicrobial peptide after treatment with 1.25-dihydroxyvitamin D. Indicating increased capacity to respond to Vitamin D.
In order to determine if Vitamin D could enhance the immunosuppressive effect of anti-TNF induced macrophages, macrophages were generated in the presence of the active metabolite of vitamin D. Addition of active vitamin D did not alter the number of regulatory macrophages. However anti-TNF induced macrophages generated in the presence of 1.25-dihydroxyvitamin D did show an increased capacity to inhibit of T-cell proliferation.
Conclusion: Anti-TNF induced macrophages show an increased activation of the vitamin D receptor pathway. The immunosuppressive properties of anti-TNF induced macrophages can be potentiated by 1.25-dihydroxyvitamin D.
Disclosure of Interest: A. Levin: None declared, M. Wildenberg: None declared, P. Koelink: None declared, F. Bloemendaal: None declared, G. D'Haens Conflict with: has served as speaker, consultant, and principal investigator for Abbott/AbbVie, AM Pharma, Centocor/Janssen Biologics, Engene, Photopill, Setpoint, Novo Nordisk, MSD, UCB, Takeda, TEVA, Millenium, Boehringer Ingelheim, Elan, Ferring Pharmaceuticals, Dr Falk Pharma, Shire, Cosmo, AstraZeneca, GSK, and PDL., G. Van den Brink Financial support for research: PPM services, Crucell and AbbVie, Lecture fee(s): AbbVie, Merck Sharp & Dohme, and Ferring Pharmaceuticals, Consultancy: AbbVie

P0276 THE AUTOPHAGY-RELATED PROTEIN CATHEPSIN S IS ESSENTIAL FOR THE INDUCTION, VIABILITY AND M2 PHENOTYPE OF ANTI-TNF INDUCED MACROPHAGES

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Introduction: We have previously shown in vitro and in vivo that anti-TNFs induce macrophages with immunosuppressive and wound healing properties. These macrophages express the M2 macrophage phenotype marker CD206. Furthermore anti-TNF induced macrophages have increased levels of autophagy and our in vitro studies have shown that the presence of the wild type allele of *ATG16L1* is associated with an increase of anti-TNF induced macrophages. The aim of this study was to further understand the effect of autophagy on anti-TNF induced macrophages.
Aims & Methods: In order to generate anti-TNF induced macrophages mixed lymphocyte reactions (MLR) were performed with peripheral blood mononuclear cells from healthy donors in the presence of anti-TNF. Anti-TNF induced macrophages were isolated by magnetic bead separation using CD14+ microbeads. IFN-γ induced macrophages were generated by culturing human monocytes in the presence of IFN-γ. Expression profile of 84 autophagy related transcripts was determined by real-time PCR array. Protein expression for Cathepsin S was determined by western blot. CD206 expression was determined by flow cytometry and viability was determined by MTS assay.
Results: Anti-TNF-induced macrophages had a different expression profile of autophagy-related transcripts compared to macrophages induced with IFN-γ. Interestingly Cathepsin S was highly upregulated in the anti-TNF-induced macrophages. Because Cathepsin S is a lysosomal protease that has previously been shown to induce M2 polarization in an autophagy dependent manner, we wanted to further study the effect of Cathepsin S on anti-TNF-induced macrophages.
Anti-TNF-induced macrophages showed increased Cathepsin S protein expression compared to IFN-γ-induced macrophages, confirming the results of the RNA array. We then tested the functional role of Cathepsin S in these macrophages. Addition of Cathepsin S inhibitor abrogated the capacity of anti-TNF to induce CD206+ macrophages. Furthermore anti-TNF-induced macrophages isolated from MLR and subsequently cultured in the presence of Cathepsin S inhibitor showed decreased viability and decreased expression of the M2 phenotype marker CD206.

Conclusion: The autophagy-related protein Cathepsin S is highly expressed in anti-TNF-induced macrophages and is essential for the induction, viability and M2 phenotype of anti-TNF-induced macrophages.
Disclosure of Interest: A. Levin: None declared, P. Koelink: None declared, F. Bloemendaal: None declared, C. Vos: None declared, G. D'Haens Conflict with: has served as speaker, consultant, and principal investigator for Abbott/AbbVie, AM Pharma, Centocor/Janssen Biologics, Engene, Photopill, Setpoint, Novo Nordisk, MSD, UCB, Takeda, TEVA, Millenium, Boehringer Ingelheim, Elan, Ferring Pharmaceuticals, Dr Falk Pharma, Shire, Cosmo, AstraZeneca, GSK, and PDL., G. Van den Brink Financial support for research: PPM services, Crucell and AbbVie, Lecture fee(s): AbbVie, Merck Sharp & Dohme, and Ferring Pharmaceuticals, Consultancy: AbbVie, M. Wildenberg: None declared

P0277 INFLIXIMAB PROMOTES MEGAKARYOCYTE DEVELOPMENT AND PRO-PLATELET RELEASE IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory disorders of the small intestine and colon. Tumor necrosis factor (TNF)-a mediates multiple pro-inflammatory signals and plays a central role in the pathogenesis of IBD. The monoclonal anti-TNF-a antibody infliximab is effective in the induction and maintenance of clinical remission in patients with IBD. Therefore, we studied the *in vitro* effect of infliximab on megakaryocyte development and pro-platelet release in IBD
Aims & Methods: Blood samples were collected from five clinically active IBD patients (two with CD and three with UC; males n = 3; mean age 38.2 yrs, range 24-64). CD45 positive cells were separated by immunomagnetic selection and cultured for two weeks in the presence of 10 ng/mL thrombopoietin together with eitgher 10 mg/mL infliximab or its isotype control (human IgG1). At the end of the culture, CD61 positive megakaryocytes and pro-platelet-forming megakaryocytes were analyzed by flow cytometry. Blood samples were also collected from five IBD (4 males, mean age 38 yrs, min 25 yrs, max 71 yrs) patients before and after 6 weeks of infliximab treatment at the dose of 5 mg/kg administered at week, 0, 2 and 6.
Results: No significant difference in *in vitro* megakaryocyte differentiation was observed in cultures stimulated with either infliximab or IgG1. However, mature megakaryocytes exhibited a significantly ($p < 0.001$) higher capacity in releasing pro-platelets in the presence of infliximab compared to megakaryocytes cultured in the presence of IgG1. Furthermore, hematopoietic progenitor cells derived from the blood of IBD patients after *in vivo* infliximab treatment showed a significantly ($p < 0.05$) higher *in vitro* differentiation in megakaryocytes in comparison to cells collected before the infiximab treatment.
Conclusion: These findings showed that infliximab promotes *in vitro* pro-platelet release in IBD patient-derived megakaryocyte cultures. Further experiments are needed to clarify whether the infliximab-induced development of pro-platelets might have a role in the wound-healing process sustained by the anti-TNF-a treatment.
Disclosure of Interest: None declared

P0278 COMPARISON OF GEBOES SCORE AND SIMPLIFIED GEBOES SCORE WITH MAYO ENDOSCOPIC SUBSCORE IN PATIENTS WITH RECENT DIAGNOSIS OF ULCERATIVE COLITIS: A RETROSPECTIVE STUDY

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Introduction: The Geboes Score (GS) is the most commonly used histological score in ulcerative colitis (UC).[1] A Simplified Geboes Score (SGS) that only includes variables linked to active inflammatory disease has been proposed in a previous study.[2] The aim of this study was to compare both scores, and to assess their correlation with the endoscopic findings in patients recently diagnosed with UC and followed up over 5 years.
Aims & Methods: Patients diagnosed with UC between 2005 and 2010, and who had serial endoscopies and biopsies, were retrospectively included. The 5-year histological evolution after diagnosis was recorded. Endoscopic results were recorded based on Mayo Endoscopic Subscore. Histological activity was scored by an experienced pathologist with the GS and the SGS. Conversions were constructed to compare endoscopic/histological scores: 2 conversions from the GS based on the results of a previous study (conversions 3 and 9) and 3 conversions from the GSG were tested, combining grade 1 and 2 (conversion 1), grade 2 and 3 (conversion 2), and grade 3 and 4 (conversion 3) of SGS.[3]
Results: We analysed 339 colonoscopies and their corresponding biopsies obtained from 103 patients with UC (51% women, mean age 40). Twenty-nine (28%) patients had proctitis, 46 (45%) left-sided colitis, and 28 (27%) extensive colitis. Forty (12%) colonoscopies presented Mayo 0, 74 (22%) Mayo 1, 107 (31%) Mayo 2, and 117 (35%) Mayo 3. A comparison of endoscopic and both histological scores of the 339 colonoscopies was performed (see Table). Patients in endoscopic remission (Mayo 0) presented with active microscopic disease (≥ Grade 3.1) in 23% of cases and those with Mayo 1 in 84%. The correlation analysis between endoscopy and both GS and SGS assessed by Kendall rank correlation coefficient (kendall τ, p value) did not show significant differences between the 2 histological scores: GS-conversion 3 (0.51, <0.001), GS-conversion 9 (0.51, <0.001), SGS-conversion 1 (0.48, <0.001), SGS-conversion 2 (0.48, <0.001), and SGS-conversion 3 (0.48, <0.001).

GEBOES S.		Mayo 0	Mayo 1	Mayo 2	Mayo 3	Total
Grade 0	**0.00.10.20,3**	91300	3300	0000	0000	121600
Grade 1	**1.11.21.3**	800	600	200	100	1700
Grade 2	**2.12.22.3**	100	000	100	000	200
Grade 3	**3.13.23.3**	200	100	300	100	700
Grade 4	**4.14.24.3**	000	101	111	000	212
Grade 5	**5.15.25.35.4**	5101	2523101	3334301	21284621	84868624
SIMPLIFIED GEBOES S.		Mayo 0	Mayo 1	Mayo 2	Mayo 3	Total
Grade 0		30	12	2	1	45
Grade 1	1.11.2	00	00	00	00	00
Grade 2	2.12.2	10	00	10	00	20
Grade 3	3.13.2	20	10	30	10	70
Grade 4	4.14.24.34.4	0601	147121	267311	0494621	31698924
Total		40	74	107	118	339

Conclusion: The assessment of histological activity based on the original GS and the SGS in a population of recently diagnosed active UC patients was comparable. Further validation should be performed in order to replace the original Geboes Score with the Simplified Geboes Score for the assessment of histological activity in UC patients' biopsies.

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Disclosure of Interest: None declared

P0279 PREDICTIVE FACTORS OF BONE LOSS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Patients with Inflammatory Bowel Disease (IBD) are at increasing risk of developing disorders in bone and mineral metabolism. Osteopenia and osteoporosis are frequent but often underestimated complications in these patients. Several factors could contribute to osteopenia, but the pathogenetic mechanisms are still not completely understood. The aim of this study is to assess the prevalence and the risk factors associated with bone loss in IBD patients.
Aims & Methods: We conducted a retrospective study from January 2007 to June 2012, including all patients with IBD who attended our department. Bone mineral density (BMD) was measured with diphotonic x-ray absorptiometry of the lumbar spine and the neck of the left femur. Results were expressed as T score (osteopenia: -2.5 standard deviation (SD) < T < -1 SD, osteoporosis: T < -2.5 SD) according to the World Health Organization (WHO).
Results: 146 patients with IBD were included, 105 had Crohn's disease (CD) (71.9%), and 41 had ulcerative colitis (UC) (28.1%). The average age at diagnosis was 33.18 years [18-46]. BMD was normal in 61 patients (41.8%) and reduced in 85 patients (58.2%). 57 cases had osteopenia (39%) and 28 patients had osteoporosis (19.2%). In patients with Crohn's disease, 60% of cases (63/105) had reduced BMD (osteopenia in 39 cases and osteoporosis in 24 cases). 53.6% of patients with UC (22/41) had reduced BMD (osteopenia in18 cases and osteoporosis in 4 patients). The univariate analysis showed a statistically significant relationship between bone loss and age over 38 years (0.032), an active tobacco consumption (0.049), low calcium intake ($p = 0.0001$), reduced physical activity ($p = 0.024$), a lower body mass index, particularly below 20 kg / m2 ($p = 0.033$), elevated markers of inflammation ($p = 0.003$), a duration of disease over 12 months (0.049), the extent of disease (0.001), and active disease (0.016), total duration of corticosteroids consumption over 12 months ($p = 0.02$), and a cumulative dose of corticosteroids > 4.5 g of Prednisone ($p = 0.001$). In multivariate analysis, the following factors were independently predictive of bone loss: limited physical activity ($p = 0.013$), body mass index < 20 kg / m2 (0.015), active disease ($p = 0.035$), the extent of the disease ($p = 0.006$), and a cumulative dose of corticosteroid exceeding 4.5g of Prednisone ($p = 0.003$).

Conclusion: Bone loss and osteoporosis are commonly reported in patients with IBD. Bone mineral density screening must be conducted systematically for patients with IBD with greater risk related to reduced physical activity, body mass index < 20 kg / m2, active disease, extensive disease, and a cumulative dose of corticosteroids > 45g.
Disclosure of Interest: None declared

P0280 ROLE OF RAGE DURING INTESTINAL INFLAMMATION AND ITS THERAPEUTIC POTENTIAL IN IBD

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Introduction: Inflammatory bowel diseases (IBD) are chronic and relapsing, life-long diseases of the gastrointestinal tract. Environmental factors which have a crucial role in the development of these diseases remain largely unknown. Few studies have described Advanced Glycation End-Products (AGE) as potential contributors of intestinal inflammation, and the role of AGE and their receptor RAGE in the pathophysiology of IBD are not yet fully elucidated.
Aims & Methods: The global aim of our study was to address the link between AGE, RAGE, and IBD which might help to better understand the role of nutrition, as a major source for AGE, in the pathophysiology of IBD.
Three different models of intestinal and colonic inflammation (indomethacin, dextran sodium sulfate (DSS) and trinitro benzene sulfonic acid (TNBS)) were induced in C57BL/6 wild type (WT) and RAGE null mice. In a second set of experiments, mice were orally administered with the food derived ligand for RAGE, carboxymethyllysine-bovine serum albumin (CML-BSA) or control BSA for 30 days; then, intestinal and colonic inflammation were induced. Severity of inflammation was evaluated using macroscopic, histologic and molecular parameters in the small intestine and colon of mice.
Results: Following indomethacin administration, a significant decrease in ulcerations number and area was observed in the duodenum, jejunum and ileum of RAGE null mice compared to WT mice. Consistently, *IL1b* mRNA levels were significantly decreased in the three intestinal segments. RAGE null mice were protected from DSS- and TNBS-induced colitis, with a significant decrease of clinical and macroscopic parameters. Myeloperoxidase (MPO) activity, reflecting the neutrophil infiltration, was also significantly reduced in the colon of TNBS-treated RAGE null mice compared to TNBS- treated WT mice. *IL1b* and *iNOS* mRNA expression were significantly decreased in colitic RAGE null mice compared to colitic WT mice. Chronic BSA-CML administration to mice worsened indomethacin-induced enteritis, as evidenced by a significant increase in ulcerations number and area in the duodenum, jejunum and ileum compared to control BSA-treated mice. Consistently, MPO activity and oxidative stress assessed by anion superoxide dosage were significantly increased in the ileum of CML BSA-treated mice compared to control BSA-treated mice. Chronic CML-BSA administration did not induce any effect on colonic inflammation.
Conclusion: We demonstrated that RAGE signaling pathway is implicated in intestinal and colonic inflammation in mice. We showed that BSA-CML might be a dietary factor involved in intestinal inflammation. The role of RAGE and AGE in IBD now merits further investigations.
Disclosure of Interest: None declared

P0281 CASP8 INHIBITION IN CD4+ T CELLS BLOCKS CHRONIC INTESTINAL INFLAMMATION

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Introduction: Caspase 8 (CASP8) is an aspartate-specific cysteine protease that has been recently linked to inflammatory bowel diseases (IBD), and CD4+ T cells are well-known key players influencing the perpetuation of mucosal inflammation in IBD patients. Previous work identified CASP8 as a central regulator of T cell fate decisions which can exert pro– as well as anti-inflammatory effector functions depending on the cellular and molecular context.
Aims & Methods: The T cell-specific role of CASP8 during intestinal inflammation has not been clarified yet. To address that topic, we have analyzed the potency of FACS-sorted naïve CD4+ T cells from several genetically modified mouse strains to induce intestinal inflammation in the adoptive transfer model of chronic colitis. Serial inspections of colonic inflammation were performed in vivo by mini-endoscopy. In addition, histopathological analyses and immunofluorescence studies were done in colon cross-sections, and immunomonitoring was performed by FACS in lamina propria and mesenteric lymph node cells.
Results: Interestingly, CASP8 deficient T cells failed to induce intestinal inflammation, produced decreased levels of pro-inflammatory cytokines and showed diminished accumulation in immunocompromised hosts, despite being highly resistant to Fas induced apoptosis. Co-transfer of congenic wildtype T cells demonstrated that the CASP8-deficient T cell population expanded less efficiently under the same in vivo conditions as wildtype cells. Additional genetic deletion of RIPK3, but not ATG7 fully restored the colitogenicity of CASP8 deficient T cells, indicating that T cell necroptosis represents a key mechanism for the blockade of intestinal inflammation. Moreover, we could show that pro-inflammatory human T cells from IBD patients can be targeted via RIPK3-RIPK1-kinase-dependent necroptosis.
Conclusion: Our study demonstrates a critical role of CASP8 in CD4+ T cells during chronic intestinal inflammation. Thus, the blockade of CASP8 and induction of necroptosis in CD4+ T cells might emerge as a novel therapeutic strategy for IBD patients.
Disclosure of Interest: None declared

P0282 DENDRITIC CELL COMPARTMENTALIZATION IN THE HUMAN INTESTINAL GUT IN HEALTH AND CROHN'S DISEASE

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Introduction: Human intestinal dendritic cells (DC) maintain a balance between tolerance to nutrients/commensals and immunogenicity against pathogens. Changes in intestinal DC properties are found in inflammatory bowel diseases including Crohn's disease (CD). Most studies, however, do not consider DC compartmentalization through the human gut. Here we studied whether DC subsets and phenotype change through the human gut in healthy controls (HC) and CD patients.
Aims & Methods: Paired biopsies from human proximal colon and the terminal ileum (TI) were obtained from HC and CD patients. DC were identified following collagenase digestion where DC phenotype were assessed by flow cytometry. Antigen presenting cells ($CD45^+HLA\text{-}DR^{high}$) were identified within single viable cells. Discrimination between DC and Mϕ was subsequently performed based on lineage marker expression (CD3,CD14,CD16,CD19,CD34) and side scatter properties of the cells identifying DC as $CD45^+HLA\text{-}DR^+lineage^-complexity^{low}$. DC were further distinguished from Mϕ as $CD64^-$ with CCR7 up-regulation following overnight culture.
Results: In all samples, intestinal DC were myeloid (mDC, $CD11c^+$) and were further divided into different subsets based on CD103 and SIRPα expression. $CD103^-SIRPa^+$ and $CD103^+SIRPa^+$were type 1 immature mDC ($CD1c^+CD141^-ILT3^+$) while $CD103^+SIRPa^-$ were type 2 mature mDC ($CD1c^-CD141^+ILT3^-$). CCR2 was expressed in all $CD103^-SIRPa^+$ DC, with expression being variable on $CD103^+SIRPa^+$and absent on $CD103^+SIRPa^-$ DC. In HC, total DC numbers were higher in the proximal colon compared with the TI with no differences in the CD103/SIRPα DC subset composition between compartments. However, the TI from HC carried higher numbers of $CCR2^+$DC and $CD11c^{dim}CD1c^-$ DC.
In CD patients compared with healthy controls, DC numbers were higher in both the colon and the TI and displayed a specific reduction of $CD103^+SIRPa^+$ DC in both tissues. CCR2 expression on ileal and colonic DC did not differ between HC and CD. In CD, however, the proportion of ileal $CD11c^{dim}CD1c^-$ DC was lower in CD patients than in HC, an effect that was not seen in the proximal colon. Finally, TLR2 and TLR4 expression were higher in both the colon and TI from CD patients, compared with the healthy matched tissue, due to a specific up-regulation of $CD11c^+CD1c^+$DC.
Conclusion: DC subsets and phenotype change through the length of the human gastrointestinal tract and display different tissue-specific alteration in CD patients. Tissue compartmentalization is, therefore, likely to affect the results of studies addressing the immune system of the human gut, both in health and disease.
Disclosure of Interest: None declared

P0283 EVALUATION OF HUMORAL IMMUNE RESPONSE TO CLOSTRIDIUM DIFFICILE INFECTION IN INFLAMMATORY BOWEL DISEASES

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Introduction: Disorder of intestinal microbes is thought to play a critical role in the pathogenesis of inflammatory bowel diseases (IBD). Evaluation of bacterial Ig could become a new approach to judge the situation of this disease.
Aims & Methods
Aim: to evaluate IgA, IgM and IgG levels to *Clostridium difficile* infection (CDI) in patients with IBD.
Methods: We prospectively included 147 pts with IBD – 92 pts with ulcerative colitis (UC) (87 in exacerbation and 5 in remission), 55 pts with Crohn's disease (CD) (44 in exacerbation and 11 in remission) and 30 healthy controls. Concentrations of IgA, IgM and IgG to lipopolysaccharide of CDI were evaluated by immunoassay. Mean age in UC was 38.18 ± 1.23 years, CD – 28.04 ± 2.11 and in control group – 30.13 ± 1.53. Severity of UC was assessed by Mayo score: mild – 28 (32.2%), moderate – 43 (49.4%), severe – 16 (18.4%). Severity of CD was assessed CDAI: mild – 15 (34%), moderate – 16 (36.4%), severe – 13 (29.6%).

Results: There was increasing of IgA, IgM and IgG levels to CDI in UC and CD compared to controls (Table 1).

Table 1: IgA, IgM and IgG levels to *Clostridium difficile* infection

	Ig A	Ig M	Ig G
control group	0.009 ± 0.005	2.99 ± 0.4	1.76 ± 0.27
exacerbation of UC	0.017 ± 0.003	5.46 ± 0.41***	6.49 ± 1.13***
remission of UC	0.06 ± 0.05	5.77 ± 2.09	6.05 ± 3.17
exacerbation of CD	0.02 ± 0.003**	6.09 ± 0.79**	8.74 ± 2.0***
remission of CD	0.12 ± 0.002	4.36 ± 1.06	5.83 ± 3.11*

*$p < 0.01$ v. control, **$p < 0.005$, ***$p < 0.001$

Immune response to CDI correlated with clinical parameters of IBD: in CD with IgM increasing faeces were more loose ($r = –0.29$; $p < 0.05$); in UC the increasing of IgA to CDI correlates with defecation rate decreasing ($r = -0.23$; $p < 0.05$), loosing of faeces ($r = -0.27$; $p < 0.05$), less weight loss ($r = -0.26$; $p < 0.05$). There is higher level of IgG to CDI in older patients with UC ($r = 0.24$; $p < 0.05$). In UC the increasing of IgA to CDI correlates with gamma-globulin blood level ($r = 0.31$; $p < 0.05$), alpha 1-globulin level increases with increasing of IgG to CDI ($r = 0.30$; $p < 0.05$).

Conclusion: The majority of pts with active IBD have increased IgM and IgG levels to CDI compared to control. Antibodies changes correlated with IBD clinical features and laboratory data.

Disclosure of Interest: None declared

P0284 ACTIVATION OF NLRP3 INFLAMMASOME IN INFLAMMATORY BOWEL DISEASE: DIFFERENCES BETWEEN CROHN'S DISEASE AND ULCERATIVE COLITIS

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Introduction: NLRP3 inflammasome is a multimolecular cytosol complex that when activated contributes to the cleavage of pro-interleukin (IL)-1β to IL-1β via caspase-1 activation[1]. NLRP3 activation can derive from both organic and inorganic substances and has been described to have in a variety of auto-inflammatory disorders. Evidence for a role of systemic NLRP3 activation in inflammatory bowel disease (IBD) is still lacking. Herein, we present the final results of our study on inflammasome activation in IBD; prelimenary results were presented at UEGW 2013[2].

Aims & Methods: Human peripheral blood mononuclear cells (PBMCs) were isolated from 20 Crohn's disease (CD) patients, 21 ulcerative colitis (UC) patients and 17 controls after gradient centrifugation of heparinized whole blood over Ficoll. PBMCs were stimulated at a density of $5x10^6$/ml with 10 and 0.1ng/ml of the TLR4 ligand lipopolysaccharide (LPS) of *Escherichia coli* O55:B5 in the absence or presence of different concentrations of NLRP3 stimulant monosodium urate (MSU). After 24h of incubation at 37^0C at $5\%CO_2$, concentrations of IL-1β, IL-6 and TNFα were measured in cell supernatants by an enzyme immunoassay. In separate experiments, PBMCs were lysed with Trizol for RNA isolation and measurements of *IL-1β* gene transcripts by RT-PCR using *β2*-microglobulin as the housekeeping gene. NLRP3 activation was considered as a more than 30% enhancement of IL-1β production after MSU addition.

Results: NLRP3 activation was found in 12 (75%) patients with CD compared to four (26.7%) controls, ($p = 0.045$) while no significant difference was detected between UC and controls (11/20 or 55% vs. 4/15 or 26.7%, $p = 0.17$), as shown in the table of mean changes of cytokine production and of respective copies. Moreover in CD patients, NLRP3 activation was proportionate to the time since the last intensification of treatment ($r = 0.95$, $p < 0.001$). Among UC patients, NLRP3 activation was found in eight (72.7%) with late (duration >1.5 years) and in nil with early disease ($p = 0.03$), respectively; no similar association was found in CD patients. No difference was detected regarding changes in IL-6 and TNFα levels and IL-1β transcripts numbers among IBD patients and controls (table). There was no association between NLRP3 activation and disease location, activity, current immunosupressive treatment and smoking status in IBD patients.

	Controls	UC	CD
% change of IL-1β	27.7 ± 26.7	258.6 ± 119.4*	$1919.2 \pm 1387.3^{\$}$
% change of IL-6	$2428 \pm 1997^{@}$	$822.3 \pm 701.4^{@}$	$919.3 \pm 599.3^{@}$
% change of TNFα	$203.5 \pm 100.2^{\#}$	$1675.3 \pm 616.6^{\#}$	$779.4 \pm 247^{\#}$
IL-1β transcripts	$206.4 \pm 188.9^{\wedge}$	$55.3 \pm 25.1^{\wedge}$	$528 \pm 510.1^{\wedge}$

*$p = 0.148$ vs. controls, $^{\$}p = 0.032$ vs. controls, $^{@}p > 0.6$ (controls vs. UC & CD), $^{\#}p > 0.082$ (controls vs. UC & CD), $^{\wedge}p > 0.82$ (controls vs. UC & CD)

Conclusion: NLRP3 is activated in CD patients, as compared to controls, and especially in those with long-term intensified treatment. Among UC patients NLRP3 inflammasome activation is detected only in those with long-standing disease.

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P0285 CIRCULATING PLATELET-DERIVED MICROPARTICLES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND THE IMPACT OF DRUG THERAPY ON THEIR LEVELS

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Introduction: Platelet activation is a consistent feature in inflammatory bowel disease and is thought to contribute to both the proinflammatory and procoagulant states of this disorder. The role of circulating platelet derived microparticles (PDMPs) and the effect of 5-amino salicylate acid (5ASA) and anti-TNF-a agents on their levels has not yet been clarified.

Aims & Methods: The aim of the study is to evaluate the levels of circulating PDMPs, as well as, the effect of 5ASA and anti-TNF-a treatments on these levels in IBD patients. Platelet-rich plasma was isolated from 47 patients with Crohn's disease (CD), 43 patients with ulcerative colitis (UC) and 26 sex and age-matched healthy controls. Clinical disease activity was assessed by Harvey-Bradshaw index for CD, Mayo score for UC and serological activity by measurement of C-reactive protein (CRP). Drug treatment at the time of blood sampling was recorded. Using flow cytometry, PDMPs were measured as the percentage of CD 36+microparticles, as well as, the percentage of CD36+microparticles expressing annexin (a phospholipid binding protein of the platelet surface expressing platelet activation) by total events with appropriate size and scatter; CD36 being a platelet surface marker.

Results: Overall, CD patients have greater percentage of CD36+microparticles ($0.31\% \pm 0.07\%$ vs. $0.14\% \pm 0.04\%$, $p = 0.02$) and of CD36+microparticles expressing annexin ($27\% \pm 2.6\%$ vs. $14.6\% \pm 2.7\%$, $p = 0.002$), in comparison with healthy controls. However, there is no correlation of percentages of both microparticles with Harvey-Bradshaw index and CRP. CD patients not receiving 5ASA have also greater percentage of CD36+microparticles expressing annexin ($25.8\% \pm 2.8\%$ vs. $14.6\% \pm 2.7\%$, $p = 0.005$), in comparison with healthy controls. Moreover, CD patients on 5ASA therapy show lower percentage of CD36+microparticles in comparison with those not receiving 5ASA ($0.30\% \pm 0.07\%$ vs. $0.32\% \pm 0.09\%$, $p = 0.048$). Anti-TNF-a treatment has no effect on both microparticle percentages in CD patients. In contrast to CD, UC patients have similar percentages of CD36+microparticles and of CD36+microparticles expressing annexin, as compared to healthy controls ($p = 0.06$ and $p = 0.2$, respectively), and there is no correlation of percentages of both microparticles and disease activity (Mayo score and CRP). Moreover, 5ASA and anti-TNF-a treatments have no effect on both microparticle percentages in UC patients.

Conclusion: Circulating levels of platelet derived microparticles are increased only in CD but they are not correlated with disease activity. The use of 5ASA is associated with lower levels of CD36+PDMPs only in CD, while anti-TNF treatment does not influence their levels in CD and UC patients.

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P0286 THE ETHANOLIC EXTRACT OF HYLOCEREUS SP. EXERTS ANTI-INFLAMMATORY EFFECTS AND PREVENTS MURINE COLITIS

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Introduction: Inflammatory bowel disease (IBD) is a chronic disorder of the gastrointestinal tract characterized by epithelial barrier disfunction and imbalance immune response. Recent pharmacological treatment has significantly improved the course of the disease but there are still a high percentage of patients that do not respond to current therapies.

Aims & Methods: We aim to evaluate the effects of the ethanolic extract of *Hylocerus sp.* (EH) in a murine model of colitis induced by TNBS. Colitis was induced in Balb/c mice by the intrarectal administration of TNBS (3.5mg/20g). Control animals received an intrarectal injection of TNBS-vehicle (EtOH 40%) (day 0). Six hours after TNBS, mice received an i.p. injection of EH (20 mg/20g mice) or its vehicle (DMEM). Changes in body weight were determined daily (results are expressed as percentage vs the weigth at day 0) and mice were sacrificed 2 and 4 days after TNBS administration. Mucosal histology was evaluated according to Wallace Score (1-10). Colons were frozen for RNA and protein isolation. The mRNA expression of *iNOS*, *Arginase I*, *COX-2*,

TNF-α, *IL-1β*, *IL-6* and *IL-10* was analysed by qPCR and protein levels of NF-κB and Iκβ-α were determined by western blot.

Results: Treatment of mice with TNBS induced a loss of body weight that peaked 2 days after treatment. Subsequently, mice began to recover and, four days after treatment, body weight reached similar values to those of control animals. In TNBS-treated mice, the administration of EH significantly ($P < 0.05$) prevented the loss of body weight ($91.97 \pm 1.65\%$) compared with the injection of vehicle ($86.40 \pm 2.05\%$), two days after TNBS. Mice receiving the EH exhibited a significant reduction in histological damage score (3.6 ± 0.6) compared with that detected in mice receiving vehicle (7.0 ± 1.0), four days after treatment. The increase in the expression of pro-inflammatory molecules detected 2 days after TNBS was significantly prevented ($P < 0.05$) by treatment with EH while no significant differences were detected in the expression of the anti-inflammatory molecule IL-10 (Table 1). Iκβ-α degradation and nuclear NF-κβ translocation were detected in the colon of TNBS-treated mice which was significantly prevented in the colon of mice receiving the EH.**Table1:** mRNA expression of different molecules detected in the colon of TNBS-treated mice. Results are expressed as fold induction vs the value obtained in mice that did not receive TNBS.

	iNOS	ArgI	COX-2	TNFα	IL-1β	IL-6	IL-10
Vehicle	5.3 ± 0.2	22.1 ± 4.1	1.7 ± 0.9	8.8 ± 1.9	1.9 ± 0.3	11.8 ± 3.8	1.2 ± 0.2
EH	0.5 ± 0.2	4.1 ± 1.3	0.5 ± 0.1	1 ± 0.2	0.8 ± 0.2	2.0 ± 0.4	1.8 ± 0.3

Conclusion: Systemic administration of the ethanolic extract of *Hylocereus sp* exerts an anti-inflammatory effect and prevents murine colitis induced by TNBS.

Disclosure of Interest: None declared

P0287 AN INTERPLAY BETWEEN AUTOPHAGY AND ER STRESS COORDINATES INTERLEUKIN-22 DEPENDENT SIGNALS IN THE INTESTINAL EPITHELIUM

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Introduction: Endoplasmic reticulum (ER) function and autophagy are necessary to maintain cellular homeostasis. Genetic variants of inflammatory bowel disease (IBD) risk genes like *ATG16L1* or *XBP1* are associated with epithelial ER stress. While *XBP1* plays a beneficial role in resolving ER stress, altered function of *ATG16L1* leads to defective autophagy and subsequent deregulation of ER function. ER stress impairs intestinal immune defense against pathogens and promotes cell death. Interleukin (IL) 22 is known to be a protective cytokine in mucosal regeneration through downstream expression of antimicrobial peptides and epithelial proliferation via STAT3 activation, respectively.

Aims & Methods: In this study, we investigate the impact of IBD risk genes *ATG16L1* and *XBP1* on regenerative function of IL22 in intestinal epithelium. Human colon carcinoma cells (HT-29 and CaCo-2) were treated with recombinant IL22 and ER stress inductors like Tunicamycin and were subjected to wound healing assays, gene expression analysis and immunoblot analysis. Intestinal organoids derived from *Xbp1* ΔIEC and *Atg16l1* ΔIEC mice were generated by culturing small intestinal crypts in collagen matrix. These were treated with recombinant IL22 and subjected to gene expression analysis. Organoids were subjected to RNA sequencing and transcriptome analysis. Secreted cytokines in supernatants from cells and organoids were detected with ELISA.

Results: IL22 induces transient self-limiting ER stress in the intestinal epithelium. Regulation of transient ER stress is dependent on *Xbp1* and *Atg16l1* as IL22 treated intestinal organoids from *Atg16l1* ΔIEC und *Xbp1* ΔIEC mice display a dramatic increase of inducible ER stress and pro-inflammatory gene expression. While IL22 improves wound healing in the absence of ER stress, IL22 leads to impaired wound closure and increased cell death under ER stress conditions. This effect is dependent on STAT3 and autophagy as STAT3 inhibition or autophagy induction through rapamycin completely neutralizes IL22 induced detrimental effect.

Conclusion: These data suggest an unexpected role of the IBD risk genes *ATG16L1* and *XBP1* in coordinating regenerative IL22 function in intestinal epithelium.

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Disclosure of Interest: None declared

P0288 MAGNESIUM IN INFLAMMATORY BOWEL DISEASE: AN UNEXPECTED PLAYER

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Introduction: Magnesium is an essential mineral that is fundamental in many pathophysiological processes. A mild hypomagnesaemia is a common condition associated to dietary deficiency of magnesium. Hypomagnesaemia is a well-known enhancer of oxidative stress and inflammation. Inflammatory Bowel Disease (IBD) is a collection of chronic inflammatory bowel diseases characterised by a variety of nutritional deficiencies due to reduced absorption and/or increased loss of essential nutrients, which among other conditions, can induce hypomagnesaemia.

Aims & Methods: To investigate the influence of magnesium availability in the diet on the severity of murine dextran sodium sulphate (DSS)-induced acute colitis. Mice were exposed to 2.5% DSS in the drinking water and fed three different diets (low (30mg/kg), normal (1000mg/kg) and high (4000mg/kg) magnesium content). Both acute colitis (5 days exposure to DSS) and recovery after the acute colitis (7 days of recovery without DSS) were studied. The severity of the colitis was scored daily using a four-point Disease Activity Index (DAI) based on the faecal consistency, weight loss and faecal blood loss. Colon, kidney and serum were collected at the sacrifice. Magnesaemia was analysed using atomic absorption spectrometry and severity of the inflammation of the colon was scored on morphological examination of haematoxylin/eosin stained slides.

Results: Dietary magnesium deficiency increased the severity of the DSS-induced colitis as scored with the Disease Activity Index, whereas magnesium supplementation seemed to score more or less like controls. Serum magnesium measurements showed that while magnesium in the diets positively correlated with the magnesaemia, the exposure to DSS reduced magnesaemia in all conditions. However, high magnesium content in the diet compensated for DSS-induced hypomagnesaemia (the colitic mice on the magnesium-enriched diet showed a magnesaemia similar to the control group on the normal magnesium diet). Interestingly, morphological analysis of the colon showed that while the low magnesium diet enhanced mucosal damage and impaired mucosal recovery, magnesium supplementation clearly protected the colonic mucosa against DSS-induced damage (much less crypt destruction and inflammatory infiltrates). And after recovery the colonic mucosa of the mice on the magnesium-enriched diet appeared to be absolutely normal.

Conclusion: Magnesium supplementation protects the colonic mucosa, compensates inflammation-induced hypomagnesaemia and seems to help the colonic mucosa restore after acute colitis. Our data suggest an active role of magnesium in the pathogenesis and in the severity of colon inflammatory diseases. The validation of these results in IBD patients is currently under study.

Disclosure of Interest: None declared

P0289 TOLL2- AND TOLL9-DERIVED SIGNALS IN DROSOPHILA MELANOGASTER PRESERVE THE INTEGRITY OF MIDGUT NEURONS

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Introduction: The gut microbiota-innate immunity axis guarantees the development, and the functional integrity of the intestine including the nervous system (ENS) embedded in the gut wall. However, the complexity of animal models is a substantial obstacle to dissect the cellular populations and the molecular pathways involved in this interplay. Since many components of innate immunity, including the sensors for conserved microbial structures such as *Toll* genes and Toll like receptors, are shared between *Drosophila melanogaster* and mammals we aimed to identify the enteric cellular populations generating trophic signals, that secure gut neuronal integrity through the Toll pathways using the *Drosophila* model.

Aims & Methods: We ablated *Toll* genes in adult flies by the expression of siRNA using ubiquitous (actin and beta-tubulin) and cellular specific (smooth muscle cells, neurons and glia) temperature inducible drivers. After 8 days of *Toll* genes silencing we: 1) dissected flies gut (20-30 individuals/measure) to perform quantitative RT-PCR for *Toll*1÷9 and *Elav* (a neuronal marker) gene expression; 2) executed immunohistochemistry on gut whole mount preparations using a neuronal (anti-HRP) marker to quantify neuronal bodies in the flies midgut; 3) exposed flies to an intestinal toxic (5% DSS) and daily recorded survival ($n = 60$-90 individuals/group).

Results: In *Drosophila* lines the expression of specific siRNA under the control of ubiquitous drivers significantly reduced in the gut the mRNA levels of *Toll1* (by 82%), *Toll2* (by 99%), *Toll4* (by 80%), *Toll6* (by 38%), *Toll7* (by 96%), *Toll8* (by 85%), *Toll9* (by 95%), as compared to W^{1118} control ($p < 0.01$). The number of neuronal bodies in the midgut was significantly reduced by the silencing of *Toll2* and *Toll9* ($p < 0.01$) but not by the other *Toll*s. Using the ubiquitous drivers actin and tubulin *Toll2* silencing reduced neurons by 92% and 81%, whereas *Toll9* silencing diminished neurons by 95% and 93% as compared to W^{1118} controls. In agreement to the loss of neurons in the midgut, *Elav* mRNA was reduced by 80% and 85%, respectively, in the gut of flies with ubiquitous *Toll2* or *Toll9* silencing. By using specific drivers to silence *Toll2* in smooth muscle and glial cells, *Toll2* mRNA levels were significantly reduced ($p < 0.01$ vs W^{1118} control) in the gut. Accordingly, the number of neuronal bodies in the midgut and the *Elav* mRNA

levels were reduced by 43% and 50% by using the smooth muscle driver and by 85% and 40%, by using the glial cells driver, respectively.
Ubiquitous *Toll2* or *Toll9* silencing reduced mortality by 32% and 31%, respectively, at the 5th day of DSS administration as compared to W^{1118}. While *Toll2* silencing in smooth muscle cells had a protective effect reducing mortality by 30%, *Toll2* silencing in glial cells exacerbated colitis inducing mortality in 95% of individuals as opposed to 86% of W^{1118} ($p < 0.01$).
Conclusion: Loss of *Toll2*- and *Toll9*-derived signals is associated to significant reduction of neuronal bodies in the *Drosophila* midgut. By using the *Drosophila* model was possible for the first time to observe that *Toll2* silencing has opposite effects in smooth muscle cells and glial cells, supporting specific effects of innate immunity-microbes interplay in specific intestinal cell population.
Disclosure of Interest: None declared

P0290 MUCOSAL FUNGAL MICROBIOTA DYSBIOSIS IN CROHN'S DISEASE

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Introduction: The gut microbiota is involved in many physiological functions. An imbalance in its composition named dysbiosis is associated with several diseases and particularly with inflammatory bowel diseases (IBD). Mucosa associated microbiota, that has been shown to differ from faecal one, could have a key role in induction of host immunity and in inflammatory process. Although the role of fungi has been suggested for a long time in IBD pathogenesis, the fungal microbiota has been poorly explored. The aim of the current study was to analyzed the composition of the mucosa associated microbiota of Crohn's disease (CD) patients and healthy subjects (HS) taking into account both bacterial and fungal fractions.
Aims & Methods: Bacterial and fungal composition of mucosa associated microbiota of 23 CD patients (16 in flare and 7 in remission) and 10 healthy subjects (HS) was determined using 16S (MiSeq) and ITS2 (pyrosequencing) respectively. The obtained sequences were analyzed using the Qiime pipeline to assess composition, alpha and beta diversity. Comparisons between clinical groups were performed using Linear Discriminant Analysis Effect Size (LEFSE). Global fungal load was assessed by real time PCR.
Results: Bacterial microbiota in CD patients was characterized by a restriction in biodiversity, a decrease of *Firmicutes* and *Bacteroidetes* and an increase of *Proteobacteria* and *Fusobacteria*. Global fungi load was significantly increased in CD flare compared to HS ($p < 0.05$). No significant difference in fungi biodiversity was observed between the studied groups. Both in HS and CD, the colonic mucosa-associated fungal microbiota was dominated by *Basidiomycota* and *Ascomycota* phyla. *Dioszegia* genera and *Candida glabrata* species were overrepresented in CD whereas *Leptosphaeria* and *Trichosporon* genera were decreased. *Saccharomyces cerevisiae* and *Filobasidium uniguttulatum* species were associated with non inflamed mucosa whereas Xylariales order was associated with inflamed mucosa.
Conclusion: Our study confirms an alteration of the bacterial microbiota and demonstrates the existence of an altered fungal microbiota in CD patients. These alterations are characterized by an increased fungal load in CD and an abnormal composition suggesting that fungi may play a role in CD pathogenesis.
Disclosure of Interest: None declared

P0291 ACTIVATION OF AUTOPHAGY BY CROHN'S DISEASE-ASSOCIATED E. COLI IS DEPENDENT OF SIDEROPHORE EXPRESSION

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Introduction: The intestinal mucosa of Crohn's disease patients are abnormally colonized by *Escherichia coli* able to invade and to replicate inside intestinal epithelial cells. Those pathogenic bacteria have been named adherent-invasive *E. coli* or AIEC. Genomic analysis of the AIEC reference strain LF82 has revealed a pathogenicity island of ~34kb (PAI II, for pathogenicity island II) closely related to the "high pathogenicity island" of pathogenic *Yersinia* sp. that encodes the yersiniabactin siderophore system. Bacteria have developed efficient high affinity iron uptake systems (siderophores) promoting their growth in iron-restricted environments.
Aims & Methods: Here, we aimed at investigating the role of the PAI II during AIEC infection. The entire PAI II was deleted and wild-type or the mutated AIEC LF82 strains were used to infect human intestinal epithelial T84 cells. Morphology of AIEC was observed using electron microscopy. AIEC intracellular survival and proliferation were assessed by counting bacterial numbers on Luria Broth (LB) plates. Activation of the transcription factor HIF-1α was assessed by Western blot and by quantifying mRNA expression levels of VEGF, a target gene of HIF-1α. Autophagy was monitored by Western blot for the conversion of LC3-I to LC3-II and by confocal microscopy.
Results: Deletion of PAI II did not alter either morphological aspects (pili, flagella…) or growth of AIEC LF82 bacteria in LB or in T84 cell culture medium. However, loss of PAI II resulted in increases in AIEC intracellular survival and proliferation in T84 cells. This was associated with inhibition of AIEC-induced HIF-1α expression and activation. HIF-1α has been associated with induction of a functional autophagic response. We observed that autophagy was induced in T84 cells infected with wild-type LF82 but not with the mutated LF82. Furthermore, siRNA-mediated HIF-1α silencing in T84 cells inhibited autophagy response, leading to increased intracellular LF82 number, confirming the key role played by HIF-1α in autophagy induction in response to AIEC infection.
Conclusion: Activation of HIF-1α and subsequently autophagy in AIEC-infected cells requires PAI II expression.
Disclosure of Interest: None declared

P0292 MICRORNA-424 MAY REGULATE TRANSCRIPTS IN THE PATHOGENESIS OF INFLAMMATORY BOWEL DISEASES - SUGGESTED MECHANISM

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Introduction: Inflammatory bowel diseases (IBD) are associated with differential expression of genes involved in inflammation and tissue remodeling. One mechanism of regulating gene and protein expression is by MicroRNAs (miRs). Recently we performed massive sequencing analysis of ileal biopsies showing that increased expression of multiple miRs occurs in intestinal inflammation, specifically that occurring in ulcerative colitis patients after total proctocolectomy and pouch surgery. miRs expression alterations correlated with disease behavior. Among the miRs with significantly altered expression, miR-424 had a robust increase: 8.4 fold change in Crohn's-like disease of the pouch (CLDP) and 2.6 in normal pouch (NP) compared to the ileum of normal controls (NC). We hypothesized that miRs may have a role in down-regulation of mRNA transcripts in IBD.
Aims & Methods: To define the interaction of candidate miRs with their potential targets and the mechanisms modifying miRs expression in intestinal inflammation. miRs and mRNAs were selected based on our previous microarray studies and *in silico* data. Levels of mature and primary miR-424 as well as its potential target genes: solute carrier family 6 member 4 (*SLC6A4*, neurotransmitter transporter) and solute carrier family 36 member 1 (*SLC36A1*, proton/amino acid symporter) were examined in patients with CLDP and NP as well as in NC and in a human epithelial cell line (HCT-116) incubated with inflammatory cytokines (TNF-α, IL-1β, INF-γ) by quantitative reverse transcription-polymerase chain reaction. Regulation of gene expression by miR-424 was assessed by transfection of specific mimic and miR-424 inhibitor.
Results: miR-424 expression was increased (3.3 fold, $p < 0.001$), while SLC6A4 mRNA expression was decreased (5.8 fold, $p < 0.01$) and SLC36A1 expression was lower in ileal biopsies of CLDP patients compared to NC. Primary to mature miR-424 expression ratios were higher in the NP compared to pouchitis (4 fold increase). Similarly, under inflammatory conditions HCT-116 cells expressed 4 fold more miR-424 ($p < 0.05$) and less SLC6A4 (2.8 fold, $p < 0.05$) and SLC36A1 (1.3 fold, $p < 0.01$) compared to untreated cells. Transfection of miR-424 mimic into HCT-116 cells resulted in a decrease in SLC6A4 and SLC36A1 expression (1.3 fold, $p < 0.05$) whereas transfection of miR-424 inhibitor resulted in an increase in SLC6A4 and SLC36A1 expression (2 fold, $p < 0.01$ and 1.3 fold, $p < 0.05$ respectively).
Conclusion: Mature miR-424 expression is increased and its target genes are decreased in intestinal inflammation suggesting its role in gene expression regulation in IBD. The processing of a primary to mature miR is increased in pouch inflammation. As miRs are robustly increased in IBD, the behavior of miR-424 may serve as a proof of concept for the role of miRs in regulating intestinal inflammation in IBD.
Disclosure of Interest: None declared

P0293 FUNGAL MICROBIOTA DYSBIOSIS IN INFLAMMATORY BOWEL DISEASES PATIENTS

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Introduction: The intestinal microbiota plays major roles in human physiology as well as in inflammatory bowel diseases (IBD). It is mostly composed of bacteria, but also contains other microorganisms such as virus and fungi. Although the bacterial part of the gut microbiota is being actively studied, almost no data are available regarding the fungal part. The presence of genes involved in sensing and response to fungi among IBD susceptibility genes and recent results in mouse models suggest a role of the fungal microbiota in IBD pathogenesis. Our aim was to characterize the fungal microbiota in IBD patients.
Aims & Methods: Bacterial and fungal composition of the fecal microbiota of 235 IBD patients and 38 healthy subjects (HS) was determined using 16S (ion torrent) and ITS2 (pyrosequencing) respectively. The obtained sequences were analyzed using the Qiime pipeline to assess composition, alpha and beta

diversity. Bacterial and fungal taxa associated with clinical parameters were identified using Multivariate association with Linear Models (MaAsLin) taking into account the following parameters: IBD status, IBD type, disease activity, ileum involvement, gender, age, smoking and treatment (5 ASA, steroids, anti-TNFa, immunosuppressant). Correlation between bacterial and fungal microbiota was investigated using spearman test.
Results: Among the 235 IBD patients (106 in flare, 129 in remission), 149 had Crohn's disease (CD) and 86 had ulcerative colitis (UC).
The results of the bacterial microbiota analysis were in accordance with published data with notably a decreased biodiversity, a decreased proportion of Firmicutes and an increased proportion of Proteobacteria in IBD patients. Beta diversity analysis showed that samples clustered according to disease activity both for bacterial and fungal microbiota. Fungal microbiota in both IBD patients and HS was dominated by the Basidiomycota and Ascomycota phyla, and by the Saccharomyces, Debaryomyces, Penicillium, and Candida genera. The fungal gut microbiota was found imbalanced in IBD patient with notably an increase Basidiomycota / Ascomycota ratio and a decreased proportion of Saccharomyces and Kluyveromyces compared to HS. The fungal biodiversity was also decreased in IBD patients, particularly in those with colon involvement. Many correlations were observed between bacterial and fungal genera abundance suggesting an inter-kingdom crosstalk. These correlations were stronger in UC patients compared to CD patients and healthy subjects. Global correlation network was homogenous and even in HS, whereas it was unbalanced and uneven in IBD patients and particularly in UC, suggesting unbalanced crosstalk.
Conclusion: The fungal gut microbiota is dominated by the Basidiomycota and Ascomycota phyla. The fungal microbiota is imbalanced in IBD patients with a reduced biodiversity and an increased Basidiomycota / Ascomycota ratio compared to HS. Correlation analyses suggest an unbalanced crosstalk globally within the microbiota and particularly between fungal and bacterial microbiota components in IBD patients.
Disclosure of Interest: None declared

P0294 ATTENUATION OF DSS-INDUCED COLITIS BY PROBIOTIC ADMINISTRATION IS ASSOCIATED WITH IMMUNOSTIMULATING EFFECTS ON REGULATORY T CELLS

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Introduction: The exact etiology of inflammatory bowel disease (IBD) remains unclear, there is much evidence supporting the hypothesis of the involvement of intestinal microbiota in IBD pathogenesis. In recent years, there is increasing interest for using probiotic in IBD. A growing body of evidence suggests that the probiotic bacteria has immune-modulatory ability. So, we investigate the effect of administration of probiotic mixture (bifidobacterium, lactobacillus and enterococcus) on colitis and regulatory T cells in DSS-induced mice.
Aims & Methods: The aim of this study is to investigate the effect of administration of probiotic mixture (bifidobacterium, lactobacillus and enterococcus) on colitis and regulatory T cells in DSS-induced mice.
An acute colitis was induced in BALB/c mice (8-10 week-old) using 3.5% w/v dextrane sulfate sodium (DSS). Mice were randomly divided into five groups: NS group (received saline), DSS group (received DSS), BB group (14-day probiotic mixture without DSS), BD group (received 7-day probiotic mixture prior to DSS administration) and BDB group (14-day probiotic mixture with DSS given at 8th day for 7 days). The Disease Activity Index was monitored daily, colon length and weight were measured and histological scores were evaluated. Regulatory T cells (CD4 + CD25 + Foxp3 + T) in spleen and blood were measured by flow cytometry.
Results: Probiotic mixture administration attenuates the DSS-induced intestinal damage. Compared with DSS group, disease activity Index (DAI) ($P < 0.001$), colonic length ($P < 0.01$), body weight ($P < 0.01$ in BD group; $P = 0.075$ in BDB group) and histological scores ($P < 0.001$) were significantly improved in mice with probiotic mixture administration. The probiotic mixture protection may be associated with a reduction in CD4 + T cells (total CD4 + T cell in BD group was lower than that of DSS group ($P < 0.05$)). Intervention with probitic mixture led to a significant increase of regulatory T cell in blood ($P < 0.05$), but not in spleen.
Conclusion: Administration of probiotic mixture (bifidobacterium, lactobacillus and enterococcus) can reduce intestinal inflammation and damage in DSS-induced colitis.This result was associated with reduction in total CD4 + T cells and increasing regulatory T cells.
Disclosure of Interest: None declared

P0295 THE ROLE OF MIR-19B TARGETING SOCS3 IN MEDIATING INTESTINAL INFLAMMATION

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Introduction: The exact etiology of inflammatory bowel disease (IBD) remains unclear. Current evidence suggested that IBD is caused by complex interactions of environmental, genetic, and immuno-regulatory factors. Of these, immune dysregulation is thought to play important roles in the pathogenesis of IBD. Intestinal epithelial cells (IECs) are prominently linked to the pathogenesis of IBD. IECs can attribute to classic inflammatory response. There is accruing evidence that miRNAs play a role in regulating inflammatory processes. Recently, unique miRNA expression profiles have been described in epithelial cells of patients with active IBD. However, the roles of miRNAs in modulating disruption of epithelia during the process of IBD remain incompletely clear.
Aims & Methods: The aim of this study is to investigate whether miR-19b targeting SOCS3 regulate activation of signal transducer and activator of transcription 3 (STAT3) in IECs and mediate intestinal inflammation.
Acute colitis was induced via an intra-rectal injection of TNBS. Levels of SOCS3 and miR-19b in colon tissues from mice were assessed by Western blot (WB) and qRT-PCR. Distribution of miR-19b in intestinal mucosal of CD patients was performed by RNA in situ hybridization (ISH). STAT3 and phosphorylated-STAT3(p-STAT3)in intestinal tissue were determined by immunohistochemical (IHC). CCK8 and flow cytometry were conducted for detection of proliferation ability in HT-29 cells. The expression of cyclinD1 was detected by WB and qRT-PCR after overexpression or knockdown of miR-19b.
Results: Compared with normal control, levels of miR-19b decreased in lesion tissue, while the expressions of SOCS3 protein increased in TNBS-treated mice. The imbalance of miR-19b and SOCS3 in TNBS-induced colitis was similar to that in CD patients. TNBS-induced colitis was improved after intracolonic administration of miR-19b mimic. Using RNA ISH, miR-19b was obviously decreased in intestinal epithelium in CD patients. Expression of p-STAT3 was decreased in CD patients. Overexpression of miR-19b in HT-29 cells downregulated the protein level of SOCS3, but not SOCS3 mRNA. The proportion of cells in phase (S + G2) was increased in HT-29 cells after overexpression of miR-19b. Downregulation of SOCS3 by miR-19b mimic caused phosphorylation of STAT3. Expression of cyclinD1 was induced in cells treated with miR-19b mimic, which was the down stream of STAT3 and associated with cell proliferation and cell cycle.
Conclusion: Intracolonic administration of miR-19b mimic improved colitis in TNBS-induced mice. MiR-19b targeting SOCS3 regulate activation of STAT3 and influence intestinal epetheliul proliferation. This pathway maybe involved in mucosal healing during intestinal inflammatory lesion.
Disclosure of Interest: None declared

P0296 LOW COLECTOMY RATE FIVE YEARS AFTER DIAGNOSIS OF ULCERATIVE COLITIS. RESULTS FROM A PROSPECTIVE POPULATION-BASED COHORT

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Introduction: The aim of the study was to analyse the first five years of a population based cohort consisting of newly diagnosed patients in all age groups with ulcerative colitis, with respect to medication, surgery and mortality.
Aims & Methods: The patients included in the study were recruited 2005-2009 in the Uppsala Health Care Region (population 642,000) and the cohort has previously been described in detail (1). The average incidence during the study period was 20.0/100 000/year. The mean age for the 526 patients was 39.2 years (median 36.0, IQR 23.0-54.0, range 3-88). The gender distribution male/female was 1.24/1. The medical notes were checked, patients that had moved before five years of observation were contacted by mail for supplementary information.
Results: Of the original 526 patients, two individuals were excluded from further analysis because of uncertain diagnose. Thus the cohort consists of 524 individuals, of whom 495 (87%) could be followed up to 5 years. Nineteen patients (3.6%) had died and two of these could be attributed to IBD (one postoperative death and one colonic cancer). The following drugs were used: 5-ASA (91%), steroids (65%), antimetabolites (28%) and anti-TNF (11%). During the 5-year observation period, 27 patients were subjected to colectomy because of ulcerative colitis, representing 5.7% using Kaplan-Meier survival function. Among patients < 17 years at diagnosis (n = 42), two were operated (4.8%) during the observation period. A multivariate analysis demonstrated that severity of symptoms at diagnosis was correlated to risk for colectomy (S2 + S3 vs SR OR = 15.2 (95% CI 1.87-124.03, $p = 0.01$)). The surgical rate varied according to the various geographical areas of the region (3.0% in the area served by the University Hospital and 11.7% in the surrounding counties).
Conclusion: Five years after diagnosis of ulcerative colitis, 5.7% had been subjected to colectomy. The geographic variation of operative treatment was considerable (3.0-11.7%) due to different approaches to severe episodes of colitis. Mortality caused by ulcerative colitis was low (0.44%)

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Disclosure of Interest: None declared

Abstract number: P0298

Table: Percentage of patients that frequently or always had negative feelings due to ulcerative colitis (n may vary from question to question due to lost answers)

	Unmotivation	Anxiety	Anger	Depression	Frustration	Embarrassment
All (n = 436)	22%	26%	23%	27%	19%	9%
GENDER						
Men(n = 229)	20%	19%	21%	25%	20%	7%
Women(n = 205)	23%	34%	24%	30%	18%	10%
PERCEPTION OF SEVERITY						
Mild (n = 227)	15%	18%	15%	19%	15%	7%
Moderate or severe (n = 169)	30%	36%	31%	37%	25%	12%
PRESENCE OF FLARE DURING PREVIOUS YEAR						
No (n = 130)	11%	14%	10%	12%	12%	3%
Yes (n = 252)	24%	30%	27%	34%	22%	11%
SYMPTOMS DURING PREVIOUS YEAR						
Symptoms under control (n = 185)	12%	16%	11%	17%	9%	4%
Yes, but not affecting my everyday life (n = 110)	20%	33%	23%	30%	18%	9%
Yes, affecting my everyday life (n = 98)	39%	37%	42%	40%	37%	15%

P0297 AFFECTIVE TEMPERAMENT TRAITS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE ASSESSED BY TEMPERAMENT EVALUATION OF MEMPHIS, PISA, PARIS AND SAN DIEGO AUTOQUESTIONNAIRE AND THEIR IMPACT ON QUALITY OF LIFE

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Introduction: Affective temperaments can be considered as the subclinical manifestation of affective disorders, which have an impact on the clinical course of chronic diseases as inflammatory bowel disease (IBD). Coping abilities of patients are influenced by their personality. Temperament variations may be useful to identify patients at risk and for further introducing the personalized therapy.

Aims & Methods: To explore the effect of affective temperament traits on disease-specific quality of life in patients with ulcerative colitis (UC) and Crohn's disease (CD).

The study embraces 116 patients with IBD: 61 with UC and 55 – with CD, aged 19-84 years (mean 43 ±7.8), in remission, without serious mental or medical conditions.

The patients completed the Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire (TEMPS-A), which is the assessment for five dimensions of temperament: depressive (TEMPS-A-D), cyclothymic(C), hyperthymic (H), irritable (I) and anxious (A).

For five temperament traits 0-1 scores were calculated. Higher score indicated the higher intensity of affective temperament. Patients Health-Related Quality of Life (HRQL) was assessed with the Inflammatory Bowel Disease Questionnaire

Results: Overall, more than 70% TEPMS-A scores were higher in IBD patients compared to general Polish population. In 25 patients (22%) we found 3 and more affective temperament traits with scores more than 0.5. In 37 patients (33%) at least one score was more than 0.7. The most common combination of affective traits was: depressive, cyclothymic and anxious and these traits reached the highest scores. Irritable temperament score was significantly higher in CD compared to UC patients ($p < 0.01$).

Mean HRQL in IBD patients were significantly decreased and mean IBDQ scores were 145/ 224. Significant negative correlation was found between HRQL in all IBDQ domains and TEMPS-A traits: D ($p < 0.001$), C ($p < 0.01$), I ($p < 0.05$) and A ($p < 0.001$).

Conclusion: The results confirmed that affective temperament traits have negative impact on quality of life in IBD patients. Personality traits should be taken into account when using IBDQ in studies as well as in management with IBD patients.

Disclosure of Interest: None declared

P0298 SYMPTOMATIC BURDEN AND EMOTIONAL HEALTH OF SPANISH PATIENTS WITH ULCERATIVE COLITIS. UC-LIFE SURVEY

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Introduction: ECCO guidelines indicates that psychological factors may have an impact on the course of ulcerative colitis (UC).

Aims & Methods: Here we describe the impact of UC on everyday life and feelings as perceived by patients followed in hospital clinics from Spain.

Methods. Thirty-nine gastroenterologists handed each a survey to 15 consecutive patients aged ≥18 years. Patients completed the survey at home and returned it by mail. The emotional impact was evaluated through questions on impact of UC on everyday life, quality of sleep, and feelings (ranked from "never" to "always").

Results: Response rate was 75% (436/585, mean age 46 years, 53% men). During the past year 51% reported at least one exacerbation and 43% perceived their UC as moderate or severe. For 79% of patients UC prevented them from doing a normal life. The figures were similar regarding age, gender or disease duration. A total of 76% reported UC affected the quality of their sleep, the percentage was higher in women (83% vs 69% in men $p = 0.001$). Those who perceived UC as moderate or severe reported more frequently impact on everyday life and rest than those describing mild disease (92% vs 69%, $p < 0.001$ and 89% vs 65%, $p < 0.001$ respectively). The percentage of patients reporting negative feelings due to UC "frequently" or "most of the time" is shown in the table. No differences were found by age ranges. Anxiety and depression were more frequently rated as "frequently" or "most of the time" by women ($p < 0.001$ and $p = 0.017$ vs men [table]). Those with higher disease burden during past year (with a flare, with perception of moderate/severe UC or with symptoms impacting everyday life), had all the feelings more frequently rated as "frequently" or "most of the time" ($p < 0.05$, table).

Conclusion: Data reported by patients underline the noteworthy impact of UC on emotions, everyday life and rest. Patients with higher burden of disease described more frequently such negative emotions. Following ECCO recommendations checking emotional aspects should be part of regular clinical practice.

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P0299 ULCERATIVE COLITIS IN THE ELDERLY: A DESCRIPTIVE ANALYSIS OF DISEASE IN THE UK

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Introduction: The presence of an ageing population combined with an increase in the incidence of inflammatory bowel disease (IBD) may mean that the burden of elderly-onset ulcerative colitis (UC) will become more apparent. Relatively limited information is available about the disease process in this group. Recent cohort studies from European IBD populations have shed some light on this issue [1,2], but equivalent data for the British population has not yet been described.

Aims & Methods: We aimed to describe demographics, therapies and outcomes in a cohort of British patients with elderly-onset UC (diagnosis confirmed after 60th birthday). Data was sourced from the Clinical Practice Research Datalink (CPRD). This is one of the largest primary care datasets in the UK and has detailed information on diagnoses, clinical events and prescription data for 8% of the British population. Data on disease parameters, medication prescriptions and surgical procedures were collected on individuals aged greater or equal to 60 years with READ codes indicating a diagnosis of ulcerative colitis, over the study period 1990 to 2012. Patients with co-morbid conditions necessitating regular steroid or immunosuppressant therapy were excluded from the final anaylsis.

Results: Over the study period, 4775 patients (52.5% male) with elderly-onset UC were identified, with a mean follow-up of 3.9 years. Mean age at diagnosis was 71.5 years. The proportion of current, non, and ex-smokers were 10.5%, 53.2% and 36.3% respectively. 58.4% of patients had received at least one prescription of 5-aminosalicylate therapy. 46.0% had received a course of oral steroids during follow up with 34.3% prescribed corticosteroid therapy within the first year after diagnosis. 18.1% of patients were classified as steroid dependent (i.e. receiving steroid course > 3 months, or needing a repeat course of steroids within 3 months of finishing the previous course). 8.7% had a prescription for thiopurine (TP) therapy with 4.6% receiving TPs in the first

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Table: Health resources consumption during previous year. (n varies among questions due to lost answers)

	Hospital Admissions	Emergency room visits	Non-scheduled visits	Steroids use
LACK OF MOTIVATIONNever (n = 119)	6%	14%	27%	28%
Sometimes (n = 187)	22%[(a)]	36%[(a)]	57%[(a)]	57%[(a)]
Frequently/always(n = 84)	31%[(a)]	42%[(a)]	61%[(a)]	62%[(a)]
ANXIETYNever (n = 115)	12%	17%	29%	35%
Sometimes (n = 174)	18%	30%[(a)]	54%[(a)]	49%[(a)]
Frequently /always (n = 102)	27%[(a)]	50%[(a,b)]	61%[(a)]	66%[(a,b)]
ANGERNever (n = 151)	16%	19%	31%	38%
Sometimes (n = 145)	17%	38%[(a)]	58%[(a)]	52%[(a)]
Frequently /always (n = 87)	25%	40%[(a)]	65%[(a)]	64%[(a)]
DEPRESSIONNever (n = 103)	11%	15%	16%	35%
Sometimes (n = 184)	18%	30%[(a)]	48%[(a)]	48%[(a)]
Frequently /always (n = 106)	30%	50%[(a,b)]	36%[(a,b)]	64%[(a,b)]
FRUSTRATIONNever (n = 154)	11%	18%	33%	32%
Sometimes (n = 152)	20%[(a)]	37%[(a)]	57%[(a)]	60%[(a)]
Frequently/always (n = 73)	32%[(a)]	46%[(a)]	65%[(a)]	62%[(a)]
EMBARRASSMENTNever (n = 240)	13%	25%	43%	42%
Sometimes (n = 107)	25%[(a)]	39%[(a)]	57%[(a)]	55%[(a)]
Frequently/always (n = 33)	36%[(a)]	52%[(a)]	64%[(a)]	73%[(a)]

(a) $P < 0.05$ vs "Never" ; (b) $P < 0.05$ vs "Sometimes"

year of diagnosis. 3.9% of elderly onset UC patients underwent colectomy during follow up versus 5.1% in patients aged less than 60 (Fisher's exact test $p = 0.009$). Over half of elderly patients requiring colectomy had surgery within the first year of diagnosis. The table demonstrates multivariate logistic regression of risk factors associated with need for colectomy in elderly patients.

	Odds Ratio	95% Confidence Intervals	p value
Smoking	1.27	0.95-1.70	0.1
5-ASA use	1.12	0.73-1.71	0.51
Thiopurine use	3.77	2.42-5.89	< 0.0001
Steroid dependency	2.05	1.35-3.12	0.001

Conclusion: Although colectomy rates appear comparitively lower than in younger populations, suggesting a more benign disease course, there is a concerning level of steroid dependency in this cohort of elderly patients who will be at particular risk from the many side effects of corticosteroid treatment. The low TP use in this group may reflect a less aggressive disease course, but may also indicate cautious prescribing in this age group.

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P0300 SELF-CONFIDENCE, EMOTIONAL HEALTH AND HEALTH RESOURCES CONSUMPTION AMONG SPANISH PATIENTS WITH ULCERATIVE COLITIS. UC-LIFE SURVEY

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Introduction: ECCO guidelines point out that psychological disorders contribute to poorer quality of life (QoL) and to increase the number of doctor visits regardless of disease severity.

Aims & Methods: We describe the prevalence of negative feelings and health resources consumption in UC patients followed in Spanish hospitals.

Methods. Thirty-nine gastroenterologists handed a survey to 15 consecutive UC patients aged ≥18 years. Patients completed the survey and returned it by post-mail. The emotional impact of UC was collected by closed questions about feelings (ranked from never to always), and self-confidence. Patients were asked about health resources consumption during the previous year.

Results: Response rate was 75% (436/585, mean age 46 years,53% men). Up to 38% felt that UC reduced their self-confidence. A higher impact of UC on self-confidence was described by older patients ($p = 0.01$), those with longer disease duration ($p < 0.001$) or higher burden of disease [i.e flares during previous year ($p = 0.05$), perception of UC as moderate or severe ($p < 0.001$) and presence of symptoms impacting everyday life ($p < 0.05$)]. The previous year 19%, 31% and 47% respectively reported hospital admissions, emergency room visits or non-scheduled visits. Negative feelings reported by patients are described in the table. Health resources consumption was significantly more frequent among those who scored negative feelings as "sometimes" or "frequently/always" (table).

Conclusion: In this survey, UC patients reported a significant impact on emotional health and self-confidence. Patients with more frequently negative feelings also described more frequency of health resources consumption.

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P0301 SURGERY IN ADULT CROHN'S DISEASE PATIENTS HAS LIMITED IMPACT ON THE MEDICAL AND SOCIAL BURDEN OF DISEASE

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Introduction: Crohn's disease is a chronic relapsing disease affecting men and woman at their prime, influencing both physical and social aspects of life. We hypothesized that surgery can be perceived as a life event that improves disease perception for the patients and those surrounding them. We investigated this issue in a community cohort of adult Crohn's patients.

Aims & Methods: Consecutive adult Crohn's disease patients were recruited from IBD clinics in 5 tertiary hospitals and from our website call, and filled out their demographics, disease status, Harvey-Bradshaw Index (HBI), and the social questionnaires: SF-36 (generic quality of life), and Brief Symptom Inventory (BSI, measures psychological stress). For the analysis parametric and nonparametric statistics were used as required. A logistic multivariate regression model was utilized to examine the associations between surgery as dependent variable with socio-demographic, HBI, BSI and SF-36 variables.

Results: The cohort comprised 518 patients, with mean (±SD) age 40.0 ± 14.8 years. Of these, 156 patients (30.1%) had undergone surgery (CD-S) and 362 (69.9%) not (CD-NS). 38.1% of 189 men underwent surgery versus 25.5% of 329 of women ($p < 0.003$). Duration of illness was greater in CD-S, 15.9 ± 9.7 years, versus CD-NS, 9.2 ± 7.3 years ($p < 0.05$), although there was no statistical difference in age between these groups. Smoking status in CD-S (18.4%) and CD-NS (19.8%) was also similar. CD-S patients had more severe present illness than CD-NS as shown by the HBI scores, with 46.8% having HBI > 7 versus 33.9%, respectively ($p < 0.001$). In the multivariate analysis CD-S was significantly associated with male sex, HBI, and selected components of SF-36 and BSI (Table).

Table: Results of multivariate analysis for Surgery (CD-S) as dependent variable*

	OR	p
Gender (male)	1.592	0.032
HBI	1.144	<0.001
BSI: somatization	0.589	0.025
BSI: global severity index	1.544	0.088
SF-36: bodily pain	1.016	0.005
SF-36: general health	0.972	<0.001
SF-36: vitality	1.026	<0.001

*Adjusted for age, education, and the other components of BSI and SF-36.

Conclusion: Crohn's disease patients who underwent surgery were more likely to be males, had evidence of greater disease activity and more psychological stress. They had reduced quality of life with more bodily pain and poorer general health.

Disclosure of Interest: None declared

P0302 COPING STRATEGIES AND DEPRESSION IN CROHN'S DISEASE

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Introduction: A significant proportion of Crohn's disease (CD) patients shows depressive and anxious disorders. Depression may also lead dysfunctional coping strategies, which implement non-adaptive and often counter-productive behaviours.

Aims & Methods: This study assessed the prevalence of anxious or depressive symptoms, and evaluated the coping strategies in CD patients with severe depressive disorders.

One hundred consecutive CD patients in clinical remission, regularly followed in our IBD Unit were included in the study. Patients with diagnosis of psychiatric disorder preceding the diagnosis of CD and patients with history of substance abuse or neoplastic diseases were excluded.

The eligible patients were screened to identify anxiety and/or depression by using Hospital Anxiety and Depression Scale (HADS). Patients with HADS scores ≥8 in the subscale "depression" were further investigated by means of Cognitive Behavioural Assessment 2.0 and Beck Depression Inventory (BDI). Afterwards the coping strategies were assessed through the Brief-COPE questionnaire.

Results: Thirty-seven patients showed psychiatric co-morbidity: 21 patients had anxious symptoms, and 16 had depressive symptoms with (15 patients) or without (1 patient) anxious symptoms. Seven of these patients (43.8%) showed significant depressive symptoms confirmed at Beck Depression Inventory. None of them had ever been treated for depressive disorder.

Compared to patients without psychiatric disorders, these patients showed lower values of "positive reframing" (p:0.017) that refers to the items "I try to see it in a different light, to make it seem more positive" and "I look for something good in what is happening"; lower values in "planning" (p:0.046) that corresponds to the item "I try to come up with a strategy about what to do". Conversely, patients with depression showed higher score in "use of instrumental social support" ($p < 0.001$) corresponding to the items "I talk to someone to find out more about the situation" and "I try to get advice from someone about what to do", in the "denial" scale (p:0.001) that refers to the items "I say to myself this isn't real" and "I pretend that it hasn't really happened", and in the "use of emotional social support" (p:0.003) that includes the item "I try to get emotional support from friends or relatives".

Conclusion: Depressed CD patients have altered coping strategies, meaning that they may not be able to implement functional strategies to manage at best stress related with their disease. These findings confirm that some CD patients may need psychiatric intervention and an interdisciplinary approach between gastroenterologist and psychiatrist.

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P0303 CRYPTOGENETIC AND CROHN'S PERIANAL FISTULA: WHAT CHANGE IN PSYCHOLOGY OF PATIENTS

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Introduction: Perianal disease has been recognized as a relevant risk factor for anxiety and depression in Crohn's disease. However, its specific impact on mood disorders in patients with cryptogenic fistula has not been reported so far.

Aims & Methods: The aim of our study was to investigate the prevalence and associations of anxiety and depressive symptoms in the subset of Crohn's patients with perianal fistula and in patients with cryptogenic fistula.

Forty-two adult patients with confirmed diagnosis of Crohn's disease, in clinical remission, with perianal fistula and 20 patients with cryptogenetic fistulae were included in the study. Patients were included irrespective to the activity of the fistula, whether actively draining or closed, and clinical history of perianal disease, whether previously operated or not.

All patients were investigated using a standard questionnaire assessing demographic and clinical features of disease, and the presence of psychiatric disorders using standardized questionnaires. The questionnaire assessed the development of psychiatric disorders after the diagnosis of perianal fistula, the use of antidepressant or anti-anxiety therapy and current anxiety or depression by means of the Hospital Anxiety and Depression Scale.

Differences in quantitative data were compared using Chi square and Fisher's exact tests.

Results: Anxiety or depression were reported by 25 (59.5%) patients with Crohn's fistula and by 2 (10%) patients with cryptogenetic fistula ($p < .0001$). Fourteen patients (33.3%) with Crohn's fistulae and 18 (90%) of patients with cryptogenetic fistulae had been operated, whilst actively draining fistula were present in 6 Crohn's patients and in 3 patients with cryptogenetic fistulae.

The prevalence of anxiety with or without depression was not significantly correlated with activity of perianal fistulae, but previous operations for perianal fistulae was significantly correlated with anxiety or depression among Crohn's patients (4.1% vs 12.5%; $p = 0.042$)

Conclusion: Perianal fistula is significantly correlated with anxiety, with or without depression, only in Crohn's disease patients. Further studies are required to assess the impact of perianal disease overall quality of life and to address the need to target interventions.

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Disclosure of Interest: None declared

P0304 ALCOHOL CONSUMPTION BEHAVIOUR AND IMPACT ON GASTROINTESTINAL SYMPTOMS AMONG SWISS IBD PATIENTS

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Introduction: Little is known about alcohol drinking behaviour and its influence on gastrointestinal symptoms among patients with inflammatory bowel disease (IBD). In a preliminary analysis of the Swiss IBD cohort data using a screening question on alcohol drinking, we estimated a prevalence of 43% (≥ 1x alcohol consumption per week). Moderate alcohol consumption was associated with a shorter disease extend in ulcerative colitis (UC), whereas a lower risk of flares and hospitalizations was observed in Crohn's disease (CD).

Aims & Methods: We aimed to assess alcohol drinking behaviour and its influence on gastrointestinal symptoms in patients with IBD. Therefore, we sent a questionnaire to patients randomly selected from 3 different groups of patients according to the reported frequency of alcohol consumption at enrolment to the Swiss IBD cohort: Group A (< 1x weekly), B (1-7x weekly) and C (> 1x daily). Data collection was based on demographic variables and disease characteristics from the most recent follow up report available, as well as the average alcohol intake per day (based on standard drinks), type of drinking, the number of days with alcohol consumption per week, influence of alcohol on gastrointestinal symptoms and smoking assessed in a dedicated questionnaire.

Results: We received 383 of 537 (72%) questionnaires from our IBD patients (56% CD and 44%UC): *Group A: 182/243 (75%), B: 175/242 (72%), C: 27/52* (52%). The rate of abstainers was similar to the Swiss population*(12%). Among drinkers, 52% drank up to 1x weekly, 29% on 2-3 and 19% on 4-7 days per week. The amount of alcohol on each occasion was 0-20g in 70% of the patients, 20-40g in 24% and 40-60g in 5% and similar for both diseases. The incidence of binge drinking was similar to the Swiss population[1] with 12% monthly (vs. 11.3%), 3% weekly (3.7%) and 1% more than weekly (6%). Binge drinkers (> 6 drinks on one occasion at least monthly) are younger than the other IBD patients (mean age 39 vs. 49 years) and more often smokers

(42.4% vs. 25.4%) whereas the amount of standard drinks per week increased with age. After IBD was diagnosed 61% of the patients did not change, 29% reduced, 6% quit or 4% increased alcohol consumption. In both, CD and UC, 30% of patients reported worsening of diarrhea and 15% worsening of abdominal pain and bloating after drinking alcohol. The type of preferred beverage did not significantly influence this changes of symptomatology. Patients did not differ significantly regarding age, disease duration, localisation, behaviour, extra-intestinal manifestation and previous surgery in our study population based on alcohol consumption.
Conclusion: Drinking behaviour in Swiss IBD patients is similar to the general population and not influenced by the type of disease. A third of IBD patients reduce or quit drinking after being diagnosed. Worsening of diarrhea, abdominal pain and bloating after drinking alcohol was reported in 15-30% by both UC and CD patients, independently of the type of drinking.

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P0306 RS2476601 POLYMORPHISM IN PTPN22 IS ASSOCIATED WITH CROHN'S DISEASE BUT NOT WITH ULCERATIVE COLITIS; A META-ANALYSIS OF 16838 CASES AND 13 356 CONTROLS

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Introduction: Although the polymorphism of *PTPN22* rs2476601 has been reported to be a susceptibility gene for Crohn's disease, results from different studies varies and remain inconclusive. Also, no association has been found between rs2476601 and the risk of ulcerative colitis. The aim of this meta-analysis is to investigate the association between *PTPN22* polymorphism (rs2476601) and the risk of Inflammatory bowel Disease (IBD), Ulcerative Colitis and Crohn's disease.
Aims & Methods: We performed a meta-analysis by two independent reviewers by identifying relevant candidate-gene based studies from EMBASE and PubMed. The Odds ratio (ORs) and 95% confident interval were calculated to estimate the strenght of the associations between rs2476601 and inflammatory bowel disease by using a fixed effect or random effect model meanwhile publication bias was assessed
Results: By pooling the results from 16 different studies, 13 356 controls, 8 182 Crohn's disease, and 8656 Ulcerative Colitis were included. We show that *PTPN22* T > C is not associated significantly with a higher risk of developing ulcerative colitis (OR = 1.06 [0.98-1.14], p = 0.16) but is associated with a decreased risk of developing Crohn's disease (OR = 1.28 [1.17 – 1.40], $p < 0.0001$). T allele in rs2476601 lower the risk of Crohn's disease by 22%.
Conclusion: This study shows that *PTPN22* (rs2476601) is associated with the risk of developing a Crohn's disease significantly but not an ulcerative colitis suggesting different pathways in the pathophysiology of the disease.
Disclosure of Interest: None declared

P0307 A COMPUTATIONAL APPROACH TO GENOTYPE-DRIVEN DRUG REPOSITIONING IN INFLAMMATORY BOWEL DISEASE (IBD)

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Introduction: Inflammatory bowel disease (IBD) is a chronic inflammation of the digestive tract, which primarily manifests in two forms, ulcerative colitis (UC) and Crohn's disease (CD). Existing therapies are partly effective, and limited understanding of IBD pathogenesis hampers the development of new therapeutic approaches. Recent applications in computational drug repositioning hold the promise for cost effective solutions.
Aims & Methods: We report an in silico pipeline for genotype-driven drug repositioning in IBD using publicly available data from genome-wide association studies (GWAS), expression quantitative trait loci (eQTL) repositories, and drug-induced gene expression profiles from the Connectivity Map (cMap).
GWAS data were retrieved from ibdgenetics.org, and significant SNPs ($p \leq 0.05$) selected at each of the 163 known IBD risk loci. Two expression quantitative trait loci (eQTLs) databases (MuTHER, mRNAbySNP) were screened in order to produce a catalog of IBD genotype-specific eQTLs in different tissues, and to link genetic risk (protection, predisposition) to effect betas (up- or down-regulation). IBD, CD and UC gene expression signatures were then built based on physical distance and consistent cis-effects. These were used for functional annotation with hypergeometric test-based tools (WebGestalt), and as input for cMap drug screening using the embedded algorithm.
Results: We found 900 IBD SNPs associated with eQTLs in 2 databases in 3 different tissues (adipose, skin and/or LCL). After data filtering and quality controls for consistency of eQTL effects across genes, these SNP-eQTL profiles gave rise to IBD- CD- and UC-specific gene expression signatures including 91 annotated genes in total. Gene set enrichment analysis of these signatures highlighted immune response and cytokines production, but also intriguingly blood pressure and sulfur compound metabolism among the involved biological pathways. Similarly, anti-inflammatory compounds were among the top ranking drugs in the cMap screening, but other unexpected high-scoring categories included antipsychotics and antimicrobial. Of note, application of our pipeline to the analysis of available IBD-risk genotypes from individual patients resulted in detectable differences in the output of the corresponding cMap screenings.
Conclusion: We devised a novel computational approach to exploit (risk) genotype and eQTL data for drug repositioning in IBD. While its potential for implementation can greatly increase with the growing number of available tissue-specific eQTL datasets, our study proposes a novel effective translation of genomic information to precision medicine in IBD and other complex diseases.
Disclosure of Interest: None declared

P0308 GENETIC POLYMORPHISM IN THE TLR4 RELATED GENE CAN BE A PREDICTIVE FACTOR OF LONG-TERM EFFECT OF INFLIXIMAB TREATMENT FOR CROHN'S DISEASE

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Introduction: Infliximab (IFX) is a chimeric anti-tumor necrosis factor-α (TNF-α) monoclonal antibody exerting therapeutic effects against Crohn's disease (CD). However, some primary failure patients have been unable to achieve remission at the short-term period of 10 weeks. Moreover, the some responders at 10 weeks did get remission at the long-term period of 1 year later. Therefore, identification of biomarkers that might predict IFX therapeutic effects is important.
Aims & Methods: The purpose of this study was to investigate whether polymorphisms of target genes in the TLR4 signaling pathway are associated with the therapeutic effects of IFX for CD patients, and whether such polymorphisms could be used as new genetic biomarkers to identify CD patients having the sensitivity or resistance to IFX for the short- or long-term treatment.
The study subjects were 127 unrelated CD patients treated with IFX in our Hospitals between 2012 and 2013. Patients were classified into two groups, responders and non-responders, based on the presence of IFX effect at 10 weeks and 1 year after IFX administration. We examined a candidate gene-based association of 29 single nucleotide polymorphisms of 8 target genes in the TLR4 signaling pathway with the therapeutic effects of IFX, using the allele, minor allele dominant, and minor allele recessive models.
Results: The genetic analyses indicated that the frequency of a C/T or T/T genotype of rs4251580 in *IRAK4* in the minor allele dominant model were significantly decreased in responders as compared to non-responders for the middle-term treatment of 1 year ($P = 0.014$, odds ratio (OR) = 0.289), implicating ~3.5-fold resistance to IFX. Conversely, a C/C genotype of rs4251580 indicated ~3.5-fold sensitivity to IFX. Likewise, the possession of a T/T genotype of rs7255265 in *TICAM1* indicated ~4-fold resistance to IFX at 1-year treatment period ($P = 0.038$, OR = 0.252). Conversely, a C/C or C/T genotype of rs7255265 showed ~4-fold sensitivity to IFX. Subsequently, we carried out a genetic test with a combination of the two genetic factors (*IRAK4* and *TICAM1* genotypes), indicating that the possession of both the C/C genotype of rs4251580 in *IRAK4* and the C/C or C/T genotype of rs7255265 in *TICAM1* strongly showed responsiveness to IFX ($P = 0.003$, OR = 4.44). The sensitivity and specificity of this genetic test were estimated at 72.2% and 63.2%, respectively.
Conclusion: This is the first report that *IRAK4* and *TICAM1* could be associated with the responsiveness to IFX in CD patients. Combination of the 2 SNPs in rs4251580 and rs7255265 could be a biomarker to predict therapeutic effects at 1 year after IFX administration as well as target molecules for new therapeutic drugs overcoming the resistance to IFX. These results suggested that certain genetic prediction in the TLR4 signaling pathway and its downstream associated molecules might be involved in IFX responsiveness, possibly through altered expression of pro-inflammatory cytokines that would be held in common between the TNF-α and TLR4 signaling and the downstream cascades.
Disclosure of Interest: None declared

P0309 THE CLINICAL RELEVANCE OF THE IBD-ASSOCIATED VARIATION WITHIN THE RISK GENE LOCUS ENCODING PROTEIN TYROSINE PHOSPHATASE NON-RECEPTOR TYPE 2 IN PATIENTS OF THE SWISS IBD COHORT

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Introduction: The gene locus encoding protein tyrosine phosphatase non-receptor type 2 (PTPTN2) has been associated with an increased risk of developing

inflammatory bowel disease (IBD). We have previously shown that PTPN2 plays a critical role in maintaining intestinal epithelial barrier function, cytokine secretion and autophagy. The single nucleotide polymorphism (SNP) rs1893217 within the PTPN2 gene locus results in a dysfunctional PTPN2 protein and is associated with Crohn's disease (CD). SNP rs1893217 is in perfect linkage disequilibrium with the CD- and ulcerative colitis (UC)-associated PTPN2 SNP rs2542151. Here, we studied the association of PTPN2 SNP rs1893217 and clinical characteristics of the affected IBD patients.

Aims & Methods: 1,073 patients with CD and 770 patients with UC or indeterminate colitis (IC) from the Swiss IBD Cohort Study (SIBDCS) were included. Epidemiologic, disease and treatment characteristics were analysed for an association with the presence of one of the rs1893217 isoforms 'homozygous wild-type' (TT), 'heterozygous' (CT) and 'homozygous variant' (CC).

Results: 2.88% of IBD patients were identified with CC, 26.8% with CT and 70.4% with TT genotype. In univariate logistic regression analysis the CC-genotype was associated with an early age of diagnosis (OR 1.315; 95% CI: 1.068-1.620; $p = 0.010$) and existence of bilestones (OR 4.793; 95% CI: 2.000-11.490; $p < 0.001$) in CD patients as well as with the presence of pancolitis (OR: 4.581; 95% CI: 1.267-16.556; $p = 0.020$) in UC patients. These factors remained significant in the subsequent multiple regression analysis. Presence of the C-allele was associated with the presence of uveitis (OR: 2.020; 95% CI: 1.201-3.398; $p = 0.008$), but protected from aphtous oral ulcers (OR: 0.578; 95% CI: 0.335-0.998; $p = 0.049$) in CD patients. UC/IC patients carrying the C-allele were diagnosed at younger age (OR: 1.122, 95% CI: 1.001-1.257; $p = 0.049$) and required intestinal surgery more frequently (OR: 3.056, 95% CI: 1.011-9.239; $p = 0.048$). Significance was seen both in univariate as well as multiple regression analyses. Both, presence of the CC genotype or the C-allele were associated with a better response to treatment with anti-TNF antibodies in both CD and UC patients (chi-square test, p-value: 0.050).

Conclusion: IBD patients carrying the C-allele of PTPN2 SNP rs1893217 are at greater risk for developing a severe disease course as indicated by younger age at diagnosis, pancolitis and higher frequency of surgeries, but are more likely to respond to treatment with anti-TNF antibodies. These findings indicate a clinical relevance of this PTPN2 risk variant in IBD patients and suggest that PTPN2 may be used as predictive marker for early treatment with anti-TNF antibodies.

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P0310 SNP RS6105269, A NEW PROGNOSIS MARKERS FOR CROHN DISEASE

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Introduction: Crohn disease (CD) is a chronic disease that can have a variable course, from a mild inflammatory effect to a severe disease with the appearance of fistulas, ulcers, abscesses, strictures that can lead to a significant impairment in quality of life. An early identification of these patients, would allow an early intensive treatment for changing the natural history of the disease. For this purpose, is essential to identify prognosis markers. The SNP rs6105269 has been identified as risk factor for CD [1].

Aims & Methods: The aim of the study is to analyze the rs6105269 polymorphism, located in the MACROD2 gene, as a prognosis marker of CD and the effect of the polymorphism in the protein expression of MACROD2. 95 patients have been enrolled and classified according to their genotype of rs6105269 polymorphism (AA, AG and GG). A Chi-square test or Fisher test have been used to study if there are significant differences among the genotypes in clinical characteristics related to a severe CD. We propose a definition of severe/disabling disease based on the development of non reversible tissue lesions as any colectomy or at least two small bowel resections or a unique resection > 50 cm or complex perianal fistulizing disease. Furthermore, plasma levels of MACROD2 protein have been analysed by ELISA assay.

Results: 43% of AA patients has family history of IBD (GG 12%, AG 9%, $p = 0.009$). The AA genotype is link to a stricturing and fistulizing patterns (AA 80% patients, GG 47% and 38% AG, $p = 0.02$) and 73% of patients with AA genotype develops a severe/disabling CD vs AG + GG 44%, ($p = 0.04$). 50% of AA patients suffers from a complex perianal disease vs 12% of GG or 19% of AG ($p = 0.01$). In particular, suprasphincteric, transsphicteric and extrasphicteric fistulas are present in 36% of AA patients vs 10% of AG + GG patients ($p = 0.03$) and 31% of AA patients have required surgical drainage of fistula abscess vs 9% of GG and 2% of AG ($p = 0.01$). Furthermore, the levels of the inflammatory marker CRP were increased in AA patients (AA: 22.5 ng/ml, GG: 3.8 ng/ml, AG: 4.2 ng/ml, $p = 0.02$), while the MACROD2 plasma levels are significantly downregulated in genotype AA (AA: 851 ng/ml, GG: 1372 ng/ml, AG: 907 ng/ml, $p = 0.04$).

Conclusion: Genotype AA of the polymorphism rs6105269 is associated with a more severe CD and the polymorphism can be used as a prognosis marker of the disabling disease. Genotype AA produces a downregulation in protein levels of MACROD2, suggesting that this protein may have a protective role in CD.

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P0311 MR ENTEROGRAPHY OR CAPSULE ENDOSCOPY - WHAT DO CROHN'S DISEASE PATIENTS PREFER?

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Introduction: Despite differences in the information obtained by capsule endoscopy (CE) and magnetic resonance enterography (MRE) regarding mucosal and intestinal wall abnormalities in Crohn's disease patients, one of these modalities may need to be chosen or may suffice when evaluating disease activity. There are no data on patients' preference that would help guide the choice between these two modalities in these instances. Despite differences in the information obtained by capsule endoscopy (CE) and magnetic resonance enterography (MRE) regarding mucosal and intestinal wall abnormalities in Crohn's disease patients, one of these modalities may need to be chosen or may suffice when evaluating disease activity. There are no data on patients' preference that would help guide the choice between these two modalities in these instances.

Aims & Methods

Aim: To compare patients' tolerance to MRE vs CE.

Methods: Patients with known small bowel CD in clinical remission (CDAI < 150) or with mild symptoms (CDAI < 220) were prospectively recruited and underwent video capsule endoscopy after verification of small bowel patency and MRE examination. Patients' were asked to fill a questionnaire addressing specific points regarding inconvenience during preparation, during procedure and post procedure. Side effects and procedure preference were addressed. Degree of severity was graded from 1 (not at all) to 5 (severe). Questionnaires were included for analysis only when more than 95% of the items were addressed.

Results: Out of 62 patients approached 56 fulfilled inclusion criteria. Results are summarized in table 1.

subject	MRE (severity degree± SD)	CE (severity degree± SD)	P value
home preparation	2.38 ± 1.32	1.13 ± 2.68	0.1215
pre-exam discomfort	1.22 ± 2.7	0.99 ± 1.5	< 0.0001
discomfort during the exam	1.22 ± 3.7	1.08 ± 2.0	< 0.0001
nausea	18. 1 ± 2.24	0.53 ± 1.29	< 0.0001
vomiting	1.05 ± 1.5	0.37 ± 1.07	0.009
bloating	1.14 ± 2.01	0.55 ± 1.25	0.0002
Abdominal pain	1.1 ± 2.24	0.63 ± 1.33	< 0.0001
tenesmus	0.87 ± 1.40	0.55 ± 1.14	< 0.0001
claustrophobia	0.7 ± 1.40	0 ± 1	< 0.0001
Time consuming	1.19 ± 3.46	1.23 ± 3.0	0.0594
Difficulty	1.13 ± 3.42	0.98 ± 2.03	< 0.0001
Drinking of contrast material	1.22 ± 3.2	NR	NR

44 patients (78%) preferred to repeat CE.

Conclusion: CE was significantly better tolerated in most parameters and preferred by 78% of patients . The superior tolerability of CE should be considered when choosing between these two modalities for suitable patients.

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P0312 EVALUATION OF NT-PROBNP IN INFLAMMATORY BOWEL DISEASE

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Variables	Se, % (95% CI)	Sp, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Altered US-BP	78.3 (69.3-85.2)	93.3 (86.6-96.9)	75.0 (65.8-82.5)	94.4 (87.9-97.6)
Mesenteric hypertrophy	65.2 (55.6-73.8)	92.2 (85.2-96.2)	68.2 (58.7-76.4)	91.2 (84.0-95.5)
BWT > 3 mm	69.6 (60.1-77.7)	96.7 (90.9-99.0)	84.2 (75.9-90.1)	92.6 (85.6-96.4)
BWT > 3 mm + US-BP + MH	56.5 (46.9-65.7)	100 (95.9-100)	100 (95.9-100)	90.0 (82.6-94.6)
BWT > 3 mm or US-BP or MH	82.6 (74.1-88.9)	86.7 (78.7-92.1)	61.3 (51.6-70.2)	95.1 (88.9-98.1)

Introduction: N-Terminal pro-Brain Natriuretic peptide (NT-proBNP) is currently used as a diagnostic marker in heart failure. Elevated NT-proBNP and significant correlation between NT-proBNP and CRP was recently reported in rheumatoid arthritis (1) and in Crohn's Disease (CD) (2). The purpose of this study was to evaluate NT-proBNPas a marker of inflammatory bowel disease (IBD) activity.
Aims & Methods: In this single-center study, NTproBNP assay was performed in patients with CD or ulcerative colitis (UC), irritable bowel syndrome (IBS) and in healthy controls. Clinical characteristics (Harvey-Bradshaw score (HB), Mayo Clinic score (Mayo)), biological (CRP) and endoscopic (CDEIS, UCEIS) data were collected at the time of NTproBNP dosage. Echocardiography was performed in case of NT-proBNPserum levels > 124pg/ml.
Results: To date, 118 patients with CD, 26 with UC, 20 with IBS and 18 healthy controls were included. The median serum NT-proBNP was 50.5 pg/ml [Q1 = 28-Q3 = 94] in CD group, 72 pg/ml [46-138] in the UC group, 43.5 pg/ml [27-111] in IBS Group and 34.5pg/ml [26-49] in the control group. A significant increase of NT-proBNPlevels was observed in CD patients with HB > 4 (p = 0.02) or UC with Mayo > 2 (p = 0.03) as compared to inactive patients. There was a significant correlation between NTproBNP and, the HB score (r = 0.31, p = 0.0005), and the Mayo score (r = 0.45, p = 0.01) respectively. A significant increase in NT-proBNP was observed in CD ($p < 0.001$) and UC ($p < 0.0016$) patients having CRP > 10 mg/l as compared to patients with CRP£10. There was a significant correlation between NT-proBNP and CRP in both CD (r = 0.64, $p < 0.001$) and UC (r = 0.8, $p < 0.001$). Among the 34 patients who had a colonoscopy a significant correlation between NT-proBNP and, CDEIS (r = 0.85, $p < 0.001$), and UCEIS (r = 0.78, p = 0.007) was observed respectively. ANTproBNP level of 57pg/ml had a sensitivity (Se) of 70% and a specificity (Sp) of 63% (AUC 0.73, 95%CI [0.63-0.83]) to predict a CRP > 10 mg/l in CD. In UC, a rate of NTproBNP of 75 pg/ml had a Se of 88% and a Sp of 75% (AUC 0.87, 95%CI [0.71-1]) to predict a CRP > 10 mg/l. All echocardiograms performed were normal.
Conclusion: NT-proBNP is correlated to the clinical, biological and endoscopic activity of CD and UC and may be a new biomarker in IBD.

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P0313 RELEVANCE OF ULTRASONOGRAPHIC PARAMETERS IN PREDICTING INFLAMMATORY BOWEL DISEASE IN A PEDIATRIC POPULATION

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Introduction: Bowel ultrasound (B-US) has been widely recognized as a useful examination in patients with suspected IBD owing to its lack of invasiveness. The relevance of increased bowel wall thickening (BWT) and the additional value of other US parameters (e.g. lymph node enlargement and mesenteric hypertrophy (MH)), in the diagnosis of IBD have not been investigated so far.
Aims & Methods: This study aims at investigating the diagnostic accuracy of several US parameters in detecting IBDs in a pediatric population.
All patients aged 2-18 years referred to the Pediatric Gastroenterology Clinic of our Hospital since 2007 to 2013 for recurrent abdominal pain and/or altered bowel habits were retrospectively considered. Patients presenting with known organic diseases or already investigated with digestive endoscopy were excluded; those with a full US report (including altered US bowel pattern (US-BP), BWT, MH, pathologic lymph nodes, free abdominal fluid, presence of stenosis, abscesses or fistulae) were considered eligible. Ileocolonoscopy, performed in patients with a high index of suspicion of IBD, on the basis of paediatrician's assessment and biochemical test results (e.g. calprotectin, CRP), has been used as reference standard. Children who initially were not selected for endoscopy, were followed for at least one year for the appearance of possible additional symptoms.
Results: 113 patients (mean age 10.8 years [range 2.1- 17.7], 65 male) were enrolled. 23 IBD (20.4%; 8 ulcerative colitis, 12 Crohn's disease and 3 indeterminate colitis) were diagnosed. Among the bowel US variables considered, only US-BP, MH and BWT > 3 mm were found useful to identify IBD on univariate binary logistic analysis. On multivariate analysis, these factors were independent predictors of IBD, even after adjustment for age and sex: US-BP (OR 9.8;95%CI 1.6-59.0); MH (OR 5.2;95%CI 1.1-25.1) and BWT > 3 mm (OR 5.4;95%CI 0.7-40.1). Diagnostic accuracy of single US parameters and their combination, in distinguish between IBD and non IBD patients, is reported in the table.
Conclusion: Among several US parameters suggestive of IBD, only the increased BWT, MH and altered echopattern are independent predictors of IBD and useful in distinguishing IBD from non-IBD patients. Owing to their high specificity and NPV, these parameters can be useful in identifying patients who do not need diagnostic invasive procedures in the short time.
Disclosure of Interest: None declared

P0314 ACCURACY OF FECAL CALPROTECTIN, BOWEL ULTRASONOGRAPHY AND INFLAMMATORY INDEXES IN THE DIAGNOSIS OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE

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Introduction: IBD in pediatric age may present with non specific gastrointestinal symptoms overlapping with functional bowel disorders or with extraintestinal manifestations making the diagnosis a challenge.
Aims & Methods: The aim of our study was to assess the accuracy of non invasive parameters including fecal calprotectin (FC), bowel ultrasound wall thickening (BWT) and blood inflammatory indexes (BII) alone or in combination as a diagnostic tool for paediatric inflammatory bowel disease (IBD).
Subjects aged 2-18 years referred to our paediatric gastroenterology clinic from 2007 to 2013 for recurrent abdominal pain and/or altered bowel habits were retrospectively considered. Subjects who underwent laboratory tests (FC, BII: white blood cell count [WBC], C-reactive protein [CRP], erythrocyte sedimentation rate [ESR]) and bowel ultrasound as initial assessment were eligible. Exclusion criteria were: signs or symptoms highly suggestive for IBD (perianal disease or haematochezia), known organic disease, previously performed endoscopy. Eligible patients were followed-up for one year.
Results: Seventy-seven patients (mean age 11.3, 44 males) were retrospectively included. One-year diagnoses were: 23 (29.9%) IBD (8 ulcerative colitis, 12 Crohn's disease 3 indeterminate colitis), 54 (70.1%) non-IBD diseases. Mean values of WBC, CRP, ESR ($p < 0.001$) and at least one BII pathological value were higher in IBD vs non-IBD patients (65.2% v 11.1%, $p < 0.001$). Pathological BWT (> 3 mm) and FC (> 200 μg/g) were more frequent in IBD than in non-IBD patients (69.6% vs 3.7%, $p < 0.001$ and 95.7% vs 27.8%, $p < 0.001$ respectively). Considering 3 (BII + FC + BWT) or 2 parameters together (FC + BWT, FC + BII) IBD patients had more simultaneous pathological results than non IBD-patients (52.2% vs 0%, $p < 0.001$; 69.6% vs 0%, $p < 0.001$; 65.2% vs 3.7%, $p < 0.001$ respectively). Diagnostic accuracy of considered parameters are described in the table.

Variables	Se, % (95% CI)	Sp, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
BII*	65.2 (53.3 – 75.6)	88.5 (78.5 – 94.4)	71.4 (59.7 – 81.0)	85.2 (74.7 – 92.0)
BWT(> 3 mm)	69.6 (57.9 – 79.3)	96.3 (88.5 – 99.1)	88.9 (79.2 – 94.6)	88.1 (78.3 – 94.6)
FC (> 200 μg/g)	95.6 (87.7 – 98.8)	72.2 (60.7 – 81.5)	59.5 (47.7 – 70.3)	97.5 (90.2 – 99.6)
FC + BWT + BII	52.2 (31.8 – 72.6)	52.2 (40.6 – 63.6)	100 (94.1 – 100)	83.1 (72.4 – 90.3)
FC + BWT	69.6 (57.9 – 79.3)	100 (94.1 – 100)	100 (94.1 – 100)	88.5 (78.7 – 94.3)
FC + BII	65.2 (48.5 – 79.1)	88.2 (73.3 – 95.7)	88.2 (73.3 – 95.7)	65.2 (48.5 – 79.1)

Se = sensitivity. Sp = specificity, PPV = positive predictive values, NPV = negative predictive values.* at least one altered

Conclusion: In initial work-up for IBD, FC alone presents highest sensitivity but poor specificity. The combination of FC + BWT presents the highest accuracy in identification of patients needing further invasive procedures in the short term.
Disclosure of Interest: None declared

P0315 DIFFERENTIAL EXPRESSION OF MICRORNAS IN SERA AND FECES OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Assessment of the disease activity in inflammatory bowel disease (IBD) is essential for appropriate treatment management. Symptom-based disease activity scores do not always correlate with endoscopic scores and are not reliable for verification of mucosal healing as a primary treatment goal. New non-invasive molecular biomarkers could substantially simplify the treatment management. MicroRNAs (miRNAs) are functionally active molecules and the

expression pattern is frequently deregulated during inflammation and carcinogenesis.
Aims & Methods: Here, we evaluate the potential of several circulating and fecal miRNAs as diagnostic biomarkers for IBD. In the proof-of-principle trial, we obtained blood or fecal specimens form patients with known or newly diagnosed IBD. From total 61 patients, 41 had histologically confirmed Crohńs Disease (CD) or indeterminate colitis and 18 patients ulcerative colitis (UC). Among them 38 patients had an active disease and 24 were in remission (CDAI < 150 for CD or Mayo-Score ≤ 1 for UC). Total RNA was isolated from sera and fecal specimens and quantitative RT-PCR analyses was performed for miR-16, miR-21, miR-223 and miR-155 using TaqMan Assay.
Results: The sera samples from IBD patients showed an increased expression level of miR-21 ($p < 0.0001$) and miR-223 ($p < 0.0001$), but not miR-155, compared to controls. The expression was higher in patients with clinically active disease compared to those in remission. In subgroup analyses, patients with CD demonstrated highest miRNA expression for both miRNAs compared to controls and UC ($p < 0.0001$, Kruskal-Wallis test). Similarly, miRNAs in feces from IBD patients showed strong increase in expression of all four miRNAs with highest expression of miR-16, miR-223 and miR-155. Opposite to miRNA expression in sera, stool samples from UC showed similarly or even higher miR-16, miR-223 and miR-155 level in feces. Clinical remission in IBD patients was associated with normalization of fecal miRNA expression. Despite the significant correlation with disease activity, only fecal miRNA, but not circulating miRNAs, correlated with surrogate parameters such as fecal calprotectin or C-reactive protein.
Conclusion: Our data provide a novel evidence for differential expression of miRNAs in sera and feces from patients with IBD. The increased expression of miRNAs correlates with disease activity especially in fecal samples. Further studies are needed to optimize this miRNA-based biomarker tool and evaluate the clinical applicability for treatment monitoring in IBD patients.
Disclosure of Interest: None declared

P0316 UROCORTIN 1 IN COLONIC MUCOSA IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is characterized by a long-standing chronic inflammation of the bowel with intermittent periods of exacerbation and remission. Its acute exacerbation appears to be related to various stresses. Urocortin 1 (Ucn1) may play important roles in integrated local responses to stress. We therefore examined local production of Ucn1 in patients with UC by immunohistochemistry
Aims & Methods: We therefore examined local production of Ucn1 in patients with UC by immunohistochemistry to detect the degree of inflammation. Ucn1 immunoreactivity was predominantly detected in lamina propria plasma cells and enterochromaffin cells. In UC patients without glucocorticoid treatment, Ucn1-positive cells and plasma cells increased in proportion to the severity of inflammation.
Results: Ucn1 immunoreactivity was predominantly detected in lamina propria plasma cells and enterochromaffin cells. In UC patients without glucocorticoid treatment, Ucn1-positive cells and plasma cells increased in proportion to the severity of inflammation ($P < 0.0001$). Ucn1-positive cells significantly increased in UC patients with advanced inflammatory grades, compared with a control group ($P < 0.0001$) and nonspecific colitis group ($P < 0.0001$). In glucocorticoid-treated patients, Ucn1-positive cells were significantly lower in number, compared with the nonglucocorticoid-treated group.
Conclusion: The present study showed that Ucn1-positive cells were correlated with the severity of inflammation in colonic mucosa with UC, and glucocorticoid treatment decreased these cells. Ucn1 therefore may act as a possible local immune-inflammatory mediator in UC.
Disclosure of Interest: None declared

P0317 USE OF FAECAL CALPROTECTIN PATHWAY IN PRIMARY CARE TO DISTINGUISH IRRITABLE BOWEL SYNDROME FROM INFLAMMATORY BOWEL DISEASE

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Introduction: Faecal Calprotectin (FCP) testing is a simple, non-invasive investigation which can differentiate Inflammatory Bowel Disease (IBD) from Irritable Bowel Syndrome (IBS). It has high negative predictive values which allow utilisation in Primary Care by reducing unnecessary referrals to secondary care & expensive/invasive diagnostic tests eg. Colonoscopy and in turn suggest potential cost-effective benefits. FC is well established in secondary care, but the literature for FC in primary care is extremely limited.
Aims & Methods
Aim: Evaluation of a pilot study of a defined FC pathway in Primary Care.
Method: A primary care referral pathway was devised to guide appropriate use of FC in Primary Care to exclude IBD in appropriate patients, particularly if secondary care referral was being considered.
A pathway proforma with initial screening tests (FBC, LFTs, TTG, CRP, TSH & stool microbiology). Inclusion/Exclusion criteria: 16-45yrs age, IBS-compatible symptoms for ≥6 weeks/recurrent, no red flags. This was based on IBS guidelines (BSG), FC literature & recent NHS Centre for Evidence-Based Purchasing report (2010).
FC results (via Quantum Blue test kits) were classified as normal, intermediate or high. Each result was advised on further appropriate action. Subsequent clinic attendances, investigations, diagnostic outcomes & associated costs were evaluated.
Results: Nineteen GP surgeries (19/22) referred 277 patients via FC pathway over 24 months (Jan 2013-Jan 2015). Forty-five samples rejected as inappropriate.

Table 1: Faecal Calprotectin results (received to date)

FCP Interpretation	FCP result (μg/g)	Patients (n = 232)	Pathway Action
Normal < 50	< 50	62.1% (144/232)	IBD excluded. Retain in primary care
Indeterminate	50-150	22.4% (52/232)	Repeat after 4-6 weeks, if repeat > 50ug/g refer to secondary care
Elevated	> 150	15.5% (36/232)	Refer to secondary care

Diagnosis outcomes were available on 175/232 patients at the time of presented data analysis: Elevated 13.7%(24),Indeterminate 19.4%(34) & Normal 66.8%(117).
In Elevated FC clinic attenders, IBD was detected in 50%(11/22).
Indeterminates were repeated in only 68%: normal repeat 52.2% (12/23), 2 IBD cases detected. After a normal FC, 12.8% were referred to secondary care anyway, but no IBD detected.
In the normal FC group alone, assuming a normal FCP avoided a secondary care referral in 87.2% (102/117), the potential cost savings = £73,468 (assuming new patient clinic + 1 colonoscopy = £741.68).
Conclusion: Preliminary data suggests a structured FC pathway is effective in distinguishing IBD & IBS in Primary Care with significant cost savings. Further refinement is required for age ranges & FC cut-off points. Based on this pilot data & latest NICE Diagnostic Appraisal 11, the local Clinical Commission Group have commissioned a secondary care supervised FC service for primary care.
Disclosure of Interest: None declared

P0318 ILEAL CROHN'S DISEASE: MAGNETIC RESONANCE ENTEROGRAPHY AS A PREDICTOR OF RELAPSE AFTER ANTI-TNF DISCONTINUATION

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Introduction: Anti-TNF therapy has proven effective in maintaining remission of Crohn's disease (CD), although the optimum duration and strategies for withdrawal in asymptomatic patients remain unclear. The discontinuation of anti-TNF may be considered due to safety and cost issues and decision should be based on clinical, endoscopic, and biological factors. However, in cases of ileal CD, ileocolonoscopy study is limited and biomarkers such as C-reactive protein (CRP) or calprotectin may be less useful in evaluating inflammatory activity.
A multidiscliplinary european expert panel (EPACT-II update) considered imaging techniques to show an "uncertain" suitability for monitoring CD activity, so that there have been few studies about their role in the decision of stopping biologicals.
Aims & Methods: The aim of this study is to evaluate the capability of MR-enterography to predict disease relapse after withdrawal of anti-TNF therapy in patients with ileal CD.
A prospective study was conducted between 2009 and 2014 in our hospital over CD patients with ileal involvement in whom anti-TNF (Infliximab or Adalimumab) was stopped. Withdrawal was only carried out in patients on deep clinical, biochemical, and endoscopic remission, defined as absence of symptoms (Harvey-Bradshaw score ≤ 3), endoscopic mucosal healing (SES-CD < 2), and CRP < 5 mg/L or Calprotectin < 150 μg/g. Follow-up visits were performed every 3 months after cessation of treatment or earlier in cases of suspected relapse.
Patients underwent a Magnetic Resonance Enterography (MRE) before drug withdrawal on a Philips Intera 1.0 scan (median 30 days, range 10-82). The degree of activity of the ileal CD was assessed by an MRE score used in our hospital.
The MRE scores of the patients with and without relapse were compared using the independent samples t-test. Furthermore, a logistic regression analysis of the total MRE score as well as each parameter individually was performed, considering the relapse as the independent variable.
Results: A total of 29 patients (16 females and 13 males) with a mean age of 36.6 years (range 16-64) were included in the study. The median follow-up time since biological withdrawal was 45.2 months (range 15-72). The average time of recurrence was 17.1 months (range 3-57). Relapse rates were 24% at 1 year and 52% at 2 years.
Patients who relapsed had higher MRE score (4.2 vs. 2.5 $p < 0.02$) than those who did not. The relative risk of relapse in patients with an MR score > 3 was 2.21 (1.1-5 $p < 0.05$), significantly higher than in patients with a score of 0-3 in the pre-withdrawal MRE.
Logistic regression analysis showed that MRE score is an independent predictor of relapse (hazard ratio 0.185 $p = 0.02$). In terms of single MR parameters,

only the presence of hyperintensity on T2-weighted sequences, which translates the bowel wall oedema, can be regarded as an independent predictor of relapse (hazard ratio 0.149 $p < 0.04$).
Conclusion: This study demonstrates that, at least in patients with ileal CD, MRE should be taken into consideration when deciding the withdrawal of anti-TNF therapy in patients who are in clinical, biological, and endoscopic remission.
A MRE score > 3 as well as the hyperintensity of the bowel wall on T2-weighted sequences increase the likelihood of relapse.
Disclosure of Interest: None declared

P0319 RELATIONSHIP BETWEEN ANTI-TNF TROUGH LEVEL THRESHOLDS AND EFFICACY LEVEL IN LUMINAL AND PERIANAL CROHŃS DISEASE: DIFFERENT STRATEGIES IN CLINICAL PRACTICE

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Introduction: Several studies have shown a correlation between antiTNF trough levels (TL) and clinical or endoscopical remission in luminal Crohńs disease (CD), but there are few data about the role of TL in perianal CD or in radiological response.
Aims & Methods: Our aim was to determine the optimal TL associated with clinical, endoscopical and radiological remission for different phenotypes of CD. We included 32 antiTNF naïve patients with moderate to severe luminal (n = 24) and perianal (n = 8) CD under antiTNF treatment over 24m. Management of patients was based on clinical assessment and investigators were blinded to the TL results.
The TL measurements were performed just before antiTNF injection simultaneously with faecal calprotectin (calprotectin < 250ug/g was defined as normal). The Harvey-Bradshaw and the Perianal Disease Activity Index (PDAI) were reported (HBI-remission < 4; PDAI-remission < 3). Endoscopic evaluation was performed at weeks 0 and 54 (SES-CD remission < 2). In case of ileal location or perianal disease, magnetic resonance enterography (MRE) or pelvic resonance were performed. The activity was assessed with our own validated MRE index (remission < 3) and the Van Assche Index for perianal disease.
Results: At 54w, 84% of patients were in clinical remission. Deep remission (clinical with endoscopical /radiological remission) was observed in 56.2%. Up to 37% of all patients required dose escalation due to a loss of response in the first year (62% of perianal CD vs 21.8% of luminal CD;$p < 0.05$). Intensification was effective in 75% of cases in whom serum TL after escalation was detected above cut-off levels. Patients in clinical remission without endoscopical or radiological remission showed calprotectin > 250 ug/g in 84%.
The optimal IFX /ADA TL cut-off associated with clinical remission in luminal CD was 1.1µg/ml and 2.51µg/ml respectively (sensitivity: 78% and 82%; specificity: 76% and 78%), while IFX /ADA TL cut-off associated with normal calprotectin, endoscopical or radiological remission in luminal disease was 2.7µg/ml and 5.4 µg/ml (sensitivity: 79% and 74%; specificity: 76% and 80%). The optimal IFX /ADA TL cut-off in perianal disease was similar for clinical, endoscopical and radiological remission: 2.7µg/ml and 5.4 µg/ml respectively (sensitivity: 79% and 74%; specificity: 76% and 80%). IFX TL > 2.7 and ADA TL > 5.4 were associated with a decreased risk of treatment failure (RR 0.34; RR 0.38).
Conclusion: 1. Serum anti-TNF TL associated to endoscopical or radiological remission are higher than TL associated to clínical remission in luminal Crohńs disease, but not in perianal disease where cut-off levels are the same in both clinical and radiological remission. Furthermore, perianal CD required dose escalation more frequently than luminal CD.
2. A calprotectin level > 250ug/g was associated with endoscopical or radiological activity in patients on clinical remission and could be useful to decide upon the need of endoscopical /radiological explorations.
Disclosure of Interest: None declared

P0320 USABILITY STUDY OF A SMARTPHONE-BASED CALPROTECTIN HOME TEST

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Introduction: Inflammatory Bowel Disease (IBD) is a chronic inflammation of the gut presenting with phases of active inflammation, remission and relapses. IBD treatment goals are mucosal healing and persistent remission. Calprotectin measured in patients' stool samples is a well-established biomarker to measure the inflammatory activity in the gut. Periodical assessment of calprotectin levels is important to measure effectiveness of the treatment as well as predicting relapses. Until now this meant that patients send in their stool sample for laboratory analysis, leading to long time spans between sample collection and final test result. To ensure real-time information about the inflammatory activities in the gut for both, the patient and the clinician, we have developed a calprotectin home test called IB*Doc*®. The IB*Doc*® consists of a stool collection and extraction device (CALEX® Valve) and an immunochromatographic calprotectin rapid test, which is measured using a smartphone App (CalApp®) controlling the phone's camera. Once the test is measured the result is sent to a webserver (IB*Doc*® Portal) allowing the treating physician immediate access to the result.
Aims & Methods: The objective of this study was to evaluate the usability of the IB*Doc*® calprotectin home test system with patients in respect of handling both, the physical test components as well as the integrated software.
10 voluntary patients suffering from IBD and naïve to the IB*Doc*® system were trained to perform the test by their IBD nurse. The patients were then asked to perform a calprotectin stool test every two weeks over a period of two months by themselves at home using the IB*Doc*® system. The patients were asked to fill in a questionnaire after the first and the last test performed. The questionnaires were based on 5-point Likert scale questions concerning all steps of the test in respect of usability aspects. It also contained free commentary sections and system usability scale (SUS) score question. The SUS is commonly used for measuring and comparing the usability of software and integrated software systems.
Results: All patients were able to able to perform home test using the IB*Doc*® system during the course of the test period. All patients (100%) felt well instructed and the instructions for the test were well understood (4.7 on a 5-point Likert Scale). When asked how easy it was to measure the test cassette with the smartphone, the patients judged this question with an average score of 4.8 on a 5-point Likert scale. The test result was displayed by the smartphone app in a clear way with a traffic light interpretation and quantitative results within the measuring range of 30-1000 µg/g of calprotectin. The test result was easy to understand for all patients (100%). All patients would use the IB*Doc*® system in the future (100%). 87% of the patients felt that the home test helps them in their disease management. The IB*Doc*® system reached a mean SUS score of 88 on a scale from 0 to 100. This SUS is well above the software industry's average score of 68.
Conclusion: This study shows that calprotectin home testing using a smartphone as measuring system was well accepted among IBD Patients. The complexity of the application is low, the entire IB*Doc*® system can be considered very user-friendly and is easy to handle by lay users without prior knowledge or experience of immunochromatographic rapid tests.
Disclosure of Interest: None declared

P0321 SELECTING IBD PATIENTS WHO WILL BENEFIT FROM THROMBOPROPHYLAXIS THROUGH A RISK ASSESSMENT THAT INCLUDES CLOT LYSIS PARAMETERS AND CLINICAL ASSESSMENT

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Introduction: Patients with inflammatory bowel disease (IBD) have a higher risk of developing thromboembolic events (TE) compared to the healthy population. TE has a substantial impact on mortality in IBD and TE prevention requires improved awareness and management.
Aims & Methods: The aim of the study is to describe the clinical characteristics of IBD patients with a history of TE and to compare markers of clot lysis between (1) IBD patients and healthy controls (HC) and (2) IBD patients with (IBD + TE) and without a history of TE (IBD-TE).
In this study, 84 IBD patients in whom a TE occurred (between January 1987 and March 2014) after the diagnosis of IBD, seen at an academic referral center between February 2009 and May 2012 were included. During the same period, 118 IBD patients without a history of TE and 113 healthy controls were selected as control groups in this case-control study. Three clot lysis parameters (area under the curve (AUC); 50% clot lysis time (CLT) and amplitude) were determined.
Results: Of the 84 IBD + TE patients (63% Crohn's disease, 44% males), 70/84 (83%) developed a venous TE and 25/84 (30%) patients were identified with recurrent TE. At time of TE, 60/84 (71%) patients had active disease and 36% received steroids. Within a 6-month period preceding the TE, 31/84 (37%) had been operated of whom only 17% received thromboprophylaxis at hospital discharge. Both the 50% CLT and AUC were significantly associated with the presence of IBD as compared to controls. Moreover, AUC (31 (24-49) vs. 22 (13-31), $p < 0.05$), 50% CLT (110 (64-132) vs. 95 (70-126) minutes, $p < 0.05$) and amplitude (0.295 (0.222-0.436) vs. 0.241 (0.168-0.308), $p < 0.05$) were significantly higher in IBD + TE vs. IBD-TE and remained higher after adjustment for age, gender, C-reactive protein, type of disease, presence of comorbidities and disease activity.
Conclusion: This study reveals that IBD patients have an altered clot lysis profile compared to healthy controls. In addition, the clot lysis parameters differ significantly between IBD patients with and without a history of TE. Of the IBD patients with a history of TE, 36% received steroids at time of TE and 37% underwent recent surgery of whom only a minority received thromboprophylaxis at hospital discharge. To date, IBD patients with a high risk for TE are given thromboprophylaxis. However, for the patients with low to moderate risk for TE it is less clear who will benefit from prophylactic therapy. Therefore, we propose to perform a risk assessment in which clot lysis parameters and IBD specific risk factors for TE are combined to identify the patients who can benefit from prophylactic therapy with low molecular weight heparins.
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P0322 VITAMIN D STATUS IN IBD PATIENTS: A COMPARISON OF THREE DIFFERENT ASSAYS

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Introduction: Vitamin D (VD) is a fat soluble secosterol that is produced in the skin after the sun exposure. Epidemiological studies show significant associations of VD deficiency and immune mediated diseases. The plasma 25-OH vitamin D3 concentration is a reliable biomarker for VD status but assays' variability makes adequate monitoring of VD difficult.

Aims & Methods: The aim of this study was to compare three different assays for measurement of 25(OH)D and to evaluate the impact of 25(OH)D assessment on clinical decision making.

Blood samples from 50 IBD patients were evaluated in a blinded way in three different laboratories using diverse assays of 25 (OH) vitamin D monitoring such as high-performance liquid chromatography (HPLC), IDS automated immunoassay (IDS) and competitive binding assay (CBP). We correlated the VD levels of different assays using Pearson correlation coefficient. To quantify the agreement between total 25(OH)D serum levels from all three assays, the interclass correlation coefficient (ICC) was calculated. We evaluated the clinical accuracy of each assay by examining the agreement of assays in sorting patients into distinct categories according to difference of VD levels using the cutoffs (< 5ng/ml) for acceptable agreement, (5-10ng/ml) significantly different and (> 10ng/ml) insufficient.

Results: The median serum 25(OH)D level measured by CBP was 17.9ng/ml (range 3.0 to 39.3ng/ml), by HPLC 27.3ng/ml (range 4.6 to 53.2ng/ml) and by IDS 24.4ng/ml (range 9.0 to 48.0ng/ml). The linear correlation between different assays was Pearson r = 0.69 for HPLC and RIA, 0.69 for HPLC and CBP, 0.63 for RIA and CBP. Comparing 25(OH)D assay HPLC with CBP gave the best agreement with an ICC 0.23 (95% CI -0.06, 0.481; p = 0.058). We saw total disagreement between assays IDS and CBP with an ICC = 0.02 (95% CI -0.258, 0.299; p = 0.439). To a lesser extent, we saw a disagreement between IDS and HPLC with an ICC = -0.22 (95% CI -0.476, 0.067; p = 0.063). By sorting individual patients samples into distinct categories according to the difference of 25(OH)D levels, we have seen the best agreement between the HPLC and IDS (64%, 29/48). Total discordance in 24% (12/50) patients was found comparing CBP and IDS. When applying the cut-off 30ng/ml for defining optimal level of 25(OH)D, the HPLC and IDS classifies 31.25% (15/48) and 26% (13/50) of patients as normal, respectively. CBP with 16% (8/50) underestimates the number of individuals having 25(OH)D concentrations above 30ng/ml.

Conclusion: The linear correlation between different assays was 0.63-0.69. We have seen a clinically significant difference between measured 25(OH)D values in 18.8-24% samples.

Disclosure of Interest: None declared

P0323 PREVALENCE AND CAUSES OF ANAEMIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES IN SOUTHERN ITALY

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Introduction: Anaemia (AN) is frequently associated with inflammatory bowel diseases (IBD) with a prevalence varying from 17% to 68%. In recent years, the management of AN in IBD has became a major issue as it negatively affects both the underlying disease and the quality of life of affected patients.

Aims & Methods:

Aim: To evaluate the prevalence and causes of AN in patients with IBD living in a region of Southern Italy.

Methods: We prospectively performed a one-year multicentre study in Campania (Italy) including all consecutive IBD cases attending 5 Units. AN was defined in presence of haemoglobin values Hb < 13 g/dl for males and Hb < 12 g/dl for females; severe AN was defined in case of Hb < 10 g/dl. To explore the causes of AN, all anaemic patients underwent a second-line haematological assessment including ferritin, transferrin, vitamin B12, folic acid and homocysteine levels and screening for celiac disease (total IgA and anti-transglutaminase antibodies). Furthermore, in all IBD cases CRP and ESR were evaluated. Iron deficiency AN (IDA) was diagnosed in case of ferritin < 30 ng/ml and transferrin saturation (TSAT) < 16%. AN of chronic disease (ACD) was diagnosed when elevated CRP/ESR values coexisted with TSAT < 16% and ferritin > 100 ng/ml; mixed type AN was considered in case of TSAT < 16% and 30 ng/ml < ferritin < 100 ng/ml.

Results: The study population included 965 IBD patients (582 CD; 383 UC) of whom 142 in- and 823 out-patients. AN was diagnosed in 134 out 965 IBD patients (14%). No significant difference was seen between CD and UC groups (81 CD vs 53 UC; 13.9% vs 13.8%; p = n.s.). The prevalence of AN was more frequent in the admitted IBD group (26% in- vs 11.7% out-patients; p < 0.01; O.R. 2.2) and in patients with active disease (CD: 34% active vs 16% in remission; p < 0.01; OR 2.1 – UC: 26% active vs 19% in remission; p = 0.03; O.R. 1.3). Furthermore, AN appeared to be more frequent in patients with ileocolic CD and in those with extensive UC (p < 0.01). Regarding the causes of AN, IDA was present in 72 patients (53.7%), ACD in 12 patients (8.2%), 11 patients (8.2%) had mixed type AN, 9 had thalassemia (6.7%), 8 (5.9%) had macrocytic AN, while in 18 patients (13.4%) the causes remained unclassifiable. Vitamin B12 deficiency was observed in 7.4% of CD patients and in no case of UC. Folic acid deficiency was detected in 6.1% of CD and in none of the patients with UC. There was no evidence of celiac disease.

Conclusion: AN is common among patients with IBD in Southern Italy and is more frequent in IBD patients with active and extensive disease and in whom needing hospitalization. Iron deficiency still remains the major cause of AN in IBD population.

Disclosure of Interest: None declared

P0324 DEFINITIONS OF THE ENDOSCOPIC LESIONS IN CROHN'S DISEASE: REPRODUCIBILITY STUDY AND GETAID EXPERT CONSENSUS

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Introduction: Emergence of mucosal healing as therapeutic goal in Crohn's disease (CD) has highlighted the need for endoscopic scores. Although other scores are available, the CD Endoscopic Index of Severity (CDEIS) [1] remains, to date, the most validated score to assess the severity of CD endoscopic lesions. Clarifying the definition of the endoscopic lesions composing this score appeared as a keypoint to optimize the CDEIS use.

Aims & Methods: This expert consensus was performed according to a Delphi-like method (12 experts) to define aphtoid erosions (AE), superficial ulcerations (SU), deep ulcerations (DU), stenosis and fistulas. These consensual definitions were then submitted to 30 other IBD physicians from the GETAID to determine an independent acceptance rate (AR). For the intra and inter-observer variation studies, 100 short films were selected (study leader), focusing on AE, SU, DU or a sham lesion (≈25% for each lesion). Overall 15 GETAID members (not the study leader) read independently the 100 films, indicating the recognized lesion. A re-reading of the same 100 films in a randomized order by the same readers was organized one month later using the same methodology. For the intra-observer variation study, the standard κ-coefficient was used from repeated readings of each observer to measure the agreement level on defining endoscopic lesions. For the inter-observer variation study, the κ-coefficient was estimated as described by Fleiss for nominal agreement among many observers.

Results: AE was defined as an ulceration with a white center whose diameter is < 5 mm with red halo (AR = 29/30). **DU** was defined as a frank depression compared to the surrounding mucosa OR striated bottom of the ulceration OR mucosal detachments OR well-like ulcerations (AR = 24/29). **SU** was defined as an ulceration whose features fit neither with that of AE nor with that of DU, as previously defined (AR = 24/29). **Stenosis** was defined as a narrowing of the intestinal lumen making impossible or difficult to pass with an adult colonoscope (AR = 25/29). **Fistula** was defined as a deep and well-limited hole whose bottom cannot be seen, with leaking faecal or purulent material OR with a suspected communication with another organ (AR = 27/29).

Intra and inter-observer agreements (κ-values)

	AE	SU	DU	sham lesions
Intraobserver estimate range	0.419-0.843	0.572-0.891	0.502-0.934	0.289-0.805
Interobserver estimate ± sd	0.554 ± 0.03	0.548 ± 0.04	0.693 ± 0.04	0.569 ± 0.03

IBD experience duration, mean endoscopies number for IBD for the last 3 years and the participation to the definition process, did not influence intra-observer agreement.

Conclusion: The definitions of CD endoscopic lesions retrieved from this GETAID expert panel, showing substantial reproducibility, should improve the standardization and the use of the CDEIS in the era of mucosal healing.

Reference

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Disclosure of Interest: None declared

P0325 DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IS EFFECTIVE TO DETECT ILEOCOLONIC ULCERATIONS IN CROHN'S DISEASE

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Introduction: Magnetic resonance entero-colonography (MREC) enables accurate assessment of ileocolonic Crohn's disease, but the need for bowel cleansing and rectal enema limits considerably its use in daily practice. Diffusion-weighted MREC (DW-MREC), with no bowel cleansing and no rectal enema, is highly accurate in assessing inflammation in ileal CD using the Clermont score ($=1.646 \times$ bowel thickness $- 1.321 \times \text{ADC} + 5.613 \times$ edema $+ 8.306 \times$ ulceration $+ 5.039$) as it is highly correlated to the Magnetic Resonance Index of Activity (MaRIA) and the simplified endoscopic score for CD (SES-CD)[1-3]. DW-MREC highly assess CD colonic inflammation using apparent diffusion coefficient (ADC), the quantitative parameter of DW-MREC, compared to the MaRIA [3]. However the ADC performances in colonic CD compared to endoscopy remain unknown.

Aims & Methods: We evaluated DW-MREC accuracy to assess endoscopic activity. Overall, 44 CD patients underwent prospectively and consecutively DW-MREC and colonoscopy within 4 weeks (mean interval $= 17 \pm 11$ days). Apparent diffusion coefficient (ADC) and Clermont score were calculated from DW-MREC. The colonoscopies were scored using CDEIS and SES-CD. Radiologists were blinded from endoscopic findings and endoscopists were blinded from radiologic findings.

Results: Mean ADC was moderately correlated with total CDEIS ($\hat{rho} = -0.40$; $p = 0.0067$) and total SES-CD ($\hat{rho} = -0.33$; $p = 0.032$).

Considering the 194 segments, ADC was moderately correlated with segmental CDEIS ($\hat{rho} = -0.48$; $p < 0.001$) and segmental SES-CD ($\hat{rho} = -0.44$; $p < 0.001$). ADC values were lower in segments with deep ulcers (1.30 ± 0.23) or superficial ulcerations (1.75 ± 0.64) than in non-ulcerated segments (2.15 ± 0.5)($p = 0.001$). Using a receiver operating curve, we determined that segmental ADC < 1.42 detected endoscopic deep ulcerations with sensitivity (se) $= 0.91$ and specificity (spe) $= 0.83$ (AUC $= 0.84$; $p < 0.001$). Segmental ADC < 1.88 detected endoscopic superficial ulcerations with se $= 0.64$ and spe $= 0.75$. The segmental ADC values decreased when the ulcerations size increased($p < 0.001$).

Considering ileal segments ($n = 36$), Clermont score was correlated with ileal CDEIS ($\hat{rho} = 0.63$;$p < 0.05$) and ileal SES-CD ($\hat{rho} = 0.58$;$p < 0.05$). Clermont score was higher in ulcerated segments (23.3 ± 8.4) than in non-ulcerated segments (12.4 ± 10.0)($p = 0.006$) and increased with ulceration size ($p = 0.012$). Clermont score > 18.9 detected ulcerations with se $= 0.79$ and spe $= 0.73$.

Among the 44 CD patients, while 10 (22.7%) were in endoscopic remission (no ulceration and no endoscopic stenosis), 8 (18.2%) were in DW-MRI remission (no segmental ADC < 1.88 AND no Clermont score ≥ 18.9 AND no MRI stenosis). The DW-MRI remission detected endoscopic remission with high Spe and NPV (90.9% and 85.7%, respectively).

Conclusion: DW-MREC using ADC and Clermont score is effective to indirectly detect endoscopic ulcerations in ileocolonic Crohn's disease.

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P0326 ENDOSCOPIC FACTORS INFLUENCING FECAL CALPROTECTIN VALUE IN CROHN'S DISEASE

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Introduction: Fecal calprotectin is usually an accurate biomarker of Crohn's disease (CD) endoscopic activity. Identifying the endoscopic situations in which fecal calprotectin is less reliable remains unexplored. We aimed to determine the endoscopic factors influencing fecal calprotectin level in CD.

Aims & Methods: Overall, 53 CD patients underwent consecutively and prospectively colonoscopy, with CD Endoscopic Index of Severity (CDEIS) calculation and stool collection. Fecal calprotectin was measured using quantitative immunochromatographic test. To calculate the overall affected or ulcerated surfaces, we considered that each segment (according to CDEIS) represented 20% of the overall surface. Correlation analysis was done with Pearson statistics. In multivariate situation, linear regression was performed according to univariate results and clinical relevance.

Results: Fifty-three CD patients were included (57% female), with a median age of 31 [21–44] years and a median CD duration of 3.5 [1.0-9.0] years at the inclusion time. Thirteen patients (24.5%) had pure ileal disease (L1 according to Montreal classification), 12 (22.7%) had colonic disease (L2), and 28 (52.8%) had ileocolonic CD (L3). The median CDAI and CRP were 198.5 [101-258] and 11.40 [4.20-33.70] mg/L, respectively. Median CDEIS was 3.6 [2.66 – 6.4]. Endoscopic ulcerations were reported in 40 patients (75.5%).

Fecal calprotectin level was correlated with CDEIS (0.66, $p < 0.001$). In univariate analysis, fecal calprotectin was correlated with the affected surface (0.65, $p < 0.001$) and the ulcerated surface (0.47, $p < 0.001$). Fecal calprotectin was significantly associated with ulcerations depth, with median fecal calprotectin values of 867.5µg/g, 1251.0µg/g and 1800.0µg/g, for non-ulcerated lesions, superficial ulcerations and deep ulcerations, respectively. Lesions locations (ulcerated or not) did not influence fecal calprotectin level.

In multivariate analysis, fecal calprotectin level was associated with affected surface ($p = 0.04$) and the presence of CD lesions. Moreover, fecal calprotectin increased with the ulcerations depth ($p = 0.03$). However, ulcerated surface and CD location did not impact fecal calprotectin.

Using a ROC curve, we showed that fecal calprotectin ≥ 400µg/g was the best compromise between sensitivity (0.76) and specificity (0.77) (AUC (95% CI) $= 0.795$, (0.624-0.966)) to detect CD superficial or deep ulcerations. A cut off value of 200 µg/g detected superficial or deep ulcerations with sensitivity, specificity, positive predictive value and negative predictive value of 0.86, 0.70, 0.86 and 0.70, respectively.

Conclusion: Fecal calprotectin is a very reliable biomarker to detect endoscopic ulcerations in CD. We suggest to repeat measurement for intermediary results (200-400µg/g) in daily practice. Fecal calprotectin level is not related to CD location but is mostly influenced by the affected surface and the presence of CD lesions (even non-ulcerated), with high impact of deep ulcerations.

Disclosure of Interest: None declared

P0327 POSTOPERATIVE RECURRENCE IN CROHN'S DISEASE: NATURAL HISTORY, RISK FACTORS AND MANAGEMENT STRATEGIES IN A RETROSPECTIVE COHORT (1986-2015)

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Introduction: As surgical resection is not curative, postoperative recurrence (POR) remains a crucial issue in Crohn's disease (CD). Several factors have been considered as POR predictors, but their true impact remains debated. Recently, the POCER trial[1] suggested that an early endoscopic-based management (EBM) decreased the risk of endoscopic POR at 18 months. However the long-term impact of EBM remains unknown.

Aims & Methods: We aimed to describe the natural history, the risk factors, and the optimal prevention strategy of POR in CD.

From the pathology department database, we retrieved the data of all the patients who underwent intestinal resection for CD in our centre between 1986 and 2015. Surgical POR was defined as re-operation for CD. Clinical POR was defined as symptoms recurrence leading to hospitalization or therapeutic modifications. Endoscopic POR was defined as a Rutgeerts' score $\geq$ i2. Patients were classified as Endoscopic-based management (EBM) if they underwent a systematic colonoscopy with no clinical POR. Considering the censored data, multivariate analyses were performed according to univariate results (log rank tests) and clinical relevance.

Results: Among the 161 CD patients, 59% were females, 33% active smokers, 33% had previous intestinal resection and 47% had previous perineal lesions (37% with abscess/fistula). Mean age at surgery was 37 ± 13.5 years.

The rates of POR were:

	1 year	5years	10 years	15 years	20 years
Surgical POR (%)	1.3	19.0	38.9	57.7	64.7
Clinical POR (%)	21.5	61.4	75.9	88.7	92.5
Endoscopic POR (%)	31.7	67.6	79.7	91.1	95.5

In multivariate analysis, fistulizing CD (B3 according to Montreal classification) (Hazard ratio: HR 1.78 [1.04-3.04], $p = 0.003$) and previous intestinal resection (HR 1.7 [1.00-2.72]; $p = 0.05$) were predictive of surgical POR. Previous intestinal resection (HR 1.65 [1.10-2.48]; $p = 0.02$) and previous perineal abscess or fistula (HR 1.48 [1.01-2.19] ; $p = 0.048$) were predictive of clinical POR. Fistulizing CD (HR 1.78 [1.04-3 .04] ; $p = 0.03$) and previous intestinal resection (HR 1.7 [1.00-2.92]; $p = 0.05$) were predictive of endoscopic POR. In our cohort, no other factor, including smoking and resection length, were POR predictors. Neither anti-TNF agents nor thiopurines therapies decreased the risk of POR.

The median interval between surgery and endoscopy was 9.5 [5.6-54.2] months) in the EBM group ($n = 49/161$). An EBM decreased the risks of clinical (HR 0.4 [0.25-0.66]; $p < 0.001$) and surgical POR (HR 0.31 [0.13-0.73]; $p = 0.007$).

Conclusion: POR remains common in CD. The identification of risk factors may enable targeted strategies to reduce this recurrence rate. EBM should be recommended in all CD patients within the first year after surgery as it highly decreased the long-term risk of POR.

Reference

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Disclosure of Interest: None declared

P0328 DEVELOPMENT OF A SMALL BOWEL CAPSULE ENDOSCOPIC INDEX OF SEVERITY IN PATIENTS WITH CROHN'S DISEASE

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Introduction: The capsule endoscopy is the most powerful exam to detect small bowel (SB) mucosal lesions in patients with Crohn's disease (CD) but the disease severity remains difficult to evaluate. The aim of this study was to develop prospectively a new index of severity devoted to the small bowel using the Pilcam® SB capsule

Aims & Methods: Patients with CD were prospectively enrolled between June 2007 and May 2013. Inclusions were stratified according to the SB disease location in a ratio 1/1/2/2 (none, ulcer at endoscopy only, non severe and severe at radiology whatever endoscopy) crossed with clinical activity in a ratio 3/1 (active or not) to ensure a wide range of severity of the SB lesions. The SB was divided into 3 tertiles from the duodenum to the caecum or to the end of the record. When possible, the terminal ileum (TI) was defined as the last 15 cm above the caecal valve. All lesions i.e. erythema, oedema, villous denudation, nodularity, lymphangiectasia, pseudo-polyp, aphtous lesions, ulcerations in relation to size, depth and shape were described, fistulas and stenosis were quantified according to predefined frequency. The extension in length of oedema, in length and circumference of ulcerations were quantified according to predefined proportions. The surface and length of lesions and ulcerations were quantified on linear analog scales. The severity physician global assessment (PGA) for each segment and for the whole SB, was assessed on a linear analog scale. Multiple linear mixed model was used to construct the new severity index in two ways as a linear combination of lesions, lengths and surfaces highly correlated either to the whole SB or to the segmental severity PGAs. Random factors were used to take into account the dependency of estimates performed in different segments of the same patient or by the same investigator on different patients.

Results: 118 patients (33 yrs [25-44]) were enrolled, 23, 21, 41 and 33 according to disease lesion strata, 76 and 42 according to clinical activity strata. Seven films were unusable for the construction of the index because of missing data or a prolonged stay in the stomach. The colon was identified in 80 patients (71%). The extension of oedema, the presence of >8 ulcerations ($>$ 10mm or superficial), the presence of deep or circular ulcerations, the extension of ulcerations in length or circumference, the lesion surface and ulceration length, and the presence of stenosis were highly related to severity, whereas the presence of villous denudation, lymphangiectasia, pseudo-polyp or aphtous lesions was clearly not

Conclusion: The preliminary results of this prospective study highlights the importance of oedema, deep and circular ulcerations and the extension of the disease in evaluating the severity of SB lesions to build this new index

Disclosure of Interest: A. Bourreille Lecture fee(s): Covidien, A. Attar: None declared, V. Maunoury: None declared, M. Simon: None declared, L. Picon: None declared, M. Fumery: None declared, S. Viennot: None declared, C. Reenaers: None declared, I. Nion-Larmurier: None declared, J. Filippi: None declared, B. Bonaz: None declared, O. Dewit: None declared, X. Dray Lecture fee(s): Covidien, J. Moreau: None declared, R. Altwegg: None declared, X. Roblin: None declared, C. Stefanescu: None declared, J.-Y. Mary: None declared

P0329 RECEIVING CORTICOSTEROIDS THERAPY IS ASSOCIATED WITH A POOR OUTCOME IN PATIENTS WITH ELDERLY-ONSET ULCERATIVE COLITIS: A POPULATION-BASED STUDY

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Introduction

Background: In elderly-onset ulcerative colitis (UC) patients, clinical course has been reported to be mild, with a rare disease extension and a majority of patients never exposed to any immunosuppressant (IS) or anti-TNF-therapy, nor operated. Nevertheless, some patients have poor clinical outcome with early resort to surgery. Along this, the impact of receiving corticosteroids (CS) therapy on the evolution of elderly-onset UC has not been evaluated.

Aims & Methods

Methods: In a French population-based cohort we identified from 1988 to 2006 473 UC patients >60 years of age at diagnosis with a median follow-up of 6.3 years [Q1 = 2.3-Q3 = 10.3]. Clinical outcome of patients undergoing CS (CS group) was compared with patients who never received CS (control group) after adjustment on receiving or not IS and/or biothérapies (as clinical surrogate marker), and on colonic location and disease duration.

Results: Among the 473 UC patients, 157 (33%) received at least one time CS therapy (prednisone or prednisolone in 97% of cases). The cumulative probabilities of receiving CS was 21% (95% CI: 17-25) at 1 year, 39% (34-45) at 5 years, and 45% (38-52) at 10 years. Gender, median age and presence of extra-intestinal manifestations at diagnosis were not different in CS and control groups. In CS group, proctitis (21%) was less frequent and pancolitis (36%) more frequent compared to control group (32% and 21% respectively, $p < 10^{-2}$). At maximal follow-up, 7% and 49% of patients in CS group had proctitis and pancolitis respectively, compared to 22% and 26% in control group respectively ($p < 10^{-4}$). Colectomy rate was higher in CS group (13%) than in control group (4%, $p = 10^{-3}$). Total number of flares and hospitalizations per year but also time spent in hospital were significantly higher in CS group compared to control group ($p < 10^{-4}$). The median duration of CS exposure was 4.6 months (2.4–9.0). Thirty-two (20%) patients were CS-dependent, 14 (9%) CS-resistant, and 15 (10%) became intolerant to CS (in which almost 30% of patients developed insulin-dependent diabetes). The cumulative probabilities of developing intolerance to CS was 1.3% (0.0 ; 4.0), 6.7% (2.6 ; 16.4) et 17.3% (8.1 ; 34.6) at 1, 5, and 10 years respectively. Four patient stopped CS because of intolerance.

Conclusion: In elderly-onset UC, receiving CS therapy is associated with a more pejorative evolution of the disease, with higher rate of surgery, flares and hospitalization. Moreover a significant proportion of patients become intolerant to CS with more than one third who developed diabetes. Unlike the majority of cases in elderly-onset UC, IS or anti-TNF treatments should be early considered in patients receiving CS.

Disclosure of Interest: None declared

P0330 SMALL BOWEL CAPSULE ENDOSCOPY IN ULCERATIVE COLITIS – THE CAPCOLITIS STUDY: A PROSPECTIVE OBSERVATIONAL STUDY IN GERMANY

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Introduction: From the genetic point of view ulcerative colitis (UC) and Crohn's Disease (CD) are not strictly separated in genome-wide association studies (GWAS). This was the reason to investigate UC-patients with a Small Bowel Capsule Endoscopy (SBCE). The nationwide BioColitis Registry (*Bio*logical Registry with Ulcerative *Colitis* Patients in Germany) of the German Competence-Network IBD is a five-year prospective registry of about 1.000 patients with ulcerative colitis (UC) in Germany. The CapColitis Study is a sub-study of the BioColitis Registry reporting the results of a SBCE in these UC-patients.

Aims & Methods: The primary study objective was to describe the type and frequency of small bowel lesions detected by SBCE in UC-patients and secondary to evaluate the prognostic impact of SBCE in new TNF-therapies. Within the framework of this non-interventional prospective online documentation, data in respect to the results of the SBCE and the course of disease, psychosocial burden, health economics and the genetic profile were analyzed. Until April 2015 about 500 UC-patients have been included in the BioColitis Study, the recruitment is ongoing. End of 2014 the recruitment of the CapColitis study was stopped having analyzed the data of 127 UC-patients with a SBCE in early disease UC-patients (disease duration < 2 years) and in UC-patients ($n = 57$) starting with an anti TNF-alpha antibody therapy (TNF) included by 11 gastroenterology practices and hospitals with IBD-experience. All patients will have a prospective 5 year follow-up period. The data of the baseline and the 6-months visit will be analyzed.

Results: 127 UC-patients have been examined with SBCE and 125 SBCE (incomplete small bowel examination ($n = 2$); no capsule retention) could be analyzed (average age: 40 years; female: 47%; disease duration: 4.5 years; pancolitis: 42%, NSAIDs 0%). Small bowel lesions/inflammation have been found in 16/125 UC patients (13%). These 16 patients with small bowel lesions/inflammation could be divided in different categories: only single-non-relevant small bowel lesions ($n = 7$) (PE-induced-lesions ($n = 3$); single-non-relevant lesions ($n = 4$)) and pathologic findings in 9 UC-patients (backwash ileitis in active pancolitis ($n = 4$); switch to Crohn's Disease ($n = 5$; 4%) after discussing all findings with the study centers). The findings in the 57 UC-patients starting a TNF-therapy have not been significantly different compared with the early disease group.

Conclusion: In this real life setting SBCE showed small bowel lesions/inflammation in 13% in these NSAIDs free UC-patients with relevant findings in 9/125 (7%), perhaps indicating an overlapping phenotyp between UC and CD as shown earlier in the partial genetic association of UC and CD in the entirety of inflammatory bowel diseases (IBD). In 5/125 UC-patients (4%) the diagnosis

have been switched following the SBCE-findings to CD. In accordance with the UC-guidelines a small bowel diagnostic is required at the point of UC-diagnosis and in this case SBCE seems to be a sensitive procedure, possibly better suited than small-bowel MRT.
Disclosure of Interest: D. Luehr: None declared, B. Bokemeyer Financial support for research: Abbvie, Ferring, UCB, Lecture fee(s): Abbvie, Ferring, MSD, Merckle, Falk, HLR, UCB; Takeda, Consultancy: Abbvie, MSD, Shire, Ferring, UCB, Hospira, U. Helwig: None declared, C. Maaser: None declared, P. Jessen: None declared, S. Schreiber: None declared

P0331 NETWORKING AND IMPLEMENTATION OF EVIDENCE-BASED PATHWAYS FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASES (IBD)

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Introduction: IBD-patients experience various somatic and psychosocial impairments. They need a comprehensive, interdisciplinary and problem-oriented health care. To improve their quality of health care IBD-pathways recommend a systematic assessment of health-related problems and focus on a multidisciplinary, patient-centered care. In a prospective controlled cohort study German gastroenterologists tried to optimize their quality of care by network activities. The impact on patient reported outcomes was evaluated.
Aims & Methods: In a region of North Germany 15 gastroenterologists recruited outpatients with IBD (IG: intervention group), outside this region 18 gastroenterologists included nationwide IBD-patients in a control group (CG). At baseline (t0), 6 (t1) and 12 months (t2) patients completed a questionnaire assessing 22 somatic and psychosocial problems. Medical data on the course of disease were gathered by the gastroenterologists. IG-patients received written feedback of their problem-profile together with individualized recommendations for appropriate treatment. Further IG-interventions were the implementation of interdisciplinary IBD-case conferences and the offer of a patient training in small groups. Main outcomes were health related quality of life (HRQoL: EQ-VAS, score: 0-100) and social participation restrictions (IMET, score: 0-10); self-management skills (heiQ) and work productivity (WPAI) were among the secondary outcomes.
Results: 282 of 349 IBD-patients (80.8%; IG: 142 of 189; CG: 140 of 160) participated in both follow-up visits. Baseline characteristics were broadly similar (age: 43 years; 61% female; 50% with Crohn's Disease; 66% in remission; 68% in full- or part time employment). Only minor differences between IG and CG for age, school education and medication could be found. Covariance analyses were used to adjust for baseline differences. No significant differences between IG and CG were seen at follow-up with respect to the primary outcomes, the entire group showed small improvements from t0 to t2 (EQ-VAS: 72.5 to 76.2, $p = 0.002$; IMET: 2.1 to 1.9; $p = 0.025$). After 12-months only the IG reported increased self-management skills, the CG remained nearly unchanged (treatment x time interaction: $p = 0.002$). Work productivity of both groups was unimproved. In contrast, the feedback of the physicians in the IG were more favourable at the 6-months follow-up. 67% of the physicians participated in IBD-case conferences, the benefit of networking has been ranked with 7 on a scale from 0 (no benefit) - 10 (best benefit).
Conclusion: Our complex intervention could not be proved as effective and beneficial in the primary outcomes. Both groups showed slight positive effects over the 12 months. In a secondary outcome (self-management skills) we found an advantage for the intervention-group. The missing differences between IG and CG could be partially explained by (i) a positive side effect in the CG caused by the systematic medical documentation during the study and (ii) by the fact, that not all network activities in the IG could have been realised in the aimed frequency. Further (sub group) analysis will promote the discussion.
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P0332 NON-INVASIVE TESTING IS DIAGNOSTIC AND PROGNOSTIC IN INTESTINAL GRAFT VERSUS HOST DISEASE

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Introduction: Intestinal graft versus host disease (iGVHD) is a debilitating and sometimes fatal consequence of bone marrow transplantation[1]. Malnutrition and profuse diarrhoea are common. The diagnosis is often based on clinical criteria alone and intestinal biopsies are frequently negative[1,2]. Even after successful treatment, iGVHD can relapse and reliable disease monitoring is unavailable.
Aims & Methods: We conducted this prospective study to evaluate the diagnostic accuracy of the xylose/rhamnose/lactulose small bowel permeability test (SBPT) and faecal calprotectin (FC) in the work-up of patients with suspected iGVHD. Prospective data was collected on all patients referred for endoscopic investigation of suspected iGVHD at KCH, from Jan-Dec 2014. All patients underwent OGD and colonoscopy to at least the caecum, with serial intestinal biopsies taken. Samples were collected for SBPT and FC. Infection and other pathologies were excluded with extensive testing. SBPT and FC results were compared to biopsy results and the site of positive biopsies was noted.
Results: 15 patients had positive intestinal biopsies (PB) with 9 negative (NB). SBPT was unavailable in 2, and FC in 1 patient in each group. SBPT was abnormal in 1/7 NB and in 11/13 PB. The sensitivity (Sn) and specificity (Sp) for SBPT in the diagnosis of iGVHD was 84.6% and 85.7% respectively; PPV 91.7%. FC was high in 2/8 NB and 9/14 PB, returning Sn 64.2% and Sp 75%. Addition of the two tests reduced sensitivity and specificity further. Mortality was high in the PB group (6/14, 43% - exclusively from gram-negative sepsis +/− multi-organ failure). FC was elevated > 300mcg/g in 5/6 deaths and 2/8 survivors. Intestinal biopsies were positive in all but one case from the right hemicolon, 3/6 ileum and only 2/15 from duodenum. At present, no significant patterns have emerged with regard to conditioning regimen or other aspects of the transplant protocol.
Conclusion: SBPT appears to be a highly sensitive and specific marker of iGVHD. A high FC does not appear to be related to iGVHD itself, but may predict severe disease and mortality. Biopsies were most often positive at full colonoscopy in our cohort. These non-invasive tests are simple and cheap and may serve to assist clinicians in the investigation and management of this debilitating condition.

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P0333 ULTRASOUND SHEAR WAVE ELASTOGRAPHY IDENTIFIES MUSCLE WALL HYPERTROPHY AND IS A NOVEL SURROGATE FOR INFLAMMATION IN CROHN'S DISEASE

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Introduction: Crohn's Disease (CD) is an inflammatory bowel disease mainly affecting the terminal ileum. Inflammation, fibrosis, and muscular hypertrophy lead to thickened and narrowed bowel detected on ultrasound (US). US shear wave elastography (SWE) assesses elastic properties of tissue through an acoustic US force providing a quantitative measurement of tissue stiffness. SWE has been described to differentiate inflammation from fibrosis in ex vivo CD bowel specimens[1]. As confirmed on histology, neo-angiogenesis is an important component of CD bowel wall inflammation. Quantification of bowel wall vascular perfusion can be uniquely detected by contrast enhanced ultrasound (CEUS).
Aims & Methods: We aim to prospectively correlate SWE of ileal CD in-vivo to CEUS peak enhancement as a measurement of inflammation, and to pathology grades of inflammation, fibrosis, and muscular hypertrophy of resected small bowel. We predict patients with a higher SWE score will have greater bowel stiffness attributable to fibrosis and muscular hypertrophy, and concurrent chronic inflammation as measured by lower CEUS peak enhancement. All consecutive CD patients (March to October 2014) attending outpatient US appointments received greyscale US. In patients with ileal CD and bowel wall thickness (BWT) > 3mm, SWE was measured at a point of maximal BWT and CEUS peak enhancement using microbubble (Definity®) contrast was performed ($n = 95$). An average of ten SWE readings were collected using Virtual Touch Quantification; Acuson S3000, Siemens Medical Solutions USA, Inc or with Philips Epiq 5, (Bothell, WA). Receiver operating characteristic (ROC) curve analysis was performed. Differences in low and high inflammation, fibrosis, and muscular hypertrophy of bowel specimens were compared using the student t-test. Of these 95 patients, fifteen had ileal resections within an average of 47 days (SD 90.4 days) from the time of CEUS. A gastrointestinal pathologist scored these specimens for inflammation, fibrosis, and muscular hypertrophy for comparison to SWE measurements of the corresponding regions.
Results: Of fifteen ileal specimens, chronic inflammatory histological change ($p < 0.001$) with lower corresponding CEUS peak enhancement ($p = 0.04$) exceeded acute inflammatory changes. Mean in-vivo SWE measurements for all patients who had and did not have surgery were 2.82 ± 0.68 m/s and 2.17 ± 0.79m/s ($p < 0.01$), respectively. Of the operated patients with a SWE > 3m/s, there was an inverse relationship with inflammation matching to lower CEUS peak enhancement ($p = 0.04$), and more smooth muscle hypertrophy ($p = 0.03$). There was no significant difference in SWE and fibrosis scores ($p > 0.05$).
Conclusion: SWE measurements of in vivo small bowel CD increases when there is smooth muscle hypertrophy. Overall, CD patients with lower CEUS peak enhancement parameters have more chronic bowel inflammation as confirmed on histology. A novel observation; higher SWE is related to bowel smooth muscle hypertrophy, and is inversely related to both chronic inflammation and CEUS peak enhancement. In vivo SWE and CEUS differentiates between acute

and chronic bowel wall inflammation and thickening, improving selection between medical therapy and surgery.

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P0334 PERFORMANCE TESTING OF A SMARTPHONE-BASED PATIENT MONITORING SYSTEM MEASURING CALPROTECTIN AS IBD THERAPY FOLLOW-UP MARKER BY LAY USERS VERSUS LABORATORY PROFESSIONALS

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Introduction: Inflammatory Bowel Disease (IBD) is a chronic inflammation of the gut comprising active inflammation, remission and flares. The disease course can be followed by biomarkers such as calprotectin which is measured in patients' stool samples. Most studies have shown that a threshold around 250 µg/g correlates well with mucosal healing. Hence, one of the therapy goals is to achieve calprotectin values below 250 µg/g and to keep them below this level. Therefore, we have developed a system, called IB*Doc*®, which allows the patient to perform calprotectin tests at home in order to regularly test that this low level is under control. The IB*Doc*® consists of a stool extraction device (CALEX® Valve) and an immunochromatographic rapid test, which is measured by a smartphone App (CalApp®) controlling the phone's camera. Results are automatically sent to and administered on a webserver (IB*Doc*® Portal) for the consulting physician or IBD nurse.

Aims & Methods: The objective of this study was to validate the IB*Doc*® home testing system by lay users vs. professional laboratory personnel and to compare its quantitative performance with routine laboratory-based methods.

Stool samples containing various levels of calprotectin (18-2582 µg/g), kindly provided by a local routine clinical laboratory, were extracted with the CALEX® Valve device by 31 lay users and two laboratory professionals. The stool extracts were then either loaded by the lay users onto immunochromatograhic test cassettes (TCs) or analyzed with a commercial ELISA test by the professional users. The lay users read the TCs via the CalApp® installed on 11 different models of iPhones and Android phones, whereas the professional users measured the TCs with the Quantum Blue® (QB) lateral flow reader. Agreement between lay users and professional users as well as quantitative performance of IB*Doc*® versus routine laboratory methods were assessed by Analyze-it for Microsoft® Excel.

Results: The IB*Doc*® test system produces a quantitative test result between 30 and 1000 µg of calprotectin/g of stool which covers the clinically relevant range of this biomarker. The total agreement (TA; based on a traffic-light system) of performing IB*Doc*® between lay users and laboratory professionals was 96.8% with 0% false positive and 0% false negative rates. The TA between measuring the TCs with 11 different smartphone models and the QB reader was 90.3%, whereas the TA of CALEX® Valve extractions performed by lay vs. professional users was 80.6%. The IB*Doc*® home test performed by 31 lay users correlated well with a state-of-the-art laboratory-based fCAL® ELISA method showing a slope of 1.03, a bias of 40 µg/g and R^2 of 0.941. The TA of these 31 single test results was 87.1%, and no false positive (red instead of green traffic-light) or false negative result (green instead of red traffic-light) was reported.

Conclusion: IB*Doc*® is the first complete and validated test system which allows the IBD patient to monitor and follow his inflammatory status by measuring the IBD biomarker, fecal calprotectin, using his/her own smartphone. The performance of the IB*Doc*® home testing system is comparable to professional, laboratory-based methods. IB*Doc*® is the first CE-marked self testing home device of its kind.

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P0335 FREQUENCY OF UNDIAGNOSED IBD AMONG PATIENTS UNDERGOING SURGERY FOR PERIANAL ABSCESS OR FISTULA

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Introduction: Many patients with penetrating Crohn's disease (CD) undergo surgery for perianal disease of presumed cryptoglandular etiology before diagnosis of IBD is established.

Aims & Methods: This study aimed for the first time (1) to determine the frequency of postoperative IBD diagnosis (Dx-POP) among patients undergoing surgery for perianal abscess or fistula, and (2) to identify predictive factors for Dx-POP.

Patients who underwent surgery for perianal abscess or fistula at two major surgical departments in the city of Graz, Styria, between 1997 and 2007 were searched electronically. Dx-POP patients were identified by a registry containing all patients who received a first diagnosis of IBD between 1997 and 2007 and were residents of Styria. Dx-POP patients were compared with sex- and age-matched non-IBD controls (CO) (ratio 1:3).

Results: Among 975 patients included (73% male; age 46 ± 14 y) 58 had a pre-existing diagnosis of IBD (52 CD, 6 UC). Twenty-two patients received a first diagnosis of IBD (18 CD, 4 UC) 0.1-70 months (median; CD 9, UC 24) after surgery. Age at surgery of patients with and without a first diagnosis of CD during follow-up was 28 ± 9 and 47 ± 14 years, respectively ($p < 0.001$). According to life-table analysis, the cumulative risk of non-IBD patients to receive a diagnosis of IBD within 11 years after surgery was 2.9% (CD 2.5%, UC 0.4%). Clinical and laboratory results of Dx-POP vs. CO are compared in the Table.

	Dx-POP	CO	p
N	22	66	
Median age (y)	28	28	
Male (%)	63.6	63.6	
Number of patients with fistula/abscess/both	4/8/10	20/36/10	0.013
Fistula simple/komplex (%)	64/36	90/10	0.039
Abscess type P/I/IR/S/H* (%)	44/17/22/6/11	85/11/4/0/0	0.004
Mean (±SD) hemoglobin (g/dL)	13.4 ± 1.5	14.8 ± 1.6	0.002
Median (IQR) platelets (10^3/µL)	321 (265-428)	249 (213-291)	0.001
Mean (±SD) ESR after 2h (mm)	57 ± 30	29 ± 28	0.026
Median (IQR) length of hospital stay (d)	5 (4-6)	4 (3-5)	0.007

*P, perianal; I, interspincteric; IR, ischiorectal; S, suprasphincteric; H, horseshoe

Conclusion: A small but important fraction of patients operated for perianal abscess or fistula will receive a diagnosis of IBD during follow-up. Young age, more complex perianal disease, low hemoglobin, and high platelets at surgery predict future diagnosis of IBD. Surgeons need to be aware of undiagnosed IBD when operating perianal lesions.

Disclosure of Interest: None declared

P0336 CLINICAL AND SONOGRAPHIC OUTCOME OF INTESTINAL FISSURING-TYPE ULCERS IN CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is frequently complicated by intestinal strictures, fistulae and abscesses. The natural course of intestinal fistulae, in particular early enteromesenteric lesions like fissuring-type ulcers originating from penetrating ulcers, is not well known.

To date, the possibility to accurately detect these lesions (IUS) by means of intestinal ultrasound, as hypoechoic irregularities of the outer margins of the intestinal wall, allows us to obtain information regarding their natural history in relation to treatment and clinical features of the disease.

Aims & Methods: The aim of this study was to evaluate the clinical features and outcome, of a cohort of patients with Crohn's disease complicated by intestinal fissuring-type ulcers.

We retrospectively identified 40 CD patients (male 23; mean age, 48 years) regularly followed in our Unit, in whom an intestinal ultrasound has detected intestinal fissuring ulcers, in absence of any other intestinal complications. All these patients had a regular clinical and sonographic follow up. The features of these patients and their clinical outcome, namely the need of surgery, biological or immunosuppressive therapy, as well as the sonographic behaviour of the lesions over time, including their disappearance or worsening into a evident intestinal fistula or abscess, have been evaluated.

Results: Eleven patients were active smokers, 22 had an ileal, 16 an ileocolic and 2 a colic CD. Four patients had a concomitant perianal disease. In 14 patients (35%) intestinal fissuring ulcers worsened, becoming an intrabdominal abscess (2 pt) or an evident internal fistula (12 pts) in a mean follow up of 2 years. Four of these patients had been treated immunosuppressive therapy, 2 also with biological therapy. Ten patients (25%) underwent surgery within 2 years, 6 of them despite the treatment with immunosuppressive therapy (2 pt) or biologics (4 pt). Fourteen patients (35%) showed the complete disappearance of the fissuring ulcers, 10 of them (71.4%) had been treated with azathioprine plus biologics (8 patients) or azathioprine alone (2 patient). Two patients (5%) under treatment with mesalamine showed the persistence of fissuring ulcer after 2 years.

Conclusion: This preliminary report showed that intestinal fissuring-type ulcers complicating CD seem to have progression into evident internal fistulae and a poor clinical outcome and in most patients. These lesions seem to disappear in less than one-third of patients and in most of these cases this is correlated with immunosuppressive and biological therapy.

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P0337 INFLAMMATORY BOWEL DISEASE ACTIVITY AND VITAMIN D DEFICIENCY: AN ASSOCIATION?

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Introduction: Vitamin D deficiency is commonly diagnosed among patients with inflammatory bowel disease (IBD). Recent studies suggest that vitamin D may have a role in clinical disease activity in ulcerative colitis (UC) and Crohn's disease (CD).
Aims & Methods: This study aims to assess an association between vitamin D levels and clinical disease activity in patients with IBD.
Prospective study with 1 year recruitment in a Southern European Center. Demographic and clinical data of patients with IBD were collected. C-reactive protein (CRP) and vitamin D levels within 30 days of their clinic visit were measured. Seasonality of the data was also considered. Patients under vitamin D replacement were excluded. Clinical activity was defined using Truelove-Witts score in UC patients and Harvey-Bradshaw score in CD patients. Vitamin D levels were defined as: normal > 30 ng/ml; insufficient 20–29 ng/ml; deficient < 20 ng/ml. Statistical analysis was performed using SPSS 21, considering statistical significance $p < 0.05$.
Results: One hundred and twenty patients; 57 females; mean age 45.8 years. 60 patients with UC and 60 patients with CD. Mean years of disease 9.69 (0-42). Seventy-seven patients presented deficient vitamin D levels and 40 patients had active disease. There was a statistically significant association between vitamin D deficiency and clinical disease activity in CD ($P = 0.005$) and in UC ($p = 0.038$). There was also a significant association between clinical disease activity and increased CRP levels in both diseases ($P = 0$), but there was no association between increased CRP and vitamin D deficiency in any type of IBD. Despite a higher percentage of vitamin D deficiency in active disease, we found that a significant percentage of patients of patients with inactive disease had insufficient or even deficient vitamin D levels. There was not season variability.
Conclusion: In our series, vitamin D deficiency is related to clinical activity of IBD, especially in CD. Vitamin D supplementation may have a potential role as a treatment for patients with active IBD.
Disclosure of Interest: None declared

P0338 ARE CLINICAL INDICES OF INFLAMMATORY BOWEL DISEASE ACTIVITY SUPERIOR TO PATIENT OPINION AT PREDICTING ACTIVITY AS DEFINED BY FAECAL CALPROTECTIN?

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Introduction: The Harvey-Bradshaw Index (HBI) and Simple Clinical Colitis Activity Index (SCCAI) are clinical scoring systems used to estimate Crohn's disease (CD), and ulcerative colitis (UC) activity respectively. However, their performance compared with patient opinion at predicting disease activity defined by faecal biomarkers of IBD activity is unclear. We conducted a cross-sectional survey of IBD activity to assess these issues.
Aims & Methods: Demographic data and patient opinion regarding whether they were, or were not having a flare of disease was assessed by standardised questionnaire. IBD activity was assessed by HBI for CD and SCCAI for UC, with active disease defined by a score of ≥5 for each. Stool was collected for faecal calprotectin (FC) analysis by enzyme linked immunosorbent assay (ELISA) (Biohit, Finland). Patients were dichotomised into those with or without active disease using a FC of ≥200μg/g of stool to define active disease. Mean FC was compared between those with and without active disease by patient opinion and clinical indices of IBD activity by independent samples t-test. The sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy of patient opinion and clinical activity indices at predicting active disease define by FC was also calculated. ROC curve for HBI and SCCAI against active disease defined by FC was used to calculate the AUC for each clinical assessment index.
Results: There was no difference in mean age, sex, education level, marital status, smoking or alcohol usage for CD or UC patients dichotomised in those with and without active disease defined by FC. In CD mean FC was lower in patients with active disease defined by HBI than those without (381 vs. 472; $P = 0.368$). Mean FC was higher in patients with active disease defined by patient opinion than those without but this failed to reach statistical significance (474 vs. 425; $P = 0.711$). In contrast, mean FC was significantly higher in UC patients with active disease defined by both patient opinion and SCCAI (919 vs. 381; $P < 0.001$ and 949 vs. 311; $P < 0.001$ respectively). The sensitivity, specificity, positive predictive value, negative predictive value, overall test accuracy and AUC for each test when used to predict disease activity defined by FC is illustrated in table 1.**Table 1:** performance of individuals IBD assessment tools

(continued)

Table 1 Continued

	Crohn's disease		ulcerative colitis	
patient opinion	HBI	patient opinion	SCCAI	
	Crohn's disease		ulcerative colitis	
patient opinion	HBI	patient opinion	SCCAI	
sensitivity	0.17	0.37	0.45	0.54
specificity	0.84	0.64	0.78	0.73
PPV	0.45	0.44	0.62	0.62
NPV	0.57	0.57	0.64	0.65
Accuracy	0.55	0.53	0.63	0.64
ROC AUC	-	0.49	-	0.66

Conclusion: The performance of clinical disease activity indices at predicting IBD activity is modest in UC and poor in CD when compared to faecal biomarkers of intestinal inflammation. Neither HBI nor SCCAI appear to outperform patient opinion. Faecal biomarker point of care testing may aid clinical decision making.
Disclosure of Interest: None declared

P0339 PREVALENCE AND IMPACT OF IRRITABLE BOWEL TYPE-SYMPTOMS IN QUIESCENT INFLAMMATORY BOWEL DISEASE

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Introduction: The prevalence of symptoms compatible with irritable bowel syndrome (IBS) in inflammatory bowel disease (IBD) has been previously described. However, the association between the presence of these symptoms and occult disease activity is less well known, as is the effect of these symptoms on psychological health. We conducted a cross-sectional survey examining these issues.
Aims & Methods: Demographic and gastrointestinal symptom data were collected from 439 adult patients via the Rome III questionnaire. IBD activity was assessed via clinical scoring systems and faecal calprotectin (FC) in a subset of patients. Mood was assessed using the hospital anxiety and depression scale, whilst somatisation and quality of life data were collected using the patient health questionnaire-12 (PHQ-12) and SF-36 questionnaire respectively. Mean FC, as well as anxiety, depression and somatisation severity and quality of life were compared between CD and UC patients meeting Rome III criteria for IBS and those who did not.
Results: More patients with CD met criteria for IBS than UC (97 (42.4%) of 229 vs. 63 (30.9%) of 204 respectively, $P = 0.01$). In CD, there was no difference in anxiety ($P = 0.106$), depression ($P = 0.156$) or somatisation severity ($P = 0.104$) when patients with IBS-type symptoms were compared to those without. Mean quality of life scores for pain ($P = 0.003$) and general health ($P = 0.009$) were significantly lower in CD patients with IBS-type symptoms. In contrast, in UC anxiety severity was higher in those with IBS-type symptoms ($P = 0.001$), and there was a trend towards greater depression and somatisation severity in patients with IBS-type symptoms ($P = 0.035$ and $P = 0.011$ respectively). UC patients with IBS-type symptoms had significantly lower mean quality of life scores for role limitations due to physical health ($P = 0.004$), energy/fatigue ($P = 0.003$), emotional wellbeing ($P = 0.002$), social functioning ($P = 0.006$), pain ($P < 0.001$) and general health ($P = 0.003$). For CD, mean FC levels were higher in those with IBS-type symptoms than those without (543.3 vs. 444.9; $P = 0.529$) and the same trend was observed in UC (423.5 vs. 282.8; $P = 0.368$). There was no difference in the proportion of individuals with a normal FC in CD patients fulfilling criteria for IBS (12 (63.2%) of 19) than those not (31 (56.4%) of 55) ($P = 0.605$). The same was true in UC (7 (50%) of 14 vs. 38 (69.1%) of 55 ($P = 0.181$).
Conclusion: The prevalence of IBS-type symptoms is higher in CD than in UC. IBS-type symptoms are associated with more severe anxiety in UC patients and lower quality of life scores in both CD and UC. Whether such symptoms arise from occult disease activity, or true coexistence of IBS, remains unclear.
Disclosure of Interest: None declared

P0340 THE FECAL NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) AS NOVEL SURROGATE BIOMARKER OF INFLAMMATION IN THE DIAGNOSIS OF INFLAMMATORY BOWEL DISEASES

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Introduction: Today there is active search of non-invasive surrogate biomarkers of intestinal inflammation in inflammatory bowel diseases (IBD). Fecal neutrophil gelatinase-associated lipocalin (NGAL) secreted by neutrophils and epithelial cells during inflammation and possibly can be used as a biomarker of inflammation.
Aims & Methods: To evaluate the fecal concentration of NGAL in different courses of inflammatory bowel disease (IBD).

We prospectively included 96 patients with IBD exacerbation [29 pts with Crohn's disease (CD) and 67 pts with ulcerative colitis (UC)] and 15 healthy controls. Fecal NGAL was determined by ELISA in fecal specimens. We used a set of Human Lipocalin-2 / NGAL ELISA, production BioVendor, Czech Republic. The average age of patients with CD was 36 ± 2 years, UC - 37 ± 1 years, in the control group - 31 ± 2 years. Severity of CD was assessed by CDAI: mild CD was seen in 7 (24%), moderate – 13 (45%), severe – 9 (31%), in UC by Mayo score: mild – 22 (33%), moderate – 28 (42%), severe – 17 (25%).

Results: Fecal NGAL level was increased in active IBD – 4122 [861; 6850] ng/ml ($p < 0.05$) compared with healthy controls – 181 [169; 720] ng/ml. Level of NGAL in UC was higher – 4668 [1298; 7792] ng/ml ($p < 0.05$) than that in CD – 2688 [200; 5710] ng/ml. In severe CD NGAL was higher – 5908 [2860; 12920] ng/ml than in moderate CD – 2236 [172; 4236] ng/ml ($p < 0.05$) and mild CD 896 [200; 3828] ng/ml ($p < 0.05$). In severe UC fecal NGAL was higher – 6044 [4605; 9632] ng/ml than in moderate UC – 4963 [2198; 7780] ng/ml ($p > 0.05$) and mild CD – 2194 [786; 4668] ng/ml($p < 0.05$).

Fecal NGAL correlated with clinical parameters of IBD: in CD with the severity of fever ($r = 0.40$; $p < 0.05$), in UC with the stool consistency ($r = 0.25$; $p < 0.05$) and the weight loss ($r = 0.27$; $p < 0.05$). Also in CD NGAL levels had a significant correlation with the C-reactive protein ($r = 0.70$; $p < 0.05$), in UC – with the erythrocyte sedimentation rate ($r = 0.44$; $p < 0.05$).

ROC-analysis defined the threshold of fecal NGAL as a marker for determining an active phase of inflammation in IBD - 1144 ng/ml, to which were empirically determined sensitivity of 72%, specificity of 100%, and AUC – 0.88. Thus, the findings suggest that studied indicator have high resolution in identifying IBD.

Conclusion: The fecal level of NGAL significantly increased during flare of IBD with a high sensitivity, specificity and AUC. The concentration of NGAL in UC was higher than that in CD. NGAL correlated with the severity and activity of CD.

Disclosure of Interest: None declared

P0341 HETEROGENEITY IN THE ENDOSCOPIC MANAGEMENT OF CROHN'S DISEASE ASSOCIATED STRICTURES: RESULTS FROM AN INTERNATIONAL INFLAMMATORY BOWEL DISEASE SPECIALIST SURVEY

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Introduction: Crohn's disease (CD) is frequently complicated by a stricturing phenotype, leading to intestinal obstruction. Endoscopic balloon dilation (EBD) represents a widely used approach for the management of intestinal strictures in CD. Available evidence in this area, however, is limited. Aim of this study was to depict heterogeneity of endoscopic management of CD associated strictures among international CD specialists to identify common treatment standards.

Aims & Methods: A questionnaire was developed by the gastroenterology faculties of the Cleveland Clinic and the University Hospital Muenster and placed on an online platform. Participants were asked about their endoscopic experience, practice setting and number of EBD annually. Two case scenarios as well as technical practice parameters were investigated. The questionnaire was distributed through the IOIBD, ECCO, PROVIT and national IBD networks. Statistical analysis was performed using appropriate tests.

Results: 126 subjects from 15 countries (11.1% colorectal surgeons; 40.5% subspecialized in interventional endoscopy; endoscopy experience 15.2 ± 8.2 years) completed the survey. The maximal length of dilated stricture was 4.5 ± 1.7 cm. The most commonly used balloon size was graded 15-18 mm with a dilation time of 1.7 ± 1.2 minutes. While 87.2% of participants favored the use of EBD for anastomotic strictures, only 58.6% did so in case of naïve strictures. Only 35.7% of physicians dilated actively inflamed strictures. Concomitant therapies employed were injection of steroids (11.2%) or infliximab (1.7%), cutting techniques (5.2%), and stent placement (0.9%). 89.7% used serial dilations in the same patient over time.

Heterogeneity in practice existed among the participants: Interventional endoscopists were more likely to dilate only clinically symptomatic strictures ($p = 0.046$). Surgeons favored surgical treatment of *de novo* ileocaecal strictures ($p = 0.026$ compared to gastroenterologists) and reported a shorter stricture length being amendable to EBD ($p = 0.045$). They more frequently used concomitant therapies ($p = 0.001$). Traversal of the colonoscope after dilation was more frequent in academic hospitals followed by community hospitals and then private practice ($p = 0.013$). Balloon inflation time was longest in Europe and shortest in North America ($p = 0.041$). Operator experience increased the likelihood of EBD in actively inflamed strictures ($p = 0.002$), maximum length of stricture and maximum balloon size ($p = 0.001$).

Conclusion: EBD is a widely used treatment approach for stricturing CD. However, individual selection of strictures appropriate for EBD and the technical approach differ widely based on individual background of the operator, experience level and practice setting. Therefore, evidence-based consensus guidelines for the practical management of EBD are highly desirable.

Disclosure of Interest: None declared

P0342 ENDOTHELIAL MICROPARTICLES AS PLASMA BIOMARKERS OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Endothelial dysfunction plays a pivotal role in the development of inflammatory bowel diseases (IBD). Activity of endothelial cells can be determined by the use of both physical and biochemical methods as well. One of the recently discovered plasma biomarkers are microparticles derived form the endothelium. They can play an important role in interactions with circulating cells and the vascular wall.

Aims & Methods: The study aimed to assess level of circulating microparticles in IBD patients as well their correlation with clinical status.

Sixty IBD patients aged 18-65 (32 Crohns's disease (CD), 28 ulcerative colitis (UC)) and 60 sex- and age-matched healthy controls were included into the study. Levels of circulating endothelial microparticles were measured and related to disease phenotype, clinical and biochemical activity.

Results: In UC group (14F and 14M) mean microparticles level was 122 +/- 70/ul of plasma and in CD group (17F and 15M) - 144 +/- 40/ul of plasma. We found statistical differences between active and inactive UC group (140 +/- 60/ul vs 96 +/- 64/ul, $p < 0.05$) as well between active and inactive CD group (176 +/- 66/ul vs 102 +/- 56/ul, $p < 0.01$). There were no differences between inactive disease and healthy controls ($p > 0.05$) Microparticles level correlated weekly positively with CD activity ($r = 0.35$) but not with UC activity ($r = 0.12$).

Conclusion: Elevated level of circulating endothelial microparticles confirms the role of endothelial dysfunction in IBD patients. It is also an indicator of the disease activity, however this relationship is more pronounced in CD patients.

Disclosure of Interest: None declared

P0343 DISPARITY OF CROHN'S DISEASE ACTIVITY BETWEEN AN OUTPATIENT VISIT AND AT HOME IS ASSOCIATED WITH POOR CLINICAL OUTCOMES; RESULTS OF A WEB-BASED, SELF-REPORTING SYMPTOM DIARY FOR CROHN'S DISEASE

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Introduction: As Crohn's disease (CD) is characterized by its unpredictable clinical course, the ideal approach for the assessment of disease activity would be real-time monitoring of patient's symptoms.

Aims & Methods: The aim of this study was to identify discordance of patients' symptoms between on routine clinic visits and at home using a web-based self-reporting Crohn's disease symptom diary (CDSD) and to evaluate its impact on clinical outcomes. CDSD consisted of 5 clinical parameters based on the Harvey-Bradshaw Index, which could easily be recorded online, by using CDSD website (www.cdsd.or.kr). Between February 2012 and October 2014 patients with CD were invited to record their symptoms at home at least once a week and on the routine outpatient clinic visit as well. We identified the patients who showed disparity of disease activity between on the regular hospital visits and at home and evaluated clinical outcomes of these patients such as biologic use, abdominal surgery, and unscheduled visits with Kaplan-Meier analysis. Risk factors related with unscheduled visits were also assessed.

Results: Among 280 patients with CD invited, 155 (male 109, age 26.17 ± 8.19 years) who recorded their symptoms weekly basis at least for consecutive 3 months were included in the study. Fifty four patients (34.8%) showed different disease activities between at home and on the hospital. Cumulative risk of abdominal surgery ($P = 0.046$) and unscheduled visits ($P < 0.001$) was significantly higher in this disparity group than concordance group. Disparity in symptoms (HR 3.61, 95% CI 1.68-7.77, $P = 0.001$), steroid exposure (HR 2.71 95% CI 1.02-7.24, $P = 0.046$) and use of biologics (HR 3.92, 95% CI 1.81-8.49, $P = 0.001$) were independent risk factors associated with unscheduled visits to the hospital.

Conclusion: Disparity in disease activity is considerable in patients with CD and is related with the negative clinical outcome. More attention should be paid to identifying patients with this unstable activity using a real-time monitoring tool.

Disclosure of Interest: None declared

P0344 ACCURACY OF CALPROTECTIN AND NGAL IN EVALUATING HISTOLOGICAL SUB-CLINICAL INFLAMMATION IN ULCERATIVE COLITIS (ACERTIVE- STUDY)

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Introduction: Fecal calprotectin (fcal) has been reported as an important biomarker of endoscopic healing in ulcerative colitis (UC).
Aims & Methods: We assessed accuracy of fcal – evaluated by 2 assays, Quantum Blue (QB) and automated fluoroimmunoassay (EliA) – and fecal Neutrophil gelatinase-associated lipocalin (NGAL), aiming to predict the histological activity in UC patients without clinical activity according to partial Mayo score. Histological evaluation was performed by 3 independent pathologists.
Results: 369 UC patients were recruited, left side colitis (57%) or pancolitis (43%). The Geboes scoring system was used to evaluate the histological activity, and 22% of UC patients were scored as $\geq$3.1. In 29% of the cases there was endoscopic activity (Mayo 1, 2 or 3). In 20% of the patients, basal plasmocytosis was observed, diffuse in 5% of the cases. Histological activity was observed in patients with Mayo score 0 (11%) and Mayo scores 1 and 2 (43% and 86%, respectively). In asymptomatic UC patients, high fcal was observed in 25% evaluated by QB ($>$250 ug/g), 20% evaluated by EliA ($>$150 ug/g), and in 31% of the cases there was a high level of NGAL($>$12 ug/g). The median values of fcal and NGAL in patients with histological remission were: QB-81.5 ug/g (IQ: 30-224); EliA- 29 ug/g (IQ: 6.8-99.5); NGAL-8.5 ug/g (IQ: 4.7-15.1). The negative predictive value (VPN) and accuracy for histological activity (Geboes $\geq$ 3.1) was the following for different assays: QB ($>$250 ug/g): VPN-83%, accuracy-70%; EliA ($>$150 ug/g): VPN-84%, accuracy-73%; for NGAL ($>$12 ug/g), the VPN-83% and accuracy 63%, respectively. The predictability of histological remission evaluated by the area under curve was: QB: 0.72 (CI:0.66-0.78); EliA 0.71 (CI:0.65-0.76); NGAL 0.66 (CI:0.58-0.74).
Conclusion: Approximately 30% of asymptomatic UC patients had high biomarkers levels and histological or endoscopic activity. Calprotectin and NGAL are reliable and accurate biomarkers to detect persistent histological inflammation in asymptomatic UC patients.
Disclosure of Interest: None declared

P0345 CHANGES OF ADALIMUMAB TROUGH LEVELS CORRELATE WITH BODY COMPOSITION PARAMETERS

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Introduction: Anti-TNF alfa adalimumab (ADA) is a well-established treatment in inflammatory bowel disease (IBD). The drug is administered subcutaneously in an uniform dose regardless of body weight. Monitoring ADA trough levels may be recommended in the future to optimize and personalize therapy and to improve efficacy. Our aim was to explore whether body composition parameters influence ADA trough levels and its variability.
Aims & Methods: Eighteen IBD patients initiating ADA treatment were included in our study. Induction therapy was started with ADA 160/80mg at weeks 0/2, then 40mg every other week as a maintenance. ADA trough levels were measured at week 6 and 12. Bioelectrical impedance analysis (BIA) was carried out and body composition was measured by InBody 720 body analyser device right before starting biological therapy. Body composition indexes were derived from the computed values (fat-free mass index [FFMI], skeletal muscle index [SMI] and body fat mass index [BFMI]) of BIA. Body surface area was calculated by using DuBois-DuBois formula.
Results: According to our findings ADA trough levels had not differ significantly at week 6 and 12 (8.00 ± 2.9µg/mL vs. 7.73 ± 3.14µg/mL). Three of the patients (6.7%) had suboptimal ADA trough levels, only one of them were detected to have antibodies, he was excluded from further investigations. The changes of adalimumab trough levels correlated with body surface area ($r = -0.682$; $p = 0.002$). We also found moderate correlation between the variability of trough levels and muscle parameters (FFMI: $r = -0.494$, $p = 0.045$, SMI: $r = -0.508$, $p = 0.038$). However the changes of ADA trough levels did not correlate with BIA fat parameters nor the proportion of extracellular and intracellular fluid (BFMI: $r = -0.099$ and extracellular/intracellular water $r = 0.089$)
Conclusion: The results of our pilot study suggest that body surface area and body muscle parameters may influence the constancy of ADA trough levels. The findings arise the question whether adalimumab dosage offerd to be adjusted to body surface area or body compostion in the future. To confirm this suspicion larger patients population and their ADA trough levels should be investigated.
Disclosure of Interest: None declared

P0346 INDICATORS OF SUBOPTIMAL THERAPY AMONG CROHN'S DISEASE PATIENTS TREATED WITH TUMOR NECROSIS FACTOR ANTAGONISTS: RESULTS FROM A MULTINATIONAL STUDY

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Introduction: Crohn's disease (CD) patients treated with tumor necrosis factor antagonists (anti-TNFs) may require therapy changes over time, which may be considered as indicators of suboptimal therapy.
Aims & Methods: A multinational, multicentre, retrospective, chart review study was conducted to assess the indicators of suboptimal therapy among adult CD patients receiving their first anti-TNF [infliximab (IFX) or adalimumab (ADA)] between June 2009 and June 2011 (index therapy). The indicators of suboptimal therapy during 2-year follow up were: anti-TNF dose-escalation (assessed $>$4 months after index to allow for initial dose adjustments), augmentation with a non-biologic drug, discontinuation of first anti-TNF, switching to another anti-TNF and CD-related surgery. Percentages of patients with each indicator type and $\geq$1 indicator by country for each anti-TNF drug are summarized descriptively.
Results: The study included 657 CD patients with mean age (SD) of 39.2 (13.2) years, 51% females, 51% with moderate to severe CD at index, 44% and 56% on ADA and IFX respectively, and 71% on combination therapy with a non-biologic drug. Overall, 56% of CD patients had $\geq$1 indicator of suboptimal therapy, 20% of patients had dose escalation, 18% needed augmentation with a non-biologic, 29% discontinued first anti-TNF, and 17% underwent a CD-related surgery. Of those who discontinued ($N = 183$), 70% switched to another anti-TNF. Patients with indicators of suboptimal therapy for each country by the anti-TNF are shown in the Table.
Conclusion: In this large multinational cohort, over half of the CD patients had $\geq$1 indicator of suboptimal anti-TNF therapy. Predominant indicators included dose escalation, discontinuation and switching to another anti-TNF.
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P0347 LONG-TERM ADALIMUMAB EFFICACY IN STEROID-DEPENDENT CROHN'S DISEASE PATIENTS: A PROSPECTIVE "REAL LIFE" STUDY

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Introduction: Adalimumab (ADA) is effective in the induction and maintenance of steroid-free remission in patients (pts) with steroid-dependent Crohn's disease (CD). We have already reported data on efficacy and prognostic factors of response of ADA (80/40 or 160/80 mg every other week followed by 40 mg every other week) in 110 steroid-dependent pts. At week 6, 91% of pts have had a clinical benefit (remission: 45.5%, response: 45.5%). At the end of the follow-up (mean 14.6 months), 80.9% of responders have maintained the clinical benefit (remission: 64.5%, response: 16.4%). Only higher induction regimen was related to remission at week 6. At the end of the follow-up, none of the variables were associated with remission. Up to now no data are available on long term efficacy of ADA in the setting of steroid dependent pts.

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Table: Indicators of suboptimal anti-TNF therapy among CD patients during 2-year follow up

Indicator of suboptimal anti-TNF therapy	Canada IFXN = 40	France		Germany		Italy		Spain		UK		Overall	
		ADAN = 24	IFXN = 50	ADAN = 26	IFXN = 43	ADAN = 66	IFXN = 75	ADAN = 69	IFXN = 66	ADAN = 78	IFXN = 91	ADAN = 29	IFXN = 365	ADAN = 292
						%								
≥1 of the following Indicators	75.0	50.0	74.0	65.4	34.9	62.1	60.0	44.9	42.4	41.0	64.8	62.1	58.6	51.71
Anti-TNF Dose escalation	40.0	41.7	32.0	23.1	9.3	18.2	18.7	14.5	9.1	11.5	17.6	31.0	19.7	19.2
Augmentation with a non-biologic drug[1]	20.0	12.5	32.0	15.4	11.6	22.7	24.0	13.0	7.6	10.3	17.6	34.5	18.6	16.8
Discontinuation of first anti-TNF[2]	27.5	16.7	36.0	30.8	20.9	31.8	34.7	21.7	25.8	17.9	38.5	13.8	31.8	22.6
Switching to another anti-TNF[3]	15.0	12.5	30.0	19.2	11.6	22.7	22.7	18.8	18.2	12.8	28.6	3.4	22.2	16.1
CD-related Surgery	20.0	16.7	24.0	15.4	7.0	16.7	21.3	18.8	13.6	15.4	16.5	13.8	17.3	16.4

[1] Augmentation defined as any new additions or increase in dose/frequency of the concurrent non-biological therapy with anti-TNF therapy. [2]Discontinuation as reported in patients' medical charts and by excluding patients that reported discontinuing first anti-TNF because it was effective. [3]Switch defined as a subset of discontinuation patients who initiated another anti-TNF therapy over the course of the follow-up period.

Aims & Methods: All the 110 pts treated in the previous study were followed up until April 2015 and the following variables were evaluated at the end of the follow up: maintenance of clinical benefit, ADA discontinuation, dose exalation, switch to another biologic, surgical treatment and side effects.
Results: At the end of the follow up (mean 74.16 ± 10.3 months) only 5 pts resulted lost during the follow-up. Concerning the remaining 105 pts, 42 pts (40%) obtained the clinical benefit: 1) 37/42 (88%) were still in maintaining treatment with ADA at the dosage of 40 mg sc (of these pts 13/37 [35%] received a weekly maintaining treatment); 2) 5/37 (12%) discontinued ADA due to mucosal healing. Sixty-three pts (60%) discontinued ADA: 1) 50/63 (79%) for lost of clinical benefit (20 of these 50 pts were operated on [40%]); 2) 6/63 (10%) for side effects; 3) 5/63 (8%) for severe endoscopic activity despite clinical response; 4) 2/63 (3%) died for reason not related to ADA treatment. Among pts who discontinued ADA 24/63 (38%) were then effectively switched to another biologic (infliximab or golimumab). At univariable analysis we did not find variables related to the treatment outcomes. ADA was well tolerated. Only one pts developed an acute leukaemia after 2 years of ADA discontinuation.
Conclusion: This long-term "real-life" prospective study showed that ADA is a good maintaining treatment in steroid dependent CD but 1/3 of them needed dose escalation to maintain clinical benefit. The rate of long term side effects that needed treatment discontinuation is quite low. In pts intolerant to or with lost of response to ADA a switch to another biologic is an effective opportunity.
Disclosure of Interest: None declared

P0348 THE COMBINATION OF MESENCHYMAL STROMAL CELLS AND INFLIXIMAB INCREASES THE ANTI-INFLAMMATORY EFFECT OF THE TREATMENT OF ULCERATIVE COLITIS

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Introduction: Mesenchymal stromal cells (MSCs) have a high immunosuppressive potential. Concentration of azathioprine, methotrexate, 6-mercaptopurine, infliximab (IFX) no effect on the viability, differentiation, phenotype MSC and ability to suppress proliferation of peripheral blood mononuclear cells. These results are important for the clinical application of MSCs in combination with immunomodulators and anti-TNF-α therapy. However, little is known about the effectiveness of the combined use of MSC and immunomodulatory drugs in the treatment of IBD. Aim. Assess the clinical and endoscopic efficacy of combination therapy of ulcerative colitis (UC) with concurrent use MSC and IFX.
Aims & Methods: 1st group patients (n = 28) who were administered MSCs twice a month at intervals of 1 week + after 6 months from the date the first administration of MSCs. 2nd group patients with UC (n = 26) received IFX. 3rd group of patients with UC (n = 10) received MSC and IFX. Follow-up was 24 months. To assess the clinical activity of ulcerative colitis, we used the index Rachmilevitz, to assess the endoscopic activity. Analysis of the effectiveness of different biologic therapy of patients with UC after 2, 6 and 12 months of therapy. Initial level clinical activity index before treatment was in group 18.98 ± 0.38 points in the 2nd - 9.1 ± 0.4, and 3rd, respectively, - 9.1 ± 0.6, the level of endoscopic activity index before treatment was in the 1st group 7.46 ± 0.2 points, in the 2nd - 7.62 ± 0.16, in the 3rd - 7.6 ± 0.4 ($p > 0.05$).
Results: After 2 months of clinical activity index decreased significantly from baseline in 1st group to 1.53 ± 0.24 points in the 2nd - to 1.27 ± 0.12, in the 3rd to 1.1 ± 0.17 points ($p > 0.05$ between groups). After 6 months of clinical activity index was in group 11.64 ± 0.24 points in the 2nd - 1.35 ± 0.14 points, 3rd - 0.7 ± 0.15 points, which was significantly lower than in the 1st and 2nd groups ($p < 0.05$). After 12 months of clinical activity index was in group 11.68 ± 0.8 points in the 2nd - 1.62 ± 0.16 points, 3rd - 0.5 ± 0.16 points, which was significantly lower than in the 1st and 2nd groups ($p < 0.05$). Index Mayo after 2 months decreased significantly from baseline in the 1st, 2nd and 3rd groups of up to 1.57 ± 0.24, 1.65 ± 0.25, 1.22 ± 0.2 scores ($p < 0.05$), respectively. After 6 months the index Mayo in 1st group was 1.6 ± 0.24 points, in the 2nd - 1.65 ± 0.19, in the 3rd - 1.1 ± 0.2 points. After 12 months, the index of the Mayo patients 3rd group was 0.8 ± 0.2 points, which was significantly lower ($p < 0.05$) than in 1st group - 1.46 ± 0.22 points and 2nd - 1.43 ± 0.1, groups of patients with UC.
Conclusion: Combined biological therapy of inflammatory bowel disease contributes to more stable clinical and endoscopic remission compared to monotherapy with biological agents after 1 years.
Disclosure of Interest: None declared

P0349 COMPARATIVE ASSESSMENT OF THE SAFETY OF STEM CELLS AND STANDARD ANTI-INFLAMMATORY THERAPY OF CROHN'S DISEASE

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Introduction: Mesenchymal stromal cells (MSCs) are now widely used in clinical studies with various diseases, providing a positive effect due to the immunomodulatory and paracrine mechanisms. However, the safety profile of these cells remains unproved.
Objective: To compare the safety of treatment of the patients with Crohn's disease (CD), receiving comprehensive anti-inflammatory therapy with the application of MSCs standard therapy with 5-aminosalicylic acid (5-ASA), glucocorticosteroids (GSCs) and immunosuppressive agents (IS).
Materials and methods.
Aims & Methods: Within the period from 2008 to 2014 the system transplantation of allogenic MSCs was carried out in 64 patients with CD. 47 patients were included in the first group, the average monitoring time averaged 62 ± 4 months. 19 of them (40.4%) were men and 28 (59.26%) women. The average age was 30.4 ± 1.2 years. 124 patients with CD, who received standard anti-inflammatory therapy with 5-ASA and GCSs, were included in the second, control group. Out of them 56 (45.2%) were men and 68 (54.8%) women. The average age was 36.8 ± 1.5 years. The patients, who received anti-cytokine therapy, were not included in this group. The safety of the used therapy was assessed by the presence of complications, arising during the observation, infectious complications, exacerbation of chronic inflammatory diseases, serious infectious complications, a malignant transformation, a lethal outcome.
Results: In the first group of patients with CD the development of non-severe infectious complications or exacerbation of chronic inflammatory diseases were registered in 7 patients out of 56, that totaled 12.5%, in the second in 14 (16.7%) patients out of 84. When comparing the two groups, no differences were found in the risk of the development of infectious complications and exacerbation of chronic inflammatory diseases on the background of the standard anti-inflammatory CD therapy or with the introduction of the MSCs (RR-0.75, 95% Cl 1.5-23.58; x^2-0.16; p = 0.66). Severe infectious complications (pneumonia, pleurisy, activation of latent TB) in the first group were detected in 1 patient (1.8%) out of 56, and in the second group in 5 (5.9%) out of 84. When comparing the two groups no differences in the risk of this type of complications were also found (RR-0.3; 95% Cl 0.04-2.5; x^2-0.59; p = 0.44). Colorectal cancer was registered only in one she-patient from the first group (1.8%). The time between the introduction of the MSCs and diagnosed colon cancer was 10 days. In the second group of patients over the 5 years of follow-up, malignant transformation was observed in 4 (4.8%) patients out of 84 (RR-0.5, 95% Cl 0.05-4.96; x^2-0.01; p = 0.97). Within 5 years of follow-up in the first and second groups of patients, fatal outcomes were registered on one occasion in each group, 1.8% and 1.2% respectively (RR-1.5, 95% Cl 0.1-23.49; x^2-0.19, p = 0.66).
Conclusion: The analysis did not reveal any differences in the development of severe infectious complications, exacerbation of chronic inflammatory diseases, serious infectious complications of malignant transformations and deaths in patients with CD, who received the MSCs and the standard anti-inflammatory therapy.
Disclosure of Interest: None declared

P0350 FINAL THIOPURINE METABOLITE LEVELS AND SHUNTER STATUS CAN BE PREDICTED AFTER SIX WEEKS OF THIOPURINE THERAPY–BIOCHEMICAL OUTCOMES FROM THE EATME STUDY

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Introduction: Dosing of thiopurines [azathioprine (AZA) and mercaptopurine (MP)] in the management of IBD has been based upon patient weight. However, it appears unreliable in predicting final levels of thiopurine metabolites. This leads to suboptimal clinical outcomes because of under- and over-dosing, and 'shunting' in 15% where toxic 6-methylmercaptopurine (6MMP) is preferentially produced over the efficacious 6-thioguianine nucleotides (6TGN), with 6MMP:6TGN ratio ≥20.
Aims & Methods
Aims: 1. To determine prospectively the clinical value of timing of measurement of thiopurine metabolites during dose-escalating regimen of thiopurine initiation in a consecutive cohort of IBD patients being initiated on a thiopurine. 2. To determine if the 6MMP:6TGN ratio changes during thiopurine dose escalation.
Methods: In this single-centre, prospective, open label study patients were commenced on either a daily dose of 50 mg AZA or 25 mg MP (physician discretion). Doses increased fortnightly by 50 mg for AZA or 25 mg for MP until target was achieved, aiming for 2–2.5 mg/kg for AZA and 1–1.5 mg/kg for MP. Hematology, CRP and liver function tests were performed fortnightly to monitor toxicity, and thiopurine metabolites were measured fortnightly until steady-state was achieved, but these results were not used for dosing decisions. Clinical and biochemical outcomes were recorded. Landmark analyses of shunter status used logistic regression models. Metabolite levels were analysed using linear regression models.
Results: 64 patients (52 Crohn's, 11 ulcerative colitis and 1 IBD-U) were enrolled. Final metabolite outcomes were: 11 (17%) patients were shunters, 27 (42%) were underdosed (6TGN level of <260 pmol/8X10^8 RBCs), 5 (8%) patients' levels were supratherapeutic (6TGN >450) and only 21 (33%) were therapeutic. 6MMP:6TGN ratios escalated over time in shunters, but not in others. After 2 weeks of therapy, a 6MMP:6TGN ratio above 9 (p = 0.058) was suggestive of shunting, while after 6 weeks, a ratio ≥12 (95% CI 7–28, p = 0.01) was predictive of shunting. 6TGN levels at week 2 (median 106, range 0–328) predicted final 6TGN outcomes (median 282, range 50–746, r = 0.681, p < .001) and 6MMP levels at week 2 (median 236, range 0-2163) predicted final 6MMP outcomes (median 1301, range 62–14600, r = 0.835, p < .001). 23% of MP and 14% of AZA patients were shunters (p = 0.395). At no time point did levels predict an adverse event to thiopurines. No correlation was detected between the weight-based dose of thiopurines and final ratios (r = −0.277), 6TGN (r = 0.044) and 6MMP (r = −0.193) levels (all p values > .10).
Conclusion: 6MMP:6TGN ratios increase during dose escalation in shunters only. Patients with a 6MMP:6TGN ratio 12 or above after 6 weeks should be considered for optimisation with allopurinol rather than waiting until 12 weeks of therapy. Weight-based dosing of thiopurines should no longer be used in standard practice.
Disclosure of Interest: None declared

P0351 IMMUNOGENICITY OF THE BIOSIMILAR INFLIXIMAB: INTERIM RESULTS FROM A PROSPECTIVE NATIONWIDE COHORT

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Introduction: Biosimilar infliximab CT-P13 received EMA approval in June 2013 for all indications of the originator product. We aimed to prospectively evaluate the immunogenicity of the biosimilar infliximab in IBD in a nationwide, multicentre cohort.
Aims & Methods: Demographic data were collected and a harmonized monitoring strategy was applied. Clinical and biochemical activity were evaluated at week 14. Trough level (TL) and anti-drug antibody (ADA) concentration were measured by ELISA (LT-005, Theradiag, France) at baseline and before each anti-TNF administration during the induction treatment.
Results: 141 consecutive IBD patients (90 CD patients and 51 UC patients) were included in the present cohort. 29% (26 and 3%) of CD patients and 22% (16 and 6%) of UC patients had received previous anti-TNF (infliximab and adalimumab) therapy. None of the patients had received infliximab within 12 months prior to initiation of the biosimilar infliximab. 62/61% of CD/UC patients received concomitant immunosuppressives at baseline. Mean TLs were 0, 19.2, 9.1. and 3.4μg/ml at weeks 0, 2, 6 and 14. There was a tendency towards lower TLs at week 2 and 6, but not at week 14 in patients with previous infliximab exposure compared to infliximab naive patients. This was coupled with higher ADA positivity. There was no significant difference in the remission and response rates between patients with or without previous anti-TNF exposure. 6 patients had allergic reactions during induction treatment, of which 4 patients had received previous infliximab treatment.
Conclusion: Patients with previous exposure to the originator infliximab had a tendency towards lower early TL coupled with ADA positivity. Although there were no significant difference in efficacy, patients with previous infliximab exposure were more likely to develop allergic reactions.
Disclosure of Interest: None declared

P0352 OPERATING PROPERTIES OF DIFFERENT PATIENT-REPORTED OUTCOME ENDPOINTS COMBINED WITH ENDOSCOPIC EVALUATION: DATA FROM EXTEND

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Introduction: Patient reported outcome (PRO) components of the Crohn's disease (CD) Activity Index (CDAI) are being explored as clinical remission (CR) endpoints,[1] as are composite measures of endoscopic remission (ER) plus CR as outcome measures in CD trials.
Aims & Methods: To explore the use of different definitions of CR, based on CDAI stool frequency (SF) and abdominal pain (AP) components, and composite endpoints on efficacy estimations in the mucosal healing study EXTEND.[2] Three CR definitions were explored in patients (pts) from EXTEND: 1) CDAI <150, 2) sum of 7 day weighted SF/AP PRO components of CDAI <69 (PRO2 <69), and 3) average (avg) daily SF ≤1.5 and avg daily AP score ≤1.0, both not worse than baseline (BL) (SF ≤1.5 and AP ≤1.0). Pooled data from 4 CD adalimumab (ADA) trials were used to identify the threshold for PRO2 which correlated best with CDAI <150 in pts with elevated BL avg daily SF ≥2.5 or AP score ≥2.0, and the combined SF/AP definition was based on a recent report.[1] In EXTEND, adults with moderate to severe CD received induction ADA 160/80 mg at weeks (wks) 0/2. At wk 4, pts were randomized to ADA 40 mg every other wk or placebo (PBO) to wk 52. Pts (N = 104) with BL avg daily SF ≥2.5 or AP score ≥2.0 and Simple Endoscopic Score for CD (SES-CD) ≥6 (or ≥4 for pts with isolated ileal disease) by central read were analyzed at wks 12 and 52. Endpoints assessed were the 3 CR definitions, ER (SES-CD ≤4 and at least 2 point reduction from BL, by central read), and composite ER and CR for each remission definition.
Results: ER was achieved by 37.3% and 15.1% of ADA- and PBO-treated pts, respectively, at wk 12 (Δ22.2%, p = 0.01); wk 52 values were 27.5% and 1.9% (Δ25.6%, p < 0.001), respectively. Compared with ER, composite endpoints generally showed diminished effect sizes for ADA vs PBO at wks 12 and 52 (Table). Overall, composite endpoint effect sizes were similar to or slightly less than CR effect sizes. At wk 52, the SF/AP definition was associated with the lowest rates of remission in both PBO and ADA groups, and the lowest effect size of all CR definitions.
Table. Effect size for various definitions of remission (NRI)
Conclusion: Use of a composite endpoint (endoscopic plus symptomatic remission) led to diminished effect sizes compared to the endoscopic definition alone. Use of new endpoints should consider the ability of the endpoint to distinguish drug effect from PBO.

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	CDAI < 150			PRO2 < 69			SF ≤1.5 and AP ≤1.0#		
	ADAN = 51	PBON = 53	Δ	ADAN = 51	PBON = 53	Δ	ADAN = 51	PBON = 53	Δ
Clinical endpoint alone, wk 12	47.1	32.1	**15.0**	51.0	32.1	**18.9**	33.3	13.2	**20.1***
Clinical endpoint plus endoscopic remission, wk 12	23.5	11.3	**12.2**	27.5	11.3	**16.1***	19.6	1.9	**17.7****
Clinical endpoint alone, wk 52	35.3	9.4	**25.9****	35.3	9.4	**25.9****	21.6	7.5	**14.0**
Clinical endpoint plus endoscopic remission, wk 52	25.5	0	**25.5*****	23.5	0	**23.5*****	15.7	0	**15.7****

Δ, Difference between treatment groups (effect size)#Each score not worse than BLNonresponder imputation (NRI) was used for pts with missing data and those who moved to open-label ADA*p < 0.05; **p < 0.01; ***p < 0.001 by Fisher's exact test

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P0353 THE LONG-TERM EFFECT OF ANTI-TNF ALPHA THERAPY ON SERUM LIPID PROFILE AND ATHEROGENIC INDEX IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Cardiovascular morbidity appears to be increased in inflammatory bowel diseases (IBD). Tumor necrosis factor (TNF) is a pivotal proinflammatory cytokine in inflammatory diseases and causes deterioration of the lipid profile in inflammatory conditions. It is postulated that in patients with IBD, proinflammatory cytokine TNFα can alter lipid profile causing dyslipidemia that promotes atherogenesis. However, previous reports investigating the effect of anti-TNFα blockers on lipid profile in IBD patients showed conflicting results.

Aims & Methods: Therefore, the aim of this study was to identify long-term effect of anti-TNFα therapy on lipid profile and atherogenic index (AI) in patients with IBD followed-up to 36 months (mos). A total of 56 patients diagnosed as having IBD [44 Crohn's disease (CD) and 12 colitis ulcerosa (CU)] and treated with anti-TNFα agents (33 received adalilumab, 23 received remicade) were evaluated by means of serum lipid profile and serum total cholesterol, triglyceride, LDL-c and HDL-c were measured within 1 month before the first dose of anti-TNFα agent and then after six-month periods. AI was also calculated by dividing total cholesterol to HDL-c before biologic agent and then every six-month periods. Patients followed-up less then 12 mos, with diabetes, receiving antilipidemic agents were not included into the study.

Results: The median follow-up period was 26.1 months. With anti-TNFα treatment, serum cholesterol level was found to be increased compared to baseline (163.1 vs 179 mg/dL, $p = 0.01$), triglyceride level increased at 24th mos compared to baseline (118 vs 152.1 mg/dL, $p < 0.001$), LDL level increased at 36th mos compared to baseline (92 vs 110.71 mg/dL, $p = 0.022$), and HDL level did not show any significant change during follow-up period. As for AI, AI significantly increased at 36th mos compared to baseline (3.84 vs 4.09, $p < 0.001$). There were no significant differences by means of lipid profile and AI between patients with CD vs UC and patients receiving adalilumab vs remicade.

Conclusion: Significant changes were observed in cholesterol and LDL levels of patients with IBD on anti-TNFα after 36 mos of treatment. A significant increase in AI was also observed in this study. Therefore, anti-TNFα treatment might affect lipid profile and AI which may contribute to cardiovascular morbidity. AI can contribute significantly in the prediction of coronary artery disease risk especially when lipid profile is not markedly deranged.

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P0354 VALPROIC ACID REGULATES MUCOSAL CYTOKINE PRODUCTION, APOPTOSIS PATHWAYS AND HISTONE ACETYLATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Novel therapeutic strategies are required for inflammatory bowel diseases (IBD), as significant numbers of patients do not respond to current treatments. Oral administration of valproic acid (VPA) has been shown to reduce acute and chronic intestinal inflammation in animal models of colitis.[1] VPA inhibits histone deacetylase (HDAC) enzymes[2] involved in the epigenetic regulation of apoptosis, cell differentiation and cytokine production. No data are available about the effect of VPA on human intestinal inflammation.

Aims & Methods: The aim of this study was to determine whether VPA induces histone hyperacetylation, influences mucosal cytokine production and impacts on apoptosis pathways in patients with IBD. Intestinal biopsies from IBD patients undergoing routine colonoscopy at the Royal London Hospital were collected and cultured with VPA (0.05 mM, 0.5 mM and 5 mM) or control media for 24 hours. Total RNA was extracted and the mRNA levels of cytokines and markers of apoptosis assessed by qPCR. The cytokine protein levels in culture supernatant were quantified using Luminex assays (IFNγ, IL-1b, IL-23, IL-6, TNFα and IL-10) and ELISA (IL-6). To confirm the proposed mechanism of action, the effect of VPA on histone-3-acetylation levels was assessed using immunofluorescence microscopy. SPSS version 22 was used for statistical analysis.

Results: Intestinal biopsies from 17 IBD patients (7 Crohn's disease, 10 ulcerative colitis) were collected and cultured with or without VPA. Relative to control, culturing with the highest concentration of VPA (5 mM) was associated to a significant reduction in IL-6, IL-22 and IL-10 mRNA expression ($p = 0.001$, $p = 0.01$ and $p = 0.001$, respectively, Wilcoxon test). VPA did not affect TNFα and IFNγ mRNA expression. Culture with VPA 5mM reduced IL-6, TNFα and IL-10 protein levels in biopsy culture supernatants ($p = 0.005$, $p = 0.002$ and $p = 0.002$, respectively, Wilcoxon test). No differences were found in the level of IFNγ, IL-1b and IL-23 protein. IL-6 concentration in the culture supernatant was confirmed to be significantly reduced by VPA 5 mM using ELISA ($p = 0.02$, Wilcoxon test). The reduction in cytokine expression was associated with a significant reduction in Bcl-3 mRNA expression ($p = 0.008$) and an increase in Caspase-9 gene expression ($p = 0.001$, Wilcoxon test), demonstrating a stimulation of pro-apoptotic pathways. The percentage of H3-acetylated positive cells was significantly higher in biopsies treated with VPA 5 mM compared with untreated ($n = 4$; $p = 0.002$, t test).

Conclusion: VPA, a broad-acting HDAC inhibitor, regulates cytokine production, increases the activity of pro-apoptotic pathways and induces histone-3 hyperacetylation in intestinal mucosa of IBD patients. These results encourage further investigation of the therapeutic role of HDAC inhibition in patients with IBD.

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P0355 FISTULIZING PERIANAL CROHN'S DISEASE TREATMENT WITH INFLIXIMAB ALONE OR COMBINED WITH SURGERY - RESULTS OF ONE YEAR FOLLOW-UP

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Introduction: Infliximab (IFX) is effective in the treatment of Fistulizing Perianal Crohn's Disease (FPCD); however, data regarding its long-term efficacy is still limited. Combined biological and surgical treatment may offer some advantages in selected patients.
Aims & Methods: The aim of this study was to assess IFX's efficacy, alone or combined with surgery, in patients with FPCD. We conducted an analysis of prospective and systematic clinical registries of patients in whom FPCD was the indication for IFX therapy, either alone or following surgery. Examination under anesthesia was executed prior to the initiation of treatment. Clinical registries were performed at weeks (wk) 0, 2, 6, 14, 30 and 54 of IFX therapy and included evaluation of Perianal Disease Activity Index (PDAI) and Fistula Drainage Assessment (FDA). Partial response (PR) was defined as at least 50% reduction in the PDAI value and at least 50% reduction in the number of draining fistulas or at least 50% healing of the perianal post-surgical wound in those who underwent surgery. Complete response (CR) was defined as a PDAI score ≤ 4 and closure of all draining fistulas or complete healing of the perianal post-surgical wound. Loss of response (LR) was defined by any increase in PDAI, by the recrudescence of draining fistulas, by the occurrence of any other perianal complication or the need for additional therapy.
Results: Thirty-six patients (19 males; average age 34 ± 14 years, range 16-75 years) with FPCD initiated IFX therapy. Seventeen (47%) patients underwent previous surgical procedure: abscess drainage (n = 9), abscess drainage and fistulotomy (n = 6) or fistulotomy/fistulectomy (n = 2); seton placement was performed in 7. At baseline (wk0), median PDAI value was 12. At wk14, 83% of patients achieved response (PR 30%, CR 53%), with an average decrease of 8.3 in PDAI score from baseline. At wk54 response was 75% (PR 19%, CR 56%); LR occurred in 7 patients (19%), all of them maintaining lower PDAI score than at baseline (average decrease of 5.6 from wk0). Biological therapy was suspended in 2 patients because of serious adverse reaction; there were no cases of perianal abscess development during follow-up.
Conclusion: Therapy with IFX, combined with surgery when appropriated, achieved early clinical response and healing in FPCD, maintaining response in 75% (partial response 19%, complete response in 56%) of patients at the 52nd week.
Disclosure of Interest: None declared

P0356 LONG-TERM OUTCOMES OF ADALIMUMAB THERAPY IN ULCERATIVE COLITIS PATIENTS BY PRIOR ANTI-TNF EXPOSURE

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Introduction: The impact of anti-TNF exposure on the outcomes of adalimumab (ADA) therapy in ulcerative colitis (UC) patients is not well known. The aim of this study was to compare the long-term outcomes of ADA in UC patients according to previous anti-TNF use.
Aims & Methods: This was a retrospective multicentre cohort study evaluating UC patients who were primary responders to ADA induction therapy and who advanced to a maintenance regimen. We compared the outcomes of the cohorts of anti-TNF-naïve patients versus anti-TNF-experienced patients. The primary endpoints were the cumulative probabilities of ADA failure-free survival and colectomy-free survival. ADA failure was defined as withdrawal of the drug due to intolerance or complete loss of response. We also assessed the need for ADA dose escalation during follow up. Predictors of event-free survival were estimated using Cox proportional hazard regression analysis.
Results: Of the 184 UC primary ADA responders included, 116 (63%) had previous anti-TNF use. During a median follow-up of 16 months (interquartile range [IQR] 7-39), 69 patients (37%) had ADA failure. Anti-TNF-naïve patients had a significantly lower adjusted rate of ADA failure compared to anti-TNF-experienced patients (hazard ratio [HR] 0.65; 95% CI: 0.52-0.80; $p < 0.001$). After a median follow-up of 21 months (IQR 12-47), 22 patients (12%) needed colectomy. Median time to colectomy was 10 months (IQR 4-18). Anti-TNF-naïve patients had a significant 74% reduction in the need for colectomy (HR 0.26; 95% CI: 0.10-0.65; p = 0.004). Seventy-six patients (41%) required escalation to weekly ADA dosing. The median time to escalation was 4 months (IQR 2-9). Anti-TNF-naïve patients had a significantly lower adjusted rate of the need for escalation (HR 0.38; 95% CI: 0.21-0.69; p = 0.002). Patients who needed escalation had a significantly higher adjusted rate of ADA failure (HR 1.78; 95% CI: 1.08-2.94; p = 0.02) and need for colectomy (HR 3.13; 95% CI: 1.22-8.03; p = 0.02).
Conclusion: In this real–life cohort of primary ADA responders with UC, 63% of patients maintained sustained clinical benefit and 88% of patients avoided colectomy. Anti-TNF-naïve patients had better outcomes in the long-term, with a significant reduction in the rates of ADA dose escalation, ADA failure and colectomy.
Disclosure of Interest: C. Taxonera Financial support for research: MDS; Abbvie, Lecture fee(s): MDS; Abbvie, E. Iglesias: None declared, F. Muñoz: None declared, M. Calvo: None declared, M. Barreiro-de Acosta: None declared, D. Busquets: None declared, X. Calvet: None declared, A. Rodriguez: None declared, R. Pajares: None declared, J. Gisbert: None declared, P. Lopez-Serrano: None declared, J. L. Perez-Calle: None declared, A. Ponferrada: None declared, C. de la Coba: None declared, F. Bermejo: None declared, M. Chaparro: None declared, C. Alba: None declared, D. Olivares: None declared, I. Fernandez-Blanco: None declared

P0357 LONG-TERM TREATMENT WITH FERRIC MALTOL IS EFFECTIVE AND WELL TOLERATED IN CORRECTING IRON DEFICIENCY ANEMIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: RESULTS FROM A PHASE-3 OPEN-LABEL STUDY

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Introduction: Iron deficiency anemia (IDA) is frequently seen in inflammatory bowel disease (IBD). Oral iron supplementation with ferrous products (OFP) is linked to possible gastrointestinal side effects and disease exacerbation in some IBD-patients. Recently, ferric maltol provided rapid and clinically meaningful improvement in Hb and showed a favorable safety profile during a pivotal 12 week study [1]. The following multicenter phase-3 open-label extension study evaluated the long-term efficacy and safety of ferric maltol.
Aims & Methods: Initially, adult patients with quiescent or mild-to-moderate ulcerative colitis or Crohn's disease, mild-to-moderate IDA, and failure on previous OFP received oral ferric maltol capsules (30 mg twice a day) or placebo for 12 weeks. Following the randomised, double-blind phase of the study, patients were eligible to receive open-label ferric maltol for up to an additional 52 weeks.
Results: In total, 111 subjects received ferric maltol for up to 64 weeks. Hb continued to rise in those previously treated with ferric maltol (mean from baseline 3.07 (SD 1.46) g/dL at week 64, n = 36). Increases were also observed in former placebo-treated subjects (mean 1.87 (SD 1.20) g/dL by week 24 (12 weeks of treatment; n = 53), and 2.19 (SD 1.61) g/dL by week 64 (52 weeks of treatment; n = 36). The proportion of subjects with normal Hb concentration continued to rise for those treated with ferric maltol initially (week 12: 71%, week 64: 86.1%;) and for those switching to ferric maltol (week 12: 15.1% and 83.3% at week 64). Ferritin rose from 8.4 ug/L at baseline (n = 128) to 24.9 ug/L at 12 weeks (n = 112) and 68.9 ug/L at 64 weeks (n = 36). In total, 80% of subjects reported at least one AE, however, only 24% of subjects reported an AE considered to be treatment related. 18 subjects (16%) discontinued due to adverse events, but only 8 (7%) of these were evaluated as treatment related AEs. The most common AEs were abdominal pain (16%), diarrhoea (14%), nasopharyngitis (18%), flatulence (8%), and arthralgia (8%). No worsening of IBD scores (SCCAI, CDAI) was observed during the entire study.
Conclusion: Long-term treatment with ferric maltol resulted in a continuous rise of mean Hb, with Hb normalisation in more than 80% of patients. Ferritin levels increased when treatment was continued past 12 weeks. The adverse event profile in the open label phase confirmed the benign safety profile of oral ferric maltol and the feasibility of long-term treatment.

Reference

1. Gasche et al., *Inflamm Bowel Dis* 2015; 21: 579–588.

Disclosure of Interest: None declared

P0358 SUBSTANTIAL HISTOLOGICAL IMPROVEMENT FOLLOWING HAEMOPOETIC STEM CELL TRANSPLANTATION FOR CROHN'S DISEASE

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Introduction: Haemopoietic stem cell transplantation (HSCT) leads to complete regression of endoscopic signs of Crohn's disease in about one third of patients, implying an alteration in the natural history of Crohn's disease. We investigated whether these substantial changes were also seen histologically.

Aims & Methods: Patients with impaired quality-of-life from active Crohn's disease not amenable to surgery despite treatment with at least 3 immunosuppressive agents all underwent stem cell mobilisation before randomisation to immuno-ablation followed by unselected cyclophosphamide-based conditioning and HSCT after one month (Early HSCT) or one-year (Delayed HSCT). They underwent full ileocolonoscopy at baseline and after one and two years. Endoscopic involvement and activity were assessed using the Simple Endoscopic Score of Crohn's disease (SES CD) in which a value of zero means no evidence of active or inactive Crohn's disease in any examined segment of the ileum or colon. In 17 patients segments were biopsied systematically for blinded histological assessment, using ECCO-approved scales for intensity and diffuseness of acute and chronic inflammation, granulomas, ulceration, distortion and metaplasia.
Results: There was a strong correlation between endoscopic findings and histology (Table).

% Normal Histology	Endoscopy: Normal	Involved	p
Ileum	78%	25%	0.001
Right Colon	90%	36%	<0.0001
Transverse Colon	83%	38%	0.003
Left Colon	93%	24%	<0.0001
Rectum	73%	27%	0.001

The % of colonic biopsy samples that were histologically normal rose from 39% (baseline) to 50% at 1 year and 78% at 2 years after Early HSCT ($p = 0.039$). In patients undergoing Delayed HSCT values were 52% (baseline), 50% 1 year after mobilisation only and 75% after a further year following delayed HSCT ($p = 0.329$). Improvements were mainly due to reduction or regression of acute and chronic inflammatory changes.
Conclusion: Blinded histological assessments fortify the evidence that HSCT can have a profound objective benefit in Crohn's disease.
Disclosure of Interest: None declared

P0359 FOUR-YEAR EFFICACY AND SAFETY OF AZATHIOPRINE TREATMENT IN THE MAINTAINANCE OF STEROID-FREE REMISSION IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Azathioprine (AZA) and thiopurine are widely used for induction and maintenance of remission in patients steroid-dependent with inflammatory bowel disease (IBD). The treatment must be withdrawn in 5-30% of patients due to the occurrence of adverse events.
Aims & Methods: Aim of this study has been to investigate its efficacy and safety in maintaining steroid-free remission in steroid dependent IBD patients four year after the institution of treatment. Data from consecutive IBD outpatients referred in our Institution, between 1985-2013, were reviewed and all patients treated with AZA were included in this retrospective study. AZA was administered at the recommended dose of 2–2.5 mg/kg. Blood chemistry was analysed before administration of the drug, every 10-15 days for the first 3 months and then every 1-2 months following the institution of treatment.
Results: Out of 2556 consecutive IBD outpatients visited in the index period, AZA was prescribed to 376 patients, 198 (52.7%) were affected by Crohn's disease (CD) and 178 (47.3%) by ulcerative colitis (UC). One hundred and four patients with a follow-up <48 months were excluded from the study. Two hundred and seventy-two patients were evaluated, 146 (53.7%) with CD and 126 (46.3%) with UC. One hundred and forty-nine (54.8%) were male and 123 (45.2%) female (average age of 33.56 ± 14.34 SD years, range 14-74 y.). Four year after the institution of treatment, 149 (54.8%) patients still were in steroid-free remission (89 CD vs 60 UC, 61% and 47.6%, respectively, $p = 0.0288$), 71 (26.1%) had a relapse requiring retreatment with steroids (42 UC vs 29 CD, 33.4% and 19.8%, respectively, $p = 0.0130$), 52 (19.1%) discontinued the treatment due to side effects (28 CD vs 24 UC, 19.2% and 19%, respectively). Loss of response from 1st to 4th year of follow-up was low, about 17%.
Conclusion: Four years after the onset of treatment 55% of patients did not require further steroid courses. After the first year loss of response was low in three subsequent years. In the present series the maintenance of steroid-free remission was significantly higher in CD than in UC patients. The occurrence of side effects leading to the withdrawal of AZA treatment has been low.
Disclosure of Interest: None declared

P0360 MAINTENANCE ANTI-TNF THERAPY HAS A BENEFICIAL EFFECT ON BONE MINERAL DENSITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: It has been well established that patients with inflammatory bowel disease (IBD), both ulcerative colitis (UC) and Crohn's disease (CD), are at increased risk of osteoporosis. Prior studies have shown that both Adalimumab and Infliximab have beneficial effects on bone metabolism in patients with CD in the short term. However, no data is available on the longer term effect of maintenance anti-TNF on bone mineral density (BMD) in patients with IBD
Aims & Methods: We aim to evaluate the medium to long-term impact of maintenance anti-TNF therapy on BMD in patients with IBD. The study was a retrospective observational cohort study of patients with IBD who were commenced on anti-TNF therapy (either Infliximab or Adalimumab). All patients underwent BMD measurement (DEXA scan) prior to commencement of anti-TNF therapy. BMD was then measured at variable intervals following commencement of therapy, with a minimum of one year prior to repeat BMD. A detailed chart review of patients' demographics, disease phenotypes and concomitant treatments was performed. This review is on- going and to date data for 30 patients has been analysed. A paired t-test was performed to evaluate the changes in BMD in patients on Adalimumab or Infliximab.
Results: To date, data for 30 patients has been analysed. There were 18 female patients and the mean age for the cohort was 45 years (SD +/- 12.8). 28 patients have CD and 2 have UC. 16 patients were on maintenance Infliximab and 12 on Adalimumab. Mean T score prior to commencement of biologic therapy was -1.68 (SD +/- 1.10). The mean T-score at follow up DEXA was -1.41 (SD +/- 1.15). The mean interval between BMD measurements was 2.9 years (SD +/- 1.5). There was a significant improvement in T score between initial and follow up BMD, $P = 0.039$ (CI:-0.531,-0.014)
Conclusion: In this study, we show a significant improvement in T scores of IBD patients following commencement of maintenance anti-TNF therapy.
Disclosure of Interest: None declared

P0361 INTERFERON-γ RELEASE ASSAY VERSUS TUBERCULIN SKIN TEST IN PATIENTS WITH MODERATE-TO-SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE PURSUIT UC PROGRAM

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Introduction: To report the results of an interferon-γ release assay (IGRA) versus standard tuberculin skin test (TST) as a screening tool for latent TB infection in patients with ulcerative colitis (UC) in PURSUIT.
Aims & Methods: UC patients with moderately to severely active UC were screened for latent TB using the standard TST and the IGRA to assess eligibility for entry into the induction studies of golimumab (PURSUIT-SC [C0524T17]and PURSUIT-IV [C0524T1]Any patient with a newly identified positive finding for TB on a diagnostic test in whom there was no evidence of active TB was permitted to enter provided appropriate treatment for latent TB was initiated before or at the time of the first dose of study agent. TST was performed according to the Mantoux method, using 5 tuberculin units (TU) of purified protein derivative (PPD) standard or 2 TU of PPD RT-23. The TST was deemed positive for latent TB infection according to the local country guidelines for defining an immunosuppressed host or, in the absence of local guidelines, according to the presence of induration $\geq$5mm. The IGRA used to screen for latent TB was the QuantiFERON-TB Gold In-Tube test. Overall IGRA and TST results were assessed. The impact of prior BCG vaccination and concomitant medication (ie corticosteroids and/or immunomodulators) on outcome was also assessed.
Results: In this analysis, 1283 patients had both IGRA and TST screening prior to GLM treatment. Among these patients, 8.7% had at least one test yielding positive findings for latent TB, including 6.2% with positive results only by TST, 3.7% with positive results only by IGRA, and 1.2% with positive results on both tests. The rate of indeterminate results for TB on IGRA was 7.7%. Agreement between the TST and IGRA results, measured by the kappa coefficient, was 0.135 (95% confidence interval [95% CI] 0.050-0.220; $p = 0.028$). Among patients with positive IGRA findings, 31.3% had positive TST results. Among patients with positive TST findings, 19.0% had positive IGRA results. Overall, 501 (40.5%) of 1283 patients had previously received BCG vaccine; among this vaccinated group, the rate of positivity for latent TB by TST was 10.4% vs 5.0% for IGRA positivity. Among patients who had not received BCG vaccine, the rate of positivity by TST was 1.9% vs 2.8% for IGRA positivity. When IGRA was repeated in patients whose results were initially indeterminant, the majority of patients (67.0%) were IGRA negative on repeat whereas the number of patients whose results were positive was 5.3%; IGRA remained indeterminate for 27.7%. Overall, 2.1% tested indeterminate on first and repeat screening. Concomitant corticosteroid and/or immunomodulator use did not appear to have an impact on results.
Conclusion: Results of this comparison of IGRA and TST in a large cohort of patients with UC suggest that the IGRA provides greater specificity and possibly greater sensitivity than the TST in patients with moderate to severe UC.
Disclosure of Interest: C. Marano Conflict with: Employee Janssen R & D, LLC, E. Hsia Conflict with: Employee Janssen R & D, LLC, S. Xu Conflict with: Employee Janssen R & D, LLC, W. Sandborn Financial support for research: Janssen R & D, LLC, P. Rutgeerts Financial support for research: Janssen R & D, LLC

P0362 THE EXPENSES OF ACADEMIC INPATIENT CARE OF INFLAMMATORY BOWEL DISEASE PATIENTS ARE ALMOST DOUBLE COMPARED WITH AVERAGE ACADEMIC GASTROENTEROLOGY AND HEPATOLOGY CASES AND NOT FULLY RECOVERED BY DIAGNOSIS-RELATED GROUP (DRG) PROCEEDS

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) challenge economies worldwide. Detailed diagnosis-related group (DRG) data of academic inpatient care for inflammatory bowel disease (IBD) patients in Europe is unavailable.
Aims & Methods: IBD was identified through ICD-10 K50 and K51 code groups. We took an actual costing approach, compared expenditures to G-DRG and non-DRG proceeds and performed detailed cost center and type accounting to identify coverage determinants.
Results: Of all 3093 hospitalized cases at our department 164 were CD and 157 UC inpatients in 2012. On average, they were 44.1 (CD 44.9 UC 43.3 all 58) years old, stayed 10.1 (CD 11.8 UC 8.4 vs. all 8) days, carried 5.8 (CD 6.4 UC 5.2 vs. all 6.8) secondary diagnoses, received 7.4 (CD 7.7 UC 7 vs. all 6.2) procedures, had a higher cost weight (CD 2.8 UC 2.4 vs. all 1.6) and required more intense nursing. Their care was more costly (means: total cost IBD 8477€CD 9051€UC 7903€vs. all 5078€). However, expenditures were not fully recovered by DRG proceeds (means: IBD 7413€, CD 8441€, UC 6384€vs all 4758€). Here, we discovered substantial disease-specific mismatches in cost centers and types and identified the medical ward personnel and materials budgets to be most imbalanced. Non-DRG proceeds were almost double (IBD 16.1% vs. all 8.2%), but did not balance deficits at total coverage analysis, that found medications (antimicrobials, biologics and blood products), medical materials (mostly endoscopy items) and in CD also non-medical intrastructure costs to contribute most to the deficit.
Conclusion: DRGs threaten sophisticated, academic care for the neediest of all IBD patients.
Disclosure of Interest: None declared

P0363 LONG-TERM OUTCOMES OF ULCERATIVE COLITIS PATIENTS ON MONOTHERAPY MAINTENANCE TREATMENT WITH THIOPURINES: PRELIMINARY DATA

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Introduction: Thiopurines have been used for the treatment of inflammatory bowel disease from several years. However there are few evidence-based data to support their efficacy in ulcerative colitis (UC).
Aims & Methods: The aim of our study was to assess the long-term outcome of UC patients receiving thiopurines monotherapy and to identify possible predictors of efficacy in a large cohort of patients.We retrospectively collected data on all UC patients who started monotherapy thiopurines at three tertiary IBD centers from February 1995 to April 2015. Associations between clinical and epidemiological characteristics and treatment efficacy were analyzed with survival regression models clustered for IBD center and adjusted for age, sex and calendar period and expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). Models incorporated treatment failure, intolerance and adverse events as competing risks. Treatment efficacy was defined as either sustained clinical remission on thiopurines treatment or withdrawal of thiopurines for remission.
Results: A total of 234 UC patients started thiopurines during the interval. The mean (SD) age at diagnosis was 39 (15) years and the median duration of disease was 4 years (range 0-32 years). One-hundred and forty-four patients (62%) had pancolitis and 90 (38%) extensive colitis. One-hundred and thirty-two patients (61%) had endoscopic moderate activity and 85 (39%) severe colitis. The main indication for treatment was steroid-dependence for 137 patients (59%). Azathioprine was prescribed to 90% of patients and mercaptopurine to 10%. Participants contributed a total of 760 person-years of follow-up (median follow-up 28 months, range 0.2-207 months). Eighty-eight of 234 patients (38%) maintained clinical remission and were still on thiopurines therapy and 37 of 234 (16%) withdrew thipurines because of sustained remission without clinical relapse. Thiopurines were discontinued in 71 patients (30%) for failure and 35 of these patients (49%) started biologics. Twenty-seven patients (12%) experienced intolerance, in particular: medullary aplasia (n = 10, 37%), hepatitis (n = 6, 22%), pancreatitis (n = 5, 19%), arthromyalgia (n = 1, 37%) and other (n = 5, 19%). Eleven patients (5%) stopped thiopurines for other reasons. Duration of disease (HR 1.02, 95% CI 0.97, 1.07), disease extension (HR for pancolitis vs extensive colitis 1.01, 95% CI 0.55, 1.85), endoscopic activity at baseline (HR for severe vs moderate colitis 0.83, 95% CI 0.59, 1.18), smoking status (HR for smoking vs non smoking 1.18, 95% CI 0.79, 1.76) and indication for treatment (HR for 5-amynosalicilates refractoriness vs steroid-dependence 1.12, 95% CI 0.72, 1.75 and HR for severe acute attack vs steroid-dependence 1.44, 95% CI 0.98, 2.10) were not significantly associated with treatment effectiveness.
Conclusion: Thiopurines monotherapy was effective in large proportion of UC patients. We could not identify any independent predictors of treatment efficacy in our sample.
Disclosure of Interest: D. Pugliese: None declared, P. M. Ferraro: None declared, A. Aratari: None declared, G. Margagnoni: None declared, R. Monterubbianesi: None declared, C. Felice: None declared, A. Papa: None declared, L. Guidi Lecture fee(s): AbbVie,MSD, Takeda, Zambon, Consultancy: AbbVie,MSD, Mundipharma, A. Kohn: None declared, C. Papi Consultancy: AbbVie,Takeda, MSD, Chiesi, Sofar, A. Armuzzi Financial support for research: MSD, Lecture fee(s): AbbVie, Astra-Zeneca, Chiesi, Ferring, Hospira, MSD, Otsuka, Takeda, Zambon, Consultancy: AbbVie, Hospira, Lilly, MSD, Mundipharma, Pfizer, Sofar, Takeda

P0364 HEALTH-RELATED QUALITY OF LIFE VARIES AS A FUNCTION OF REMISSION STATUS IN PATIENTS WITH MILD-TO-MODERATE ULCERATIVE COLITIS RECEIVING SHORT-TERM AND LONG-TERM DAILY THERAPY WITH MULTIMATRIX MESALAZINE

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Introduction: Studies have shown an inverse relationship between disease activity and health-related quality of life (HRQL) for patients (pts) with ulcerative colitis (UC), such that decreases in disease activity predict better HRQL. Consistent with this are findings that pts with UC in complete (clinical and endoscopic) remission (CR) exhibit better HRQL than pts not in remission (NR). What has not been established is whether HRQL for UC pts in partial remission (PR) is more similar to pts in CR or NR.
Aims & Methods: Data were from a multinational, open-label, prospective trial of multimatrix mesalazine (NCT01124149). During induction treatment, pts with active mild-to-moderate UC received 4.8 g multimatrix mesalazine once daily (QD) for up to 8 weeks. Pts in CR or PR at Week 8 were eligible to receive 12 months of maintenance treatment with 2.4 g multimatrix mesalazine QD. Remission status at Week 8 or early withdrawal (EW) visit during the induction phase (induction endpoint) and at Month 12 or EW visit of the maintenance phase (maintenance endpoint) was determined using a modified UC-Disease Activity Index (UC-DAI). CR was defined as UC-DAI $\leq$1 with scores of 0 for both rectal bleeding (RB) and stool frequency (SF) components and $\geq$1-point reduction from baseline for the endoscopy component. PR was defined as UC-DAI $\leq$3, RB + SF $\leq$1, and not in complete remission. All EW pts were classified as NR. Pts completed measures of generic HRQL (12-item Short-Form survey [SF-12v2]) and disease-specific HRQL (Shortened Inflammatory Bowel Disease Questionnaire [SIBDQ]) at baseline and at the end of induction and maintenance treatment. Analysis of variance models tested if HRQL scores at both endpoints differed as a function of pts' remission status. Repeated-measures mixed-effects models (RMMM) tested if changes in HRQL over time varied by maintenance endpoint remission status. All tests used Bonferroni-adjusted P values to control for multiplicity.
Results: The numbers of pts in CR, PR, and NR (including EW pts) were, respectively, 186 (26.6%), 282 (40.3%) and 231 (33.0%) at Week 8, and 159 (39.7%), 103 (25.7%) and 139 (34.7%) at the end of maintenance (Month 12). At both time points, pts in CR and PR scored significantly better on all 8 SF-12v2 and all 4 SIBDQ domains than NR pts (all $P < 0.0001$). Including EW pts in all analyses, there were no statistical differences between scores of CR and PR pts on 7 of 8 SF-12v2 domains (all but bodily pain, $P = 0.013$) or any SIBDQ domains at Week 8, while at Month 12, there were no statistical differences between CR and PR pts on any SF-12v2 or SIBDQ domains (all $P \geq 0.251$). Estimated parameters and means from RMMM indicated that pts in CR or PR showed similarly larger improvements and better maintenance of HRQL over time than did NR pts.
Conclusion: HRQL was similar for pts whose UC was in CR or PR following both short-term and long-term daily treatment with mesalazine. Furthermore, at both endpoints, CR and PR pts exhibited better HRQL than NR pts. These results indicate that improvement and maintenance of HRQL for pts with UC in PR was comparable with those in CR.
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P0365 REMISSION STATUS PREDICTS WORK-RELATED OUTCOMES FOR PATIENTS WITH MILD-TO-MODERATE ULCERATIVE COLITIS RECEIVING SHORT-TERM AND LONG-TERM DAILY THERAPY WITH MULTIMATRIX MESALAZINE

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Introduction: Studies have shown that increased disease activity for patients with ulcerative colitis (UC) predicts impairment in work-related outcomes (WRO),

such as decreased productivity and increased absenteeism. In addition, patients whose UC is in complete (clinical and endoscopic) remission (CR) demonstrate less impairment in WRO than patients whose UC is not in remission (NR). The objective of the current study was to examine WRO of UC patients in partial remission (PR) relative to WRO of patients in CR or NR.

Aims & Methods: Data were from a multinational, open-label, prospective trial of multimatrix mesalazine (NCT01124149). In the induction phase, patients with active mild-to-moderate UC received 4.8 g of multimatrix mesalazine once daily (QD) for 8 weeks. Patients in CR or PR after induction were enrolled in the maintenance phase, during which they received 2.4 g of multimatrix mesalazine QD for 12 months. Remission status at induction endpoint (Week 8 or early withdrawal [EW] visit) and at maintenance endpoint (Month 12 or EW visit) was determined by a patient's score on a modified UC-Disease Activity Index (UC-DAI). CR was defined as UC-DAI $\leq$1 with scores of 0 for both rectal bleeding (RB) and stool frequency (SF) components, and $\geq$1-point reduction from baseline for the endoscopy component. PR was defined as UC-DAI $\leq$3, RB + SF $\leq$1, and not in complete remission. Patients who did not complete the full course of treatment were classified as NR.

A UC-specific version of the Work Productivity and Activity Impairment (WPAI:UC) questionnaire measured the impact of UC on 4 WRO domains – absenteeism, presenteeism, overall work impairment (OWI), and activity impairment – at baseline, Week 8, and Month 12 (including EW patients at all time points). Analysis of variance models compared WPAI:UC scores at these time points among CR, PR, and NR patient groups. Changes in OWI scores over time as a function of remission status was examined using a repeated-measures mixed-effects model (RMMM). All tests used Bonferroni-adjusted *P* values to control for multiplicity.

Results: The numbers of patients in CR, PR, and NR (including EW patients) were, respectively, 186 (26.6%), 282 (40.3%) and 231 (33.0%) at Week 8, and 159 (39.7%), 103 (25.7%) and 139 (34.7%) at Month 12. Patients in CR and PR had significantly lower (better) scores on all WPAI:UC domains than did NR patients at both time points ($P < 0.05$ and $P < 0.001$, respectively). Further, at both induction and maintenance endpoints, WPAI:UC domain scores did not statistically differ between CR and PR patients (all $P \geq 0.415$). Estimated parameters and means from the RMMM indicated that patients in CR or PR showed similarly larger improvements and better maintenance of improvements in OWI over time than did NR patients.

Conclusion: Patients whose UC was in CR or PR following both short-term and long-term daily treatment with multimatrix mesalazine exhibited better WRO than NR patients. Furthermore, WRO was equivalent for patients in CR and PR groups, indicating that improvement and maintenance of WRO for patients who achieved PR was just as good as for those in CR.

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P0366 MILD TO MODERATELY ACTIVE ULCERATIVE PROCTITIS: ORAL MESALAZINE MMX PLUS RECTAL MESALAZINE VS RECTAL MESALAZINE ALONE

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Introduction: Mesalazine (MSZ) 1 g suppository once daily is the preferred initial therapy for the treatment of mild to moderately active ulcerative proctitis (UP). Whether the use of oral mesalazine MMX (MMX) together with rectal MSZ improves the clinical outcome of UP is not known.

Aims & Methods: The aim is to evaluate the efficacy of combination therapy with MSZ suppository plus MMX vs rectal MSZ alone in inducing remission of UP. Secondary endpoint was to assess whether combined therapy had any effect on the extension of the inflammation at 6 months follow-up compared with rectal MSZ alone.

We retrospectively studied 156 consecutive patients (pts) (81males, 75 females) with mild to moderately active UP admitted to our IBD Units, from 2010 to 2014. Forty pts (26%) were excluded from the analysis because they had been treated with oral MSZ other than MMX. Therefore 55 (35%) pts treated with MMX 1200 mg/die plus MSZ suppositories 1g/die and 61 (39%) pts treated with MSZ 1 g suppositories/die alone were included in the study. Patients on combined therapy, stopped daily MSZ suppository after two months and continued MMX 1200 mg/die plus MSZ suppository every other day up to 6 months. Patients treated with MSZ suppository alone, stopped daily rectal MSZ after 2 months and continued with MSZ suppository every other day up to 6 months. After 2 months pts were clinically evaluated according to the partial Mayo score. After 6 months follow-up, pts underwent control endoscopy. Significance of differences was assessed by X_2 test.

Results: After two months follow-up, 46 pts (84%) on combined therapy and 49 pts (80%) on rectal MSZ alone reached clinical remission. At 6 months follow-up, proximal extension of the inflammation both at the endoscopy and histology level was observed in 8/55 (14%) pts on combined therapy and in 18/61(29%) pts on rectal MSZ alone ($p < 0.05$).

Conclusion: 1) Combined therapy with oral MMX plus rectal MSZ or rectal MSZ alone are equally effective in inducing clinical remission in pts with UP, however, 2) combined oral MMX plus rectal MSZ is associated with a significant reduction in the proximal extension of the disease compared with rectal MSZ alone.

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Disclosure of Interest: None declared

P0367 EFFICACY, SAFETY AND LONG-TERM OUTCOME OF ENDOSCOPIC DILATION THERAPY FOR STRICTURING CROHN'S DISEASE - A COMBINED ANALYSIS OF 3252 ENDOSCOPIC BALLOON DILATIONS PROCEDURES

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Introduction: Intestinal strictures are a frequent complication of Crohn's disease (CD), leading to intestinal obstruction. Endoscopic balloon dilation (EBD) represents a widely used approach for the management of intestinal stenosis in CD patients. Available evidence in this area, however, is limited. We therefore performed a combined efficacy and safety analysis based on all studies of endoscopic balloon dilation available in the literature.

Aims & Methods: A systematic literature search regarding EBD in CD was performed. Available technical and clinical variables were extracted from studies with > 15 patients for a descriptive pooled data analysis. Weighted efficacy averages were calculated for sub-groups. Study authors were contacted to provide individual patient data. Frailty models were used with study as a random effect for heterogeneity between studies. An automated stepwise variable selection method was used to choose variables in the multivariable models. In addition, generalized linear mixed models were used to assess associations. Binomial distribution with log link was used for all the other outcomes.

Results: 34 studies with a total of 1500 CD patients and 3252 performed dilation procedures were included. 82.7% of intestinal strictures were located in the ileum and 66.4% were anastomotic strictures (33.6% *de novo*, respectively). Technical success rate was 89.9% of all patients, resulting in clinical efficacy in 79.5% of patients. Major complications, defined as perforation, bleeding or dilation-related surgery, occurred in 2.6% of all procedures. During a mean follow-up period of 39.8 months, 48.6% of patients reported symptomatic recurrence, while 30.2% of all patients had to undergo surgical intervention. Concomitant therapy with steroid injection and cutting techniques post dilation was associated with a poorer dilation efficacy (all $p < 0.001$).

Multivariate analysis of 676 individual patients from 12 studies identified a 50% higher hazard of re-dilation in CD with *de novo* strictures as compared to anastomotic strictures ($p = 0.014$). Additionally, concomitant therapy with steroid injection doubled the hazard of need for re-dilation ($p = 0.029$). A greater maximum dilation diameter (per 1 mm increase) was found to be associated with a higher likelihood of both, technical success ($p = 0.004$) and scope passing ($p = 0.001$). Finally, every 1 cm increase of stricture length increased the hazard of need for surgery by 8% ($p = 0.008$).

Conclusion: EBD has a high rate of short-term technical and clinical success with substantial long-term efficacy and acceptable complication rates. Main predictors of successful EBD are a greater maximum caliber of dilation and anastomotic stricture. Steroid injection and an increased length of stricture reduced time to surgical intervention. EBD is a valuable alternative to surgery in patients with CD associated strictures.

Disclosure of Interest: None declared

P0368 IN VITRO AND IN VIVO PROPERTIES OF NR11/1943, A NEW CCR9 RECEPTOR ANTAGONIST

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Introduction: Inflammatory bowel disease (IBD) is a chronic inflammatory disorder in which tissue damage and inflammation lead to long-term, often irreversible, impairment of the structure and function of the gastrointestinal tract. Chemokine Receptor 9 (CCR9) is expressed on lymphocytes in the circulation, and is the key chemokine receptor that enables these cells to home to

the small intestine due to the localised expression of its ligand, Chemokine (C-C) Ligand 25 (CCL25). It has been suggested that CCR9 antagonism represents a means to prevent the aberrant immune response in IBD. NR11/1943 has been identified as a promising, small-molecule candidate by a medicinal chemistry programme, aimed at producing an orally-available CCR9 antagonist with a superior pharmacokinetic (PK) profile to vercirnon, a first generation compound of this class.

Aims & Methods: In this study we describe the *in vitro* and *in vivo* properties of a new, orally-available CCR9 antagonist molecule using various calcium-flux and chemotaxis based assays and *in vivo* procedures and models commonly used in the early discovery and development phases of new IBD therapies.

Results: In a number of experiments, studying the interaction between the CCR9 receptor and NR11/1943, inhibitory constants (Ki) were obtained ranging from 6nM to 24nM showing the compound to be a potent antagonist of the receptor. PK data demonstrated that the molecule has an excellent profile, being highly bio-available and with a long half-life in all the species studied. Following BID oral dosing, the molecule also demonstrated efficacy in three different models of colitis in mice (3 mg/kg to 100mg/kg) and rats (30 mg/kg and 120 mg/kg), showing significant protection against DSS- and TNBS-induced weight loss and other adverse effects, especially with respect to faecal consistency and intestinal bleeding.

Conclusion: NR11/1943 is an orally available CCR9 antagonist with a superior pre-clinical PK profile to vercirnon and with suitable pharmacological properties, both *in vitro* and *in vivo*, to allow it to progress towards the clinic.

Disclosure of Interest: S. B. Kalindjian Conflict with: Employee of Norgine, S. Kadnur Conflict with: Contractor to Norgine, R. Fairclough Conflict with: Employee of Norgine, C. Hewson Conflict with: Employee of Norgine, S. Juluri Conflict with: Contractor to Norgine, Z. Mohamed Conflict with: Contractor to Norgine, R. Saxena Conflict with: Contractor to Norgine, J. Aiyar Conflict with: Contractor to Norgine, D. McVey Conflict with: Employee of Norgine

P0369 CROSS-SPECIES TRANSLATABILITY OF NONCLINICAL SAFETY ASSESSMENTS OF A HUMAN INTERLEUKIN-22FC, AN IG FUSION PROTEIN FOR THE POTENTIAL TREATMENT OF INFECTIOUS OR INFLAMMATORY DISEASES

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Introduction: Interleukin 22 (IL22) belongs to the IL10 cytokine family (Ouyang et al. 2011) and binds specifically to the IL22 receptor (IL-22R) heterodimer, expressed on a variety of epithelial tissues (Gurney 2004). Due to its ability to modulate innate immunity via activation of the transcription factor, STAT3, and subsequent regenerative and protective properties (Wolk et al. 2004), IL-22 is thought to have therapeutic potential in treating tissue injury or chronic tissue damage.

Aims & Methods: To assess the pharmacological activity of IL-22 recombinant fusion protein (IL-22Fc) that links the human cytokine IL-22 with the Fc portion of a human immunoglobulin, STAT3 activation was evaluated in primary hepatocytes isolated from human, cynomolgus monkey, minipig, rat, and mouse after incubation with IL-22Fc. The nonclinical safety profile of IL-22Fc was evaluated to establish a safe clinical starting dose for humans in Phase I trials and support clinical intravenous (IV) and/or subcutaneous (SC) treatment regimen. Studies included pilot systemic toxicity studies in mice, rats, and cynomolgus monkeys; and repeat-dose GLP systemic toxicity studies, one in rats and one in cynomolgus monkeys. In addition, a pilot single-dose SC local toxicity study was performed in minipigs; and a tissue cross-reactivity study was conducted ex vivo using human and cynomolgus monkey tissues.

Results: Results demonstrated that all species achieved similar levels of STAT3 phosphorylation but higher concentrations of IL-22Fc and longer incubation times were required to achieve equivalent levels of STAT3 phosphorylation in rat hepatocytes when compared to hepatocytes from other species. Taken together, these results confirmed that the cynomolgus monkey, minipig, rat, and mouse were all appropriate nonclinical species for toxicology studies, and that the rat was not as sensitive to the effects of IL-22Fc as the cynomolgus monkey. Systemically administered IL-22Fc was well tolerated in both cynomolgus monkeys and rats up to highest doses tested. In monkeys, skin reddening with microscopic findings of dose-dependent epidermal hyperplasia or acanthosis, sometimes accompanied by variable increased vascularity in the superficial dermis was observed. In addition, cynomolgus monkeys exhibited transient and dose-dependent increases in acute phase reactants (Sonnenberg et al. 2011), without a concomitant increase in any proinflammatory cytokines or chemokines. Epidermal hyperplasia was also observed in mice, rats and minipigs.

Conclusion: Results from these nonclinical studies demonstrate the cross-species translatability of the biological response in activating the IL-22 pathway as well as the translatability of findings from *in vitro* to *in vivo* systems. The predicted safety risks for IL-22Fc are exaggerated pharmacologic effects of epidermal hyperplasia and a transient increase in acute phase proteins, both of which are considered predictable, manageable, monitorable, and reversible in the clinic.

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P0370 FIRST OBSERVATIONS OF THE USE OF BIOSIMILAR INFLIXIMAB FOR TREATMENT OF ULCERATIVE COLITIS AND CROHN DISEASE IN PAEDIATRIC POPULATION

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Introduction: Biosimilar infliximab (Remisma/Inflectra) was introduced into therapy in European Union and also in Poland at the beginning of 2014. Biosimilar infliximab (BI) was authorised based on preclinical and clinical studies and is considered therapeutically equivalent in terms of safety and efficacy to the reference infliximab.

Aims & Methods: The aim of the study was to present first, to our knowledge, observation on the safety and efficacy of BI in children with ulcerative colitis and Crohn disease. From the beginning of 2014 we start treatment with biosimilar infliximab Remsima (5mg/kg) patient with ulcerative colitis (9 patients) and Crohn disease (16 patients). Patients received BI at weeks 0, 2 and 6. Disease activity (PUCAI/PCDAI) and laboratory values (CRP, ESR, platelet count) were assessed at qualification for the biological treatment and after induction treatment at week 10. Mean and range of clinical values is reported.

Results: Median age of 9 patients with UC was 15 years (range 4.5-17.5). Mean PUCAI before infliximab initiation was 48 (range 5-85). Mean (range) CRP, ESR and platelet count before initiation were 1.95 mg/dL (0.03-8.05), 31 mm (25-38) and $451x10^9$/L ($259-786x10^9$). For 2 patients it was the second course of biological treatment. For 2 from 9 patients treatment was discontinued, in 1 due to lack of response after first dose (disease flare), in second due to allergy reaction during dose 3 infusion. As of April 2014, 6 patients received 3 doses and were evaluated at week 10. After 3 doses of biosimilar infliximab mean PUCAI values decreased to 30 (range 0-65). CRP, ESR and platelet count were 0.6 mg/dL (0.02-1.77), 29 mm (18-65) and $510x10^9$ (236-706), respectively. In the group of patients with Crohn disease (16 patients) median age was 17.7 years (range 3-18). At BI start mean PCDAI was 45 (range 15-65); CRP, ESR, platelet count values were 2.05 mg/dL (0.14-6.92), 30 mm (3-93), $362x10^9$/L ($235-573x10^9$), respectively. Eight out of 16 patients were previously treated with a biologics (7 with reference infliximab, 1 with adalimumab). Time of previous treatment was mean 20 months (6-59) with biologic-free interval of 23 months (10-72). Actual treatment was discontinued in 2 from 16 patients, after first BI dose due to lack of response, accompanied by adverse event in one patient and withdrawal of consent in second patient. As of April 2014, 10 out of 14 patients received all 3 induction doses. For those patients, median initial PCDAI was 47 (15-62.5) and decreased to 6.75 (0-27.5) . Before treatment and at week 10 CRP, ESR and platelet count were 2.8 (0.15-6.92), 35.4 (3-93), $375x10^9$ (235-573) and 0.53 (0.03-2.62), 18 (6-52), $285x10^9$ (228-340), respectively. Adverse events during infusion were observed in 2/16 patients: one allergic reaction leading to treatment discontinuation and one blood pressure rise that resolved after infusion rate lowering.

Conclusion: In this preliminary report BI appears to be safe and efficacious in inducing remission in ulcerative colitis and Crohn disease paediatric patients. No unexpected safety and product quality issues were identified. Further studies with larger patient groups are required.

Disclosure of Interest: None declared

P0371 CORTICOSTEROID DOSE REDUCTION WITH VEDOLIZUMAB TREATMENT OF CROHN'S DISEASE

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Introduction: Corticosteroids (CS) can effectively induce remission of Crohn's disease (CD), but serious side effects prohibit long-term use. Vedolizumab (VDZ) maintenance therapy resulted in a greater percentage of patients (pts) with CS-free remission at week (wk) 52 versus placebo (PBO) in the phase 3 GEMINI 2 study of moderately to severely active CD.[1]

Aims & Methods: In GEMINI 2, pts who responded to VDZ induction therapy at wk 6 were re-randomised to PBO or VDZ for 46 wks. From wk 6 onward, pts with clinical response discontinued CS use. With exploratory and post hoc analyses, we characterised CS dose reductions following VDZ therapy in pts on stable CS doses (≤30 mg/day prednisone or equivalent) at wk 0. Median CS dose over time, change from baseline CS dose, and CS-free status at wk 52 were summarised overall and by anti-tumour necrosis factor (anti-TNF) treatment (naïve or failure) history. Median-based analyses were used since the data were not normally distributed.

Results: At wk 52, numerically similar percentages of VDZ- and PBO-treated pts had reductions from baseline CS dose (**Table**). The median CS dose in either treatment group (VDZ or PBO) at wk 52 was 5 mg/day. Higher percentages of pts (overall and anti-TNF-naïve) had doses ≤7.5 mg/day with VDZ versus PBO (**Table**). In anti-TNF-naïve pts, the median CS dose at wk 52 was 2.7 mg/day with VDZ (vs 5.0 mg/day with PBO). Higher percentages of VDZ-treated pts were CS-free for 90 and 180 days at wk 52 than PBO-treated pts (**Table**).

Conclusion: VDZ therapy was associated with a numerically higher percentage of CS-free pts and a longer duration of being CS-free than PBO. Interpretation of these post hoc analyses, including the degree of dose reduction, is limited by CS discontinuation on study and small sample sizes.

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Abstract number: P0371
Table: CS Dose Reductions at Wk 52

Wk 52 No. of Pts (%)	Anti-TNF-Naïve PBOn = 29[b]	VDZ[a] n = 55[b]	Anti-TNF-Failure PBOn = 33[b]	VDZ[a] n = 68[b]	Overall PBOn = 65[b]	VDZ[a] n = 127[b]
No change in CS dose	6 (21)	8 (15)	7 (21)	20 (29)	14 (22)	28 (22)
CS dose increased	5 (17)	3 (5)	6 (18)	10 (15)	11 (17)	13 (10)
CS dose decreased	18 (62)	44 (80)	20 (61)	38 (56)	40 (62)	86 (68)
By <25%	2 (7)	5 (9)	2 (6)	1 (1)	5 (8)	6 (5)
By 25 to <50%	2 (7)	1 (2)	2 (6)	5 (7)	4 (6)	6 (5)
By 50 to <75%	2 (7)	5 (9)	4 (12)	4 (6)	6 (9)	9 (7)
By 75 to <100%	4 (14)	8 (15)	9 (27)	13 (19)	13 (20)	21 (17)
By 100% (CS-free)	8 (28)	25 (45)	3 (9)	15 (22)	12 (18)	44 (35)
CS-free for 90 days[c]	16 (40)	36 (49)	5 (13)	18 (21)	23 (28)	57 (35)
CS-free for 180 days[c]	12 (30)	34 (46)	4 (11)	17 (20)	18 (22)	53 (33)
Daily CS dose ≤7.5 mg	13 (45)	36 (66)	14 (42)	30 (44)	28 (43)	70 (55)

[a]VDZ every 4 or 8 wks.[b]Pts on CS according to the interactive voice response system (IVRS) at screening and also on steroids for CD at baseline (wk 0).[c]Pts on CS according to the IVRS at screening; anti-TNF-naïve: PBO n = 40, VDZ n = 74; anti-TNF-failure: PBO n = 38, VDZ n = 84; overall: PBO n = 82, VDZ n = 162.

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P0372 CORTICOSTEROID DOSE REDUCTION IN ULCERATIVE COLITIS PATIENTS TREATED WITH VEDOLIZUMAB

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Introduction: Corticosteroids (CS) are effective for the short-term treatment of patients (pts) with ulcerative colitis (UC), but serious side effects prohibit long-term use. In the GEMINI 1 study, a higher percentage of pts with moderately to severely active UC were in CS-free remission at week (wk) 52 with vedolizumab (VDZ) treatment than with placebo (PBO).[1]
Aims & Methods: In GEMINI 1, pts who responded to VDZ induction therapy at wk 6 were re-randomised to PBO or VDZ for 46 wks. From wk 6 onward, pts with clinical response discontinued CS use. We characterised CS dose reductions achieved with VDZ therapy in exploratory and post hoc analyses of pts with baseline (wk 0) CS use (≤30 mg/day prednisone or equivalent). Median CS dose over time, change from baseline CS dose, and CS-free status at wk 52 were summarised overall and by anti-tumour necrosis factor (anti-TNF) treatment (naïve or failure) history.
Results: Of pts with baseline CS use, 74% decreased their CS dose with VDZ treatment (vs 57% with PBO) (**Table**). At wk 52, 56% of VDZ-treated pts were on ≤7.5 mg/day of CS (**Table**), and the median CS dose was 2.5 mg/day for VDZ-treated pts and 10.0 mg/day for PBO. Numerically higher percentages of VDZ-treated pts were CS-free for 90 and 180 days at wk 52 than PBO-treated pts (**Table**). Similar trends were observed in the anti-TNF-naïve and anti-TNF-failure populations.
Conclusion: At wk 52, numerically greater reductions in CS use were achieved with VDZ compared with PBO. VDZ therapy was associated with a numerically higher percentage of CS-free pts and a longer duration of being CS-free than PBO. Interpretation of these post hoc analyses, including the degree of dose reduction, is limited by CS discontinuation on study and small sample sizes.

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Abstract number: P0372
Table: CS Dose Reductions at Wk 52.

Wk 52 No. of Pts (%)	Anti-TNF-Naïve PBOn = 40[b]	VDZ[a] n = 82[b]	Anti-TNF-Failure PBOn = 21[b]	VDZ[a] n = 42[b]	Overall PBOn = 67[b]	VDZ[a] n = 140[b]
No change in CS dose[c]	8 (20)	13 (16)	4 (19)	5 (12)	14 (21)	21 (15)
CS dose increased[c]	8 (20)	4 (5)	5 (24)	2 (5)	14 (21)	10 (7)
CS dose decreased[c]	24 (60)	63 (77)	12 (57)	33 (79)	38 (57)	104 (74)
By <25%	1 (3)	2 (2)	2 (10)	2 (5)	4 (6)	4 (3)
By 25 to <50%	4 (10)	5 (6)	0 (0)	4 (10)	4 (6)	12 (9)
By 50 to <75%	9 (23)	8 (10)	2 (10)	6 (14)	11 (16)	15 (11)
By 75 to <100%	0 (0)	11 (13)	5 (24)	9 (21)	6 (9)	19 (14)
By 100% (CS-free)	10 (25)	37 (45)	3 (14)	12 (29)	13 (19)	54 (39)
CS-free for 90 days[d]	13 (30)	52 (63)	3 (13)	16 (36)	17 (24)	73 (51)
CS-free for 180 days[d]	12 (28)	50 (60)	2 (9)	14 (31)	15 (21)	69 (48)
Daily CS dose ≤7.5 mg[d]	13 (30)	52 (63)	9 (39)	23 (51)	23 (32)	80 (56)

[a]VDZ every 4 or 8 wks.[b]Pts on CS according to the interactive voice response system (IVRS) at screening and also on steroids for UC at baseline (wk 0).[c]Pts with missing data; anti-TNF-naïve: VDZ n = 2 (2%); anti-TNF-failure: VDZ n = 2 (5%); overall: PBO n = 1 (1%), VDZ n = 5 (4%).[d]Pts on CS according to the IVRS at screening; anti-TNF-naïve: PBO n = 43, VDZ n = 83; anti-TNF-failure: PBO n = 23, VDZ n = 45; overall: PBO n = 72, VDZ n = 143.

The clinical study was funded by Millennium Pharmaceuticals, Inc (d|b|a Takeda Pharmaceuticals International Co). Medical writing assistance was provided by inVentiv Medical Communications and supported by Takeda Pharmaceuticals International, Inc.

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P0373 PROGNOSIS OF PATIENTS WITH ULCERATIVE COLITIS IN SUSTAINED REMISSION AFTER THIOPURINES WITHDRAWAL

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Introduction: The ideal length of treatment with thiopurines in ulcerative colitis (UC) patients in sustained remission remains unknown. It is widely accepted that the withdrawal of these drugs is associated with a worse outcome of the disease.

Aims & Methods: The aim of this study is to analyze the clinical outcome after this withdrawal and to identify possible predictors of clinically significant relapse (CSR).

A multicenter, observational and retrospective study was designed. 102 patients with UC who discontinued thiopurines in a situation of sustained free-steroid clinical remission were included. All the patients were followed up until last revision or until CSR (understood as the occurrence of signs and symptoms of UC that required a rescue treatment).

Results: The mean duration of the disease in all patients was 13 +/- 0.61 years, the median time from diagnosis to the start of thiopurines was 48.14 +/- 5.51 months and the mean duration of total treatment with thiopurines was 60.87 +/- 4.89 months. After thiopurines withdrawal, overall CSR was recorded in 32.35% of the patients. The cumulative percentage was 18.88% in the first year, 36.48% in the third year and 43.04% in the fifth year after withdrawal. On multivariate analysis, predictors of relapse were the time from diagnosis of UC until the starting of thiopurines (HR 1.01; 95% CI, 1.01-1.02; $p = 0.039$), the duration of treatment with thiopurines (HR 0.15; 95% CI, 0.03-0.66; $p = 0.013$), the situation of biological remission at withdrawal (HR 0.004; 95% CI, 0.0001-0.14; $p = 0.0021$), the number of relapses before the withdrawal (HR 1.3; 95% CI, 1.01-1.66; $p = 0.029$) and pancolitis (HR 5.01; 95% CI, 1.95-26.43; $p = 0.0277$).

Conclusion: The withdrawal of thiopurines in patients with UC, although in sustained remission, is related to a high relapse rate. Clinical variables such as the extent of the disease, the total duration of treatment or time from diagnosis to the start of thiopurines should be considered before stopping these drugs. Further controlled, randomized and prospective studies with long follow-up periods are required to clarify this issue.

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P0374 CUMULATIVE INCIDENCE OF, RISK FACTORS FOR AND OUTCOME OF DERMATOLOGICAL COMPLICATIONS OF ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASE: A 14-YEAR EXPERIENCE

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Introduction: The broader and prolonged use of anti-tumor necrosis factor (TNF) agents in inflammatory bowel disease (IBD) could expose patients to an increased risk of adverse reactions, including dermatological complications.

Aims & Methods: We assessed the cumulative incidence of anti-TNF-induced cutaneous adverse reactions in IBD patients, their risk factors, their dermatological management and their outcome in a large cohort of IBD patients.

In a single-center observational retrospective study including all consecutive adult IBD patients treated with anti-TNF agent between 2001 and 2014, all patients with dermatological complications under anti-TNF therapy were identified in a well-defined cohort of IBD patients. We conducted a survival analysis to determine the cumulative incidence of dermatological complications and risk factors for developing any dermatological complications, cutaneous infections and psoriasiform lesions. Survival curves were estimated by the Kaplan-Meier method, and we used a Cox proportional hazards model to test the association between parameters and time to each event: any dermatological complication, cutaneous infections, and psoriasis lesions.

Results: Among 583 IBD patients, 176 dermatological complications occurred, involving 20.5% of patients. Median duration of follow-up was 38.2 months (Range: 1-179). Psoriasiform lesions (10.1%; 59/583) and cutaneous infections (11.6%, 68/583) were the most frequently observed, with a cumulative incidence of respectively 28.9% and 17.6% at 10 years. They led to anti-TNF discontinuation respectively in 18.6% and 2.9% of patients. In case of switching to another anti-TNF agent for psoriasiform lesions, recurrence occurred in 57% of patients. Ulcerative colitis was associated with a lower risk of developing cutaneous infections than Crohn's disease (HR 0.25; 95% CI, 0.09-0.68; $p = 0.007$). Higher dosing of infliximab, longer duration of treatment, and maintenance regimen were associated with a higher risk of developing cutaneous infections (respectively $p = 0.01$, $p < 0.001$, and $p = 0.04$). A younger age at time of anti-TNF initiation was associated with a risk of psoriasiform lesions (HR 5.11; 95% CI, 2.43-11.16; $p < 0.001$).

Conclusion: Dermatological complications involve one of 5 patients treated with anti-TNF therapy after a 14-year follow-up. Association of cutaneous infections with higher infliximab dosing, shorter intervals between infliximab infusions, and maintenance regimen suggests a dose-dependent effect. Discontinuation of anti-TNF therapy due to dermatological complications is required in one out of 5 patients with psoriasiform lesions, but specific dermatological treatment allows to continue anti-TNF therapy in half of them.

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P0375 AN EVALUATION OF A PHARMACIST-LED TELEPHONE CLINIC WITH REGARD TO MONITORING, SAFETY AND QUALITY OF SERVICE ON PATIENTS TAKING THIOPURINES FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE (IBD) AND AUTOIMMUNE HEPATITIS (AIH) AT BARNSLEY HOSPITAL NHS

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Introduction: Monitoring of patients on immunomodulators increases the workload of consultants in gastroenterology outpatient clinics. This study evaluates how a clinical pharmacist can improve drug monitoring outcomes, safety and quality of service for patients taking thiopurines for IBD and AIH[1,2]

Aims & Methods: The number of patients seen at the pharmacist-led IBD clinic for the research period of three months was 81. Patients were seen initially once face to face then follow-up by telephone consultation. Three different quantitative forms were designed and validated for the evaluation of the study. The first one evaluated the quality of the service, the second evaluated each blood test

requested in clinic and the third evaluated the overall patient's clinical performance for the research period. The satisfaction questionnaires were posted to them, advising them to return it anonymously.
Results: The number of patients in the study were 81 [(45 Female); median age 46 years; range age [18-74]]. Indications were IBD (n = 75), AIH (n = 6). The questionnaires were posted to each patient (n = 81), 51.8% (n = 42) were returned anonymously with responses. A vast majority found the telephone follow up clinic to be conventient 92.9% (n = 39) and 95.2% (n = 48) were satisfied with the clinic service.
The therapeutic target was not achieved in 39.5% (n = 32) of the patients due to drug intolerance. Consequently, 29.6% (n = 24) of the patients needed a check of the level of thioguanine nucleotides (TGN) for better dose adjustment.[3] The results showed sub-therapeutic TGN levels in 13.6% (n = 11), a high TGN level in 14.8% (n = 12) and 1.2% (n = 1) shows non-adherence to therapy.
The total number of blood tests monitored were 304; 85.5% (n = 260) were scheduled as expected, 12.8% (n = 39) were rescheduled by the pharmacist and 1.6% (n = 2) did not attend so therapy was discontinued. The number of blood tests identified in clinic with white cell counts and neutrophils below lower limit is 6.9% (n = 21) but only 2.5% (n = 2) of the blood tests led the pharmacist to stop therapy and refer back to gastroenterologist.
Conclusion: In conclusion, the pharmacist-led clinic is a safe alternative to traditional clinical monitoring of patients initiated on immunomodulators. It reduces the number of patients who had to discontinue treatment due to myelosuppression, optimises dosage by TGN level, and increases adherence to blood monitoring. It reduces the number of doctor visits due to monitoring and thereby proves to be a cost-effective strategy.

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P0376 AN OPEN-LABEL, PILOT STUDY TO ASSESS FEASIBILITY AND SAFETY OF FECAL MICROBIOTA TRANSPLANTATION IN PATIENTS WITH MILD-MODERATE ULCERATIVE COLITIS: PRELIMINARY RESULTS

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Introduction: Fecal microbiota therapy (FMT) has been successful in treating *Clostridium difficile* (CDI) colitis, while its possible application in the management of inflammatory bowel disease (IBD) remain unclear.
Aims & Methods: We report preliminary results of an open label feasibility trial on fecal microbiota transplantation in mild to moderate ulcerative colitis. Outpatients affected by active ulcerative colitis (UC) (partial Mayo score ≥4 with an endoscopic Mayo score ≥ 1 with no upper limit on Mayo score), negative for *C. difficile* toxin were enrolled. Concomitant medications were admitted if stable 2 weeks before and thought the trial. Enrolled patients underwent to colonoscopy and received three administration of FMT using 200 cc of fecal slurry from an healthy donor proposed by the patient, negative for active infections. Primary outcome was feasibility and safety of FMT in UC. Secondary end points were: clinical remission defined as partial Mayo score ≤ 2 with no subscore ≥ 1 and clinical response, defined as reduction of Mayo score of at least 2 points at week 2, 6, 12; endoscopic remission defined as Mayo score = 0 at week 6. Consecutive patients with similar clinical features, candidates to anti-TNF-a or immunosuppressant, acted as a "real life" controls (standard therapy, ST).
Results: We enrolled 8 patients for FMT group and 7 patients for ST. Baseline characteristics were similar between FMT (6M, 2 F; mean age 37 ± 7 yo) and ST group (5M, 2 F, mean age 37 ± 10 yo): Pancolitis in 47%, left-side colitis in 33%; 80% were on steroids and 5-ASA, 40% on immunemodulators. In FMT group we observed: 1 SAE (kidney stone) and 2 drop out for disease worsening, while in ST group: 1 SAE (cerebral arterial thrombosis), 2 drop out for disease worsening, 1 infusion reaction. Clinical remission and clinical response for FMT and ST group were respectively: 37.5%/50% and 28.6%/28.6% at week 12, 25%/25% and 14.3%/57.1% at week 2, 25%/50% and 42.8%/42.8% at week 6. Endoscopic remission was observed in 33.3% of FMT group of patients while it was not evaluated in ST group.
Conclusion: The proposed protocol for FMT seems to be safe and well-accepted by UC patients. This FMT protocol have a good potential in inducing clinical response in real life mild-moderate UC patients. Further studies are mandatory.
Disclosure of Interest: None declared

P0377 ROLE OF BMI, USE OF IMMUNE SUPPRESSANT AND PHARMACOKINETIC OF INFLIXIMAB-PATHWAY IN DETERMINING PROSPECTIVE AND RETROSPECTIVE RESPONSE TO THE DRUG IN COHORT OF IBD PATIENTS UNDER MAINTENANCE THERAPY WITH INFLIXIMAB

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Introduction: Response to infliximab (IFX) depends on use of immune suppressants and BMI/body fat content. Few informations however exist on how these factors interact with pharmacokinetics of IFX.
Aims & Methods: Assess a possible correlation between BMI, body fat and use of immunosuppressants with serum IFX, TNF-α and ATI before and after drug administration (trough levels, post-infusion levels). Assess a possible correlation between the serum concentrations of IFX, TNF-α and ATI before and after drug administration (trough levels, post-infusion levels) with the prospective and retrospective clinical response. We enrolled 12 Crohn's disease (CD) patients and 12 ulcerative colitis (UC) patients, in maintenance treatment with IFX, for at least 14 weeks. Blood samples were collected from each patient before infusion of the drug (trough levels) and half hour after the end of the infusion (post-infusion levels). Clinical data were registered 2 months before the infusion (for retrospective analisis) and also 2 months following the infusion (prospective analysis). Trough levels and post-infusion levels of infliximab, TNF-α and anti-infliximab (ATI) were measured by ELISA (Immunodiagnostik). Body fat levels were measured by DEXA.
Results: As expected, higher BMI and body fat levels were associated to reduced response to IFX. Higher IFX trough levels correlated to retrospective response to IFX. ATI associated to lower IFX trough levels and also post-infusion levels. BMI and body fat levels correlated to IFX postinfusion levels, suggesting that IFX does not distribute in the adipose tissue. Patients under immunosuppressant display higher IFX post-infusion levels and reduced ATI levels. The ration between IFX trough levels/TNF-α trough levels predicted the response to IFX at 2 months following IFX infusion.
Conclusion: Patients lacking response to IFX have higher values of body fat and BMI, which directly influence IFX post infusion levels, suggesting that the drug does not distribut in adipose tissue. Immunosuppressants also associate to higher IFX post infusion levels but with lower ATI levels. Finally, for the first time, our study showed that the ratio between IFXtrough-levels and TNF-αtrough-levels in serum, predict clinical response to the drug at 2 months. If confirmed in wider population, the last is a good parameter in order to promote a personalized therapy, based on the study of a specific pathogenic pathway.
Disclosure of Interest: None declared

P0378 INFLIXIMAB TROUGH LEVELS AND ANTI-DRUG ANTIBODIES AFTER INDUCTION PREDICT LONG TERM CLINICAL REMISSION IN INFLIXIMAB-TREATED PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The treatment paradigm of Inflammatory Bowel Disease is dramatically changed in the past decades, thanks to the development of biological drugs. However, approximately 40% of primary responder patients to anti-TNF therapy experience a loss of response (LOR) during the first year of treatment. Recently, drugs trough levels (TL) and anti-drug antibodies (ADA) presence were proposed as useful tools in the management of patients who have a LOR. Currently, one of the most important issue in IBD patients on biological therapy is to timely identify patients at risk of anti-TNF therapy failure.
Aims & Methods: The aim of our prospective study was to evaluate TL and ADA presence after Infliximab (IFX) induction and their correlation with clinical activity in a series of patients with Inflammatory Bowel Disease (IBD) followed-up for at least 48 weeks. We included 32 consecutive Inflammatory Bowel Disease patients [20 Crohn's Disease (CD) and 12 Ulcerative Colitis (UC); 17 males, median age 42 years, range 18-69] who underwent IFX therapy and achieved clinical remission after induction (schedule: 5 mg/kg at week 0, 2 and 6). Blood samples were drawn at standardized time points (i.e., 0, 2, 6, and 14 week) before IFX infusion. TL and IFX ADA were measured using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). Disease activity was assessed both at week 14 and week 48 by the Harvey-Bradshaw Index (HBI, remission defined by HBI < 5) in CD patients and by the Mayo score for UC patients (remission defined by Mayo score <2). Also, protein-C reactive and erythrocyte sedimentation rate (ESR) were measured.
Results: During 48 weeks follow-up, 14 patients (43.8%) experienced LOR. We found significantly lower IFX TL after induction in patients who experienced LOR as compared to patients who maintained clinical remission during the follow-up period (0.78 mcg/ml, range 0-14.97 mcg/ml *versus* 10.01 mcg/ml, range 0.00-42.83 mcg/ml; $P = 0.0018$). Moreover, IFX TL were significantly lower in ADA positive patients as compared to ADA negative ones (0 mcg/ml, range 0-9.66 mcg/ml *versus* 11.91 mcg/ml, range 2.00-42.83 mcg/ml;

$P < 0.0001$). Lastly, ADA concentration after induction was significantly higher in relapsers as compared to patients in remission (3.13 U/ml, range 0-30.52 U/ml *versus* 0 U/ml, range 0-16.83 U/ml; $P = 0.02$).
Conclusion: Patients who experienced LOR to IFX mono-therapy during long-term follow-up (48 weeks) had significantly lower IFX TL and higher ADA serum concentrations after IFX induction (i.e., 14 weeks). Therefore, assessment of IFX TL and of ADA serum concentrations after IFX induction can be used as a predictive tool for estimating the long-term clinical response to biological therapy.
Disclosure of Interest: None declared

P0379 GRANULO-MONOCYTES APHERESIS INDUCE TGFβ1 MODULATION IN NEUTROPHILS OF PATIENTS SUFFERING FROM ULCERATIVE COLITIS: A POSSIBLE ROLE OF SOLUBLE HLA-I MOLECULES

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Introduction: Plasmapheresis is used in immune-mediated disease in order to remove humoral factors and, in addition, to modulate cellular immunity. It has been shown that during aphaeretic centrifugation, whole and/or re-folded soluble HLA class I molecules (sHLA-I) bind to the circuit surfaces. Similarly, neutrophils can bind sHLA-I molecules with immunoglobulin-like transcript (ILT) membrane receptors, becoming hereafter sensitive to the immunomodulation of sHLA-I such as transcriptional and post-transcriptional transforming growth factor (TGF)-β_1 modulation. On the other hand, TGFβ signaling plays a major role in the pathogenesis of inflammatory bowel diseases and it is known to directly induce Foxp3 expression. Besides, Foxp3 expression has been reported increased in patients who responded to granulocytes apheresis with remission of clinical symptoms.
Aims & Methods: The aim of this prospective study was to evaluate a possible sHLA-I mediated immunomodulation in granulocytes and monocytes apheresis in ulcerative colitis patients who responded to therapy. We prospectively enrolled a total of 10 patients (4M/6F; mean age 49, range 27-73) who achieved clinical remission with GMA. The GMA sessions (5 cycle/session) were performed using Adacolumn device. Instantly before each single apheresis and immediately after each procedure, neutrophils were analyzed for a possible *in vivo* aftermath of sHLA-I binding with corresponding ligands Ig-like-transcripts. The concentrations of sFasL molecules were determined by double-determinant immunoassay (DDIA) and the concentrations of $TGFb_1$ were determined by double-determinant immunoassays utilizing a commercially available kits.
Results: Between every GMA cycle a significant upregulation of intracytoplasmic $TGF\beta_1$ molecule or $TGF\beta_1$-mRNA was observed in neutrophils and $CD8^+$ T lymphocytes drawn along the apheretic therapeutic treatments. In particular, the greatest mean increase was found after the first and the forth GMA cycles (from +1% to +30%). A significant up-regulation of sFasL and TGFβ1 concentrations in plasma was observed along the procedures. Similarly, the mean difference increases in comparison with previous samples were constantly found raising during scheduled blood sampling for both molecules. In $CD4^+$ T lymphocytes, unable to bind sHLA-I, the aphaeretic procedures never induced $TGF\beta_1$ modulation
Conclusion: Our findings suggest that the immunosuppressive effects following therapeutic apheresis might at least in part depend on activated leukocyte sensitivity to sHLA-I molecule bioactivity.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 09:00–17:00
OTHER LOWER GI DISORDERS I – HALL 7

P0380 PREDICTIVE FACTORS OF IN-HOSPITAL AND SHORT-TERM MORTALITY ISCHEMIC COLITIS

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Introduction: Ischemic colitis is the most common form of intestinal ischemia with a wide spectrum of severity, with possible risk of death.
Aims & Methods: Evaluate predictive factors of in-hospital and short-term mortality, in a cohort of patients with ischemic colitis. Retrospective analysis of ischemic colitis cases diagnosed between 2008 and 2013 in a single center, with assessment of factors at diagnosis associated with in-hospital mortality and at 3 months.
Results: Of the 203 patients included (132 women), 47 (23%) died during the follow-up (median: 16 months). 21 (45%) died during hospitalization and at three months there were 30 deaths (64% of total). In the univariate analysis, higher values of LDH ($p = 0.004$), urea ($p < 0.001$), creatinine ($p = 0.001$) and leukocytes, more days of hospitalization ($p = 0.006$), male gender ($p = 0.006$), atrial fibrillation (AF) ($p = 0.03$), intestinal occlusion ($p < 0.001$), recent intravascular intervention ($p = 0.001$), endoscopic severity ($p = 0.02$) need for surgery ($p < 0.001$) or vasopressor support ($p < 0.001$), parenteral nutrition ($p < 0.001$) or antibiotic use ($p = 0.013$), prophylactic anticoagulation ($p = 0.02$) and hospitalization in intermediate/intensive care (ICU) ($p < 0.001$) were associated with in-hospital mortality. In the multivariate analysis, AF, vasopressor support and ICU admission for in-hospital mortality. These factors have been used for the creation of a risk score that showed high acuity with an area under the curve (ROC) of 0.89 (S = 89%; E = 78% - mortality 32%). At 3 months, the presence of chronic renal failure ($p = 0.002$) and lower values for hemoglobin ($p = 0.006$) at admission were also independently associated with mortality.
Conclusion: Multiple clinical and analytical factors at admission were associated with in-hospital mortality, and the presence of AF, vasopressor support or admission in ICU proved to be independent factors (risk score probability of 32%). The mortality rate at 3 months presented similar risk factors.
Disclosure of Interest: None declared

P0381 ISCHEMIC COLITIS: THE EXPERIENCE OF A REFERRAL TERTIARY CENTER

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Introduction: Ischemic colitis is the main form of intestinal ischemia, especially in the elderly population, it is essential to have an early diagnosis with subsequent treatment.
Aims & Methods: Evaluate the demographics, etiology, clinical manifestations and prognosis of ischemic colitis in a referral tertiary center. Retrospective analysis of patients with ischemic colitis histologically confirmed between 2008 and 2013.
Results: 205 patients included (64% women), mean age of 75 years. Median follow-up time of 16 months, with an overall mortality rate of 22%. The majority of patients was admitted in the emergency department (88%) and presented with rectal bleeding and/or abdominal pain (87%). The main medical problems were HTA (65%), diabetes mellitus (24%), cerebrovascular disease (21%), heart failure (18%), coronary artery disease (17%), renal failure (15%) and atrial fibrillation (10%). The most prevalent medications were antihypertensives, diuretics and aspirin/NSAID. At admission, the majority presented with leukocytosis and renal dysfunction, without anemia. The diagnosis was established by colonoscopy in the majority of cases (87%), with a correlation of 94% with the histology. Urgent surgery was necessary in 11% of cases (due to peritonitis in half of them) and 12% of patients required blood transfusions. The main complication reported was acute kidney injury (10%). 80% underwent antibiotic therapy. The median length of hospital stay was 8 days, with need for intermediate/intensive care in 19% of cases. The in-hospital mortality rate, at 30 days and at 3 months was 9%, 10% and 14%, respectively. The recurrence rate was 6.5%.
Conclusion: We observed a high incidence of ischemic colitis in the elderly females, especially in the presence of cardiovascular risk factors. Colonoscopy was the preferred method of diagnosis. The vast majority recovered after medical support. The in-hospital mortality represents approximately half of the overall mortality.
Disclosure of Interest: None declared

P0382 ENDOSCOPIC BAND LIGATION (EBL) IS SUPERIOR TO ENDOSCOPIC CLIPPING FOR THE TREATMENT OF COLONIC DIVERTICULAR HEMORRHAGE

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Introduction: Colonic diverticular hemorrhage is a common cause of lower gastrointestinal bleedings. However, low detection rate of a responsible diverticulum for bleeding, less than 20%, and high early re-bleeding rate, more than 30%, are clinical problems. Recently, there were several reports of high successful rate of endoscopic band ligation (EBL) for colonic diverticular hemorrhage. Therefore, we retrospectively compared the efficacy of hemostasis for colonic diverticular hemorrhage in our hospital.
Aims & Methods: From April 2012 to March 2015, total 149 cases of 90 patients in whom colonic diverticular hemorrhage was diagnosed or clinically suspected (mean age 73.5 years (41-95 years); male: 66, female: 24) were retrospectively enrolled. Urgent colonoscopy was performed within 24 hours from arrival to our hospital by colonoscopy with a water-jet function. To better identify a responsible diverticulum, a transparent soft hood (Olympus Optical Co, Ltd, Tokyo, Japan) was attached to the tip of the scope. Diverticular hemorrhage was definitely diagnosed when active bleeding from a diverticulum, a visible non-bleeding vessel within a diverticulum, or a densely adherent clot despite vigorous irrigation, was recognized. After identifying a responsible diverticulum a marker clip was placed near the diverticulum. Hemostasis was selected from following three methods; closing an orifice of the responsible diverticulum with clipping device (closing method); clipping a vessel within a diverticulum (clipping method); EBL (Sumitomo Bakelite Co Ltd, Tokyo, Japan) method. Early re-bleeding rates within a week were evaluated.
Results: Colonic diverticular hemorrhage was diagnosed in 55 of 149 cases (36.9%); active bleeding in 46, non-bleeding visible vessels in 4, and a densely adherent clot in 5 cases. Hemostatic treatments were done in 53 of 55 cases; closing method in 20, clipping method in 27, and EBL method in 6. Residual 2 cases could not received hemostatic treatment because of inappropriate cases for endoscopic hemostasis. Respective re-bleeding rates within a week were 11 (55%), 10 (37%), and 0 (0%). There was a significant difference of re-bleeding rate between closing and EBL methods ($p = 0.02$), although no significant difference was found between clipping and EBL methods ($p = 0.145$). There was no significant adverse event related to endoscopic hemostasis. One case refractory to closing method required surgery.
Conclusion: EBL would be safe, effective, and superior to hemoclips for the treatment of colonic diverticular hemorrhage. The hood method is useful to identify the responsible diverticular hemorrhage.
Disclosure of Interest: None declared

P0383 POST-POLYPECTOMY BLEEDING: FACTORS ASSOCIATED AND ROLE OF THIENOPYRIDINES

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Introduction: Limited data exist for clinically significant (that requires transfusion or hospitalization) post-polypectomy bleeding (PPB) risk factors and the role of thienopyridines (ticlopidin, clopidogrel, prasugrel, ticagrelor).

Aims & Methods: To determine factors associated with PPB and if thienopyridines use prior to colonoscopy increases the risk of clinically significant PPB. A case-control study of patients with clinically significant PPB was performed at our Hospital. Information collected included age, gender, uninterrupted assumption (within five days of colonoscopy) of thienopiridines, aspirin, low weight molecular eparine (LWMH), comorbidities, polyp characteristics, and polypectomy technique. The control group consisted of patients matched with the controls for the same characteristics

Results: During the study period (from 2007 to 2014), 15,946 patients underwent colonoscopy with polypectomy at our institutions and 84 patients presented with clinically significant PPB. Three patients were excluded from analysis because of lack of informations about the patient. The remaining 81 patients with removal of 130 polyps (32 immediated bleeding and 49 delayed bleeding) were well matched to 443 patients who had undergone colonoscopy with 855 polypectomies without complications. Uninterrupted thienopyridine use prior to polypectomy was 5% in the bleeding group and 7% in the control group. Mean ± standard deviation dimensions of polyps wiht PPB and in the control group was 18.4 mm ± 15 mm and 7.7 ± 7.9 mm respectively. Median size of polyps removed during thienopyridine assumption was 7.5 mm. According to a multivariate logistic regression analysis that included significant factors from the univariate logistic regression and known risk factors for bleeding, polyps superior than 10 mm (OR 3.6; 95% CI 2.1-6.2; $P < 0.0001$), polyps located in the right colon (OR 2.13; 95% CI 1.3-3.4; $P = 0.003$) aspirin use (OR 7.7; 95% CI 3.2-18.7; $P < 0.0001$) and LWMH use (OR 10.8; 95% CI 5.6-20.7; $P < 0.0001$) were significantly associated with the development of PPB. Polypectomies under thienopyridine showed a positive association without significance (OR 1.4; 95% CI 0.3-7.0; $P = 0.6$) possibly for minor dimensions of the polyps removed. Preventive measures for bleeding were found to be protective for only immediate PPB (OR 3.7; 95% CI 1.4-9.3; $P = 0.005$).

Conclusion: Polypectomies under thienopyridines are safe for polyps less than 10 mm. Polyp ≥10mm, located in the right colon, aspirin or LWMH is associated to PPB while prophylactic clip are protective only for immediate bleeding.

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Disclosure of Interest: None declared

P0384 CAUSES OF HEMATOCHEZIA AND ANTIBIOTIC-ASSICIATED COLITIS IN CHILDREN AND ADOLESCENTS

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Introduction: Diseases causing hematochezia in children are diverse and range from benign to potentially life-threatening. Systematic pediatric data on the causes of hematochezia are scarce. We aimed at elucidating the range of disorders causing hematochezia in children. A second aim was to investigate antibiotic-associated colitis (AAC) presenting with hematochezia, focusing on antibiotic-associated hemorrhagic colitis (AAHC), a recently described entity caused by *Klebsiella* (*K.*) *oxytoca*.

Aims & Methods: Infants, children and adolescents with visible bloody stool were recruited at 5 Austrian pediatric hospitals. Patients were grouped in infants (<1 year), young children (1-5 years), children (6-13 years) and adolescents (≥14 years). As an addition to routine diagnostics a stool culture for *K. oxytoca* was done (API 20E test). Further clinical investigations or therapy were not influenced by the study. We collected data on history, laboratory findings, infectiological investigations, imaging, final diagnosis and clinical course.

Results: We included 221 patients (female n = 102, 46%): 57 infants, 64 young children, 46 children and 54 adolescents. 17 (7.7%) had a positive stool culture for *K. oxytoca*. In 129 (58%) hematochezia was caused by infectious diseases. In 51 (23%) no final diagnosis could be made and hematochezia resolved spontaneously. Thirty (14%) patients underwent endoscopy, which led to a definite diagnosis in 17/30 (57%). 21 (9.5%) were diagnosed with diseases occurring only once or twice within this study. The most common diagnoses in regard to age groups were: Food protein-induced proctocolitis in infants (n = 19, 33%), bacterial enterocolitis (*Campylobacter*/*Salmonella*; n = 34, 53%) in young children and inflammatory bowel disease in children (n = 10, 22%) and adolescents (n = 11, 20%). AAC was diagnosed in 12 (5%) patients: 2 infants with AAHC, 2 young children with *C. difficile*; in the remaining 8/12 (67%) with the clinical diagnosis of AAC no known pathogen was identified.

Conclusion: Hematochezia was caused by infections in the majority of patients. In most patients invasive diagnostic procedures were not necessary. Thus, in children with hematochezia indication for endoscopy should be restrictive, especially in infants and young children. AAC presenting with hematochezia might be caused by pathogens other than *C. difficile* and *K. oxytoca*. AAHC, caused by *K. oxytoca*, was a rare diagnosis in our pediatric cohort.

Disclosure of Interest: None declared

P0385 EFFICACY OF CT DIAGNOSIS OF LOWER GI BLEEDING WITH ISCHEMIC COLITIS

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Introduction: Ischemic colitis (IC) is one of the most frequent causes of sudden bloody bowel discharge, melena. It is generally accepted in Japan to perform emergency colonoscopy (E-CS) for detection of causative lesion of melena, and as necessary, endoscopic treatment for the bleeding from such lesions as diverticulum, tumor etc. However, for IC, such as endoscopic intervention is rarely needed because the bleeding quite often spontaneously ceases. Thus, less invasive modality than CS which is useful only for diagnosis would be much beneficial for IC patients with melena. Edematous swelling of colon wall on CT has been widely accepted as a target sign of IC.

Aims & Methods: In the present study, its diagnostic value for IC was elucidated. 249 patients with a complaint of melena were enrolled and target sign in 177 patients who underwent both CT and CS were analyzed. The Toshiba Aquilion64 (64DAS) CT scanner was used for CT. Scans were acquired with use of 130kVp, 0.5 s/rot and 0.5mmx64 HP53, respectively. Images were retrospectively reconstructed by using a 0.5 mm section index.

Results: Of 177 patients, 94 showed typical sign of IC on CS. Of these 94 patients, 80 were demonstrated to have a target sign on CT (85.1% sensitivity). Of 83 patients who were negative for CS sign, 72 patients were target sign free (86.7%specificity). When the analysis was carried out on only those patients who received CS within 48hrs, sensitivity increased to 92.9%(75/83).

Conclusion: CT at an early stage after the episode of melena showed similar sensitivity and specificity as E-CS for detection of IC. Thus this less invasive modality can be used, replacing E-CS for patients with IC.

Disclosure of Interest: None declared

P0386 THE HISTORY OF COLONIC DIVERTICULAR HEMORRHAGE AND COLONOSCOPIC HEMOSTASIS ARE INDEPENDENT PREDICTORS FOR RECURRENT HEMORRHAGE

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Introduction: Colonic diverticular hemorrhage (CDH) is a common health care problem, and it is reported to occupy 40% of lower gastrointestinal hemorrhage. Although it is often self-limited and eventually ceases spontaneously in up to 70-90% of cases, recurrence of CDH is not so rare and it occurs in about 30%. It has also been reported that once hemostasis was obtained for CDH endoscopically, recurrent hemorrhage significantly decreases (*Jensen* et al. *N Engl J Med 2000*). However, it is not easy to perform colonoscopy urgently, and therefore, narrowing down candidates is necessary who would be more benefited by colonoscopy from the viewpoint of long-term outcome.

Aims & Methods: The aim of this study was to clarify risk factors of recurrent CDH.This was a retrospective cohort study from a tertiary hospital. A total of 265 patients who were diagnosed as CDH from March 2004 to October 2014 were enrolled. CDH was defined as apparent hematochezia in patients with known colonic diverticulum diagnosed by computed tomography, colonoscopy, and/ or barium enema examination without any other causes. We analyzed the association between patients' characteristics (age, gender, history of CDH, arteriosclerotic disease, antiplatelet use, anticoagulant use, to be obtained hemostasis by colonoscopy) and recurrence of CDH using Cox proportional hazards model. The cumulative recurrent curve was plotted using Kaplan-Meier methods.

Results: Of 265 patients, 170 were men and 95 were women, and median age was 75 [IQR 63-83]. The median observation period was 276 [IQR 29-1047]

days. A total of 227 patients underwent colonoscopy while hospitalized, and 22 patients (10%) obtained colonoscopic hemostasis. One patient obtained hemostasis by interventional radiology. The other patients eventually obtained spontaneous hemostasis. Recurrent CDH was seen in 54 patients (20%). Univariate analysis showed significant association of history of CDH and colonoscopic hemostasis with recurrent CDH. Multivariate analysis showed that history of CDH is an independent risk factor for recurrent CDH (OR 2.26 [95%CI 1.15-4.16], p = 0.0192), and obtained colonoscopic hemostasis independently reduces recurrent CDH (OR 0.30 [95%CI 0.05-1.0], p = 0.0492). One year cumulative recurrent hemorrhage rate was 35% in those with history of CDH, whereas 15% in those without (log rank test, p = 0.0047).

Conclusion: History of CDH and colonoscopic hemostasis were independent predictors for recurrent CDH. Although the identification rate of bleeding point remained only 10%, colonoscopic hemostasis could reduce 70% of recurrent hemorrhage. Therefore, patients with past history of CDH should be aggressively considered to undergo urgent colonoscopy, since they are at high risk for recurrent CDH.

Disclosure of Interest: None declared

P0387 DIABETES MELLITUS IS A PREDICTIVE FACTOR OF THE DIVERTICULAR RE-BLEEDING OF THE COLON IN JAPANESE PATIENTS

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Introduction: Diverticular bleeding of the colon occurs in 2-4% of colonic diverticula diseases and it has been reported to be the most common cause of lower gastrointestinal bleedings. In general, the treatment strategy for diverticular bleeding of the colon is endoscopic hemostasis or interventional radiology (IVR) in cases of the colonic diverticula in which bleeding points are able to be detected. However, it is difficult to precisely detect the bleeding point in most of diverticular bleedings by colonoscopy or enhanced computed tomography. There have been few reports regarding the recurrence of diverticular bleeding, and the rate of recurrence of diverticular bleedings was reported from 10.8 to 43.4%. However, the risk factors of recurrent bleedings of colonic diverticula are still unknown. Thus, we assessed the risk factors of recurrent bleedings to estimate the prognosis of the patients with bleeding colonic diverticula.

Aims & Methods: We aimed to investigate the risk factors of diverticular re-bleeding in the colon. Ninety-three patients who were referred to our hospital due to lower gastrointestinal bleeding and were diagnosed as colonic diverticular bleeding between January 2008 and December 2014 were analyzed. The patients with melena or hematochezia who had no other bleeding lesions except for colonic diverticula were diagnosed as diverticular bleeding by colonoscopy. Ninety-three patients were divided into two groups; 38 patients without repeated diverticular bleeding, non-recurrence group; 55 patients requiring more than two hospitalizations due to diverticular bleeding, recurrence group). Patients' backgrounds such as sex, age, comorbidities and use of medicines were compared between the two groups.

Results: Thirty-eight patients (40.9%) (24 men and 14 women; median age, 70.4 ± 11.0 years old) were included in the recurrence group. Antiplatelet or anticoagulant drugs were administered in 14 patients (38.8%), and NSAIDs were administered in 4 patients (10.5%). Ten patients (26.3%) had diabetes mellitus, 3 patients (7.9%) had ischemic heart diseases. On the other hand 55 patients (59.1%) (33 men and 22 women; median age, 73.7 ± 10.5 years old) were included in the non-recurrence group. Antiplatelet or anticoagulant drugs were administered in 17 patients (30.9%), NSAIDs were administered in 3 patients (5.4%). Five patients (9.1%) had diabetes mellitus, 7 patients (12.7%) had ischemic heart diseases. Univariate analysis revealed that the patients with diabetes mellitus significantly harbored higher frequency of diverticular re-bleeding than those without diabetes mellitus ($p = 0.043$). However, there were no significant differences in other factors between the two groups. Multivariate analysis showed that diabetes mellitus was an independent and significant predictor for diverticular re-bleeding of the colon (odds ratio, 3.60; 95% confidence interval, 1.1-11.8; $p = 0.035$).

Conclusion: Patients with diabetes mellitus harbored about a 4-fold higher risk of diverticular re-bleeding compared with patients with other comorbidities. Patients with diabetes mellitus suggested to be carefully observed after initially diverticular bleeding.

Disclosure of Interest: None declared

P0388 ANTITHROMBOTIC AGENTS AND POST-POLYPECTOMY BLEEDING

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Introduction: It is still controversial whether antithrombotic agents, i.e., antiplatelets and anticoagulants, increase post-polypectomy bleeding (PPB).

Aims & Methods: The aim of this study was to elucidate risk factors for PPB including antithrombotic agents.This was a case-control study based on medical records of single center. PPB was defined as bleeding that occurred 6 hours to 10 days after colonoscopic polypectomy and required endoscopic hemostasis. All colonoscopic polypectomies performed between January 2011 and December 2014 were reviewed.

Results: PPB occurred in 29 (3.7%) of 788 polypectomies performed during the period. Four PPB cases required transfusion and no PPB cases required surgery. Any antiplatelets or anticoagulants were prescribed to 210 (26.6%) patients; antiplatelets to 155, anticoagulants to 83 and both to 28 patients. All anticoagulants and antiplatelets except for aspirin or cilostazol in 19 cases were ceased before polypectomy. Anticoagulants were significantly associated with PPB ($P < 0.0001$) while antiplatelets were not. Bridging therapy using intravenous unfractionated heparin was adopted to 73 patients and also significantly correlated with PPB ($P < 0.0001$). None of the followings correlated with PPB; age, gender, polyp location, size, shape (flat vs. sessile vs. pedunculated), histology, number of polyps resected, prophylactic clipping, resection method (polypectomy vs. endoscopic mucosal resection vs. endoscopic submucosal dissection). Thromboembolic event occurred in one patient taking anticoagulant after cessation.

Conclusion: Patients taking anticoagulants have increased risk of PPB, even if anticoagulants are interrupted before polypectomy. Heparin-bridge therapy might be responsible for the increased PPB in patients taking anticoagulants.

Disclosure of Interest: None declared

P0389 COST-EFFECTIVENESS OF ROUTINE SCREENING FOR LYNCH SYNDROME IN COLORECTAL CANCER PATIENTS UP TO 70 YEARS OF AGE

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Introduction: Lynch syndrome (LS) is the most common hereditary cause of colorectal cancer (CRC). Identifying LS carriers among CRC patients is of great importance, since surveillance programs for their affected relatives can reduce CRC morbidity and mortality by 56-70%. However, many LS carriers are still not identified. The aim of this study was to assess the cost-effectiveness of routine molecular screening for LS in CRC patients up to 70 years of age.

Aims & Methods: A population-based series of CRC patients aged ≤70 years was routinely screened for LS by analysis of microsatellite instability, immunohistochemistry and *MLH1* hypermethylation, followed by germline mutation analysis in indicated cases. Effectiveness of screening was expressed in life years gained (LYG), based on the number of LS carriers detected among CRC patients and their relatives. Total costs consisted of LS diagnostics and surveillance, including gynaecological surveillance and prophylactic surgery for female LS carriers. We calculated incremental cost-effectiveness ratios (ICERs) comparing different age cut-offs and comparing age-targeted screening with the revised Bethesda guidelines. One-way sensitivity analyses were performed to test the robustness of ICERs.

Results: Screening among 1117 CRC patients identified 23 LS carriers, of whom 7 were ≤50, 7 were 51-60 and 9 were 61-70 years of age. Additionally, 70 LS carriers were identified among relatives (14, 42 and 14 per age category respectively). Overall, screening amounted to 68.1 LYG or 14.4, 39.1 and 14.6 LYG per age category. Total costs for LS screening and surveillance increased from €232,395 (€11,066 per LS carrier detected) for LS screening among CRC patients ≤50 years of age to €1,056,191 (€11,357 per LS carrier detected) for screening CRC patients ≤70 years of age. ICERs were €12,941/LYG for LS screening in CRC patients ≤60 years compared with ≤50 years and €21,728/LYG for screening CRC patients ≤70 years compared with ≤60 years. The revised Bethesda guidelines identified 17/23 (74%) LS carriers among CRC patients and 53/70 (76%) LS carriers among relatives. The ICER for LS screening in CRC patients ≤70 years of age was €22,485/LYG compared with LS screening according to the revised Bethesda guidelines. The ICERs were most sensitive to the assumed LYG by relatives. All ICERs remained < €30,000/LYG in sensitivity analyses.

Conclusion: Routine LS screening by analysis of microsatellite instability, immunohistochemistry, and *MLH1* hypermethylation in CRC patients up to 70 years of age is a cost-effective strategy according to currently accepted standards, with important clinical benefits for LS carriers among CRC patients and their relatives.

Disclosure of Interest: None declared

P0390 CEA AND CYFRA21-1 IMPROVE THE SPECIFICITY OF A 29-GENE BLOOD-BASED TEST FOR EARLY DETECTION OF COLORECTAL CANCER

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Introduction: An effective and convenient test for colorectal cancer (CRC) screening is needed in order to increase compliance and reduce mortality from CRC. Recent studies[1,2] demonstrate that an effective blood test could be an attractive alternative to increase participation rate to CRC screening. Previously[3] we validated a novel blood test for the detection of CRC and large adenomas based on a 29-gene panel in peripheral blood mononuclear cells.

Aims & Methods: The aim of this study was to investigate how addition of CEA, CYFRA21-1, CA125 and CA19-9, circulating protein tumor biomarkers used in the management of different cancers, could improve accuracy of the 29-gene test.

Subject enrolled in the DGNP-COL-0310 study, a multi-center case-control study previously described[3], were older than 50 years and referred for screening/diagnostic colonoscopy or scheduled for surgical removal of CRC. 371 plasma samples from the Swiss participants, including 118 samples from CRC patients, 103 from patients with adenomas $\geq$1cm and 150 from subjects without colorectal lesions (controls), were used to measure protein concentration on the Architect platform (Abbott Diagnostics). Subjects were assigned to training, validation, and test set, using the same design used to develop the 29-gene classifier. Training and validation set were used to select the most relevant circulating protein tumor markers and to determine a new predictive algorithm combining the protein biomarkers with the existing 29-gene classifier. The test set was used to validate the predictive algorithm on the independent data set.

Results: Among the 4 tested proteins, CEA and CYFRA21-1, alone or in combination, showed the highest predictive accuracy for CRC discrimination and were included in the final predictive algorithm. When validated on an independent test set, including 73 CRC, 42 adenomas and 74 controls, the algorithm showed a specificity of 92% and a sensitivity of 78% for CRC and of 52% for adenoma detection.

Conclusion: The addition of the tumor biomarkers CEA and CYFRA21-1 improved the specificity of our 29-gene algorithm, which increased from 88% to 92%. Sensitivity for CRC and large adenomas increased only slightly. Thus, we confirmed that this blood test could be an effective complement to colonoscopy to increase compliance to CRC screening. The test has now been launched on the Swiss market under the trade name Colox®.

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P0391 NEW HORIZONS IN T1 CANCERS: DIFFERENT METASTATIC RISK PARAMETERS ARE PROBABLY NEEDED FOR CRC SCREENING POPULATIONS

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Introduction: Actually we don't know how long does it takes for a preneoplastic lesion to become a cancer invading the submucosal layer (pT1). We don't know, also, how long a pT1 lesion rest in the submucosal layer before going deeper to reach the muscolaris propria becoming pT2. At present, in these neoplasic lesions hystological parameters alone determine wether a low (7%) or high (35%) risk of metastasis exists[1,2].

Aims & Methods: The aim of this study was to assess the metastatical risk in pT1 lesions diagnosed during routine colonoscopies (RC) in comparison with those found during CRC screening colonoscopies (SC). We retrospectively reviewed the files of 17587 colonscopies (8343 RC and 9244 SC) performed in our Endoscopy Unit from july 2009 to january 2015 and extracted all the pT1 CRC. pT1 patients gone for a strict follow-up: first visit in 6 months, then a visit every year. The schedule was: physiscal examination, CEA marker and colonscopy every year, CT scan and liver Ultrasonograpy every other year.

Results: In 67 months 144 pT1 (80M, 55F) tumors were detected, 115(79.9%) during SC and 29(20.1%) during RC. The median follow-up was 39 months. Overall pT1 prevalence was 115/9244(1.2%) in SC and 29/8343(0.3%) in RC (Pearson $\chi^2 = 43.4$, $p < .0001$). 71(49%) patients undergone for surgery because considered at high metastatic risk, 3 refused. During the follow-up only 5 patients (5/144, 3.4%) presented limphnode metastasis. In high-risk group 2/7 (28%) in RC and 3/61 (4.7%) in SC presented metastatsis (Pearson χ^2, $p = 0.019$). No patient 0/73 with low metastatic risk presented metastsis during follow-up. Population mean age was higher in RC 72 vs 62 ($p < 0.00001$). High risk pT1 were more frequent in SC (53% vs 24%, $p < 0.01$). No differences were found in the two populations for: dimension, tumor grading, deep/extent of invasion, vascular invasion, budding, polypectomy resection margin ($p = ns$). Presence of tumor budding was higher in male (21% 16/77 vs 5% 3/61, $p = 0.006$). Survival curves for metastatic risk shows a non significative difference between SC and RC (Breslow test $\chi^2 = 1.528$, $p = 0.216$; Long Rank Mantel-Cox $\chi^2 = 1.137$, $p = 0.286$).

Conclusion: CRC pT1 are 4 times more frequent in SC than in RC. However, only in the RC group the real risk of limph node metastsis justfy the surgical resection. In the SC one, the present series highlighted a remarkable overtreatment and the pressing need to identify new parameters more strongly associated to limph node metastasis in this kind of patients.

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Disclosure of Interest: None declared

P0392 FIT-BASED COLORECTAL CANCER SCREENING: DO WE NEED TO TAILOR SCREENING FOR MEN AND WOMEN?

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Introduction: Colorectal cancer (CRC) screening programs are implemented worldwide. Many are based on biennial fecal occult blood testing (FOBT). Despite well-known differences between men and women in incidence of CRC and its precursors, screening programs invariably use the same strategy for both genders. In recent years fecal immunochemical tests (FITs) replace guaiac FOBTs. The quantitative nature of FIT allows tailored screening by using different cutoffs. We aimed to evaluate whether different cutoffs should be used in men and women.

Aims & Methods: Participants (50-75 years) in an invitational primary colonoscopy screening program were asked to complete one sample FIT (OC-sensor, Eiken, Japan) before colonoscopy. We determined FIT positivity rates, sensitivity, specificity, detection rate and false-positivity rate in detecting advanced neoplasia (AN) for cutoff levels of 10 (FIT10), 20 (FIT20), 30 (FIT30) and 40 (FIT40) µg Hb/g feces in both men and women, corresponding to 25, 50, 75 and 100 ng Hb/ml feces. A receiver-operating-characteristic (ROC) curve was calculated for both men and women at multiple cutoffs to calculate the highest predictive ability.

Results: In total 1,256 invitees underwent FIT and colonoscopy, 638 men and 618 women, with a median age of 61 years (IQR 56-66) and 60 years (IQR 55-65). The prevalence of AN was 10.6% in men and 8.3% in women. At all FIT cut-offs, men had higher positivity rates than women. These ranged from 10.8% (95% CI 8.6-13.5%) to 3.8% (95% CI 2.5-5.6%) in men, and 8.4% (95% CI 6.5-10.9) to 3.2 (95% CI 2.1-5.0) in women. Sensitivity in men ranged from 40% (95% CI 29-52%) for FIT10 to 25% (95% CI 16-37%) for FIT40, and in women from 35% (95% CI 24-49%) for FIT10 to 22% (95%CI 12-35%) for FIT40. The highest predictive ability was similar for men and women with a maximum AUROC of 0.72, at different thresholds of 30 µg Hb/ml and 20 µg Hb/ml respectively. More advanced neoplasia was found and missed in absolute numbers in men for all cutoffs.

Conclusion: FIT-based CRC screening has a lower sensitivity and specificity for advanced neoplasia in women than in men. However, in absolute numbers more advanced neoplasia was both detected and missed in men compared to women at all cut-offs. When implementing a FIT-based CRC screening program these gender differences should be taken into account when aiming for optimal use of colonoscopy capacity.

Disclosure of Interest: None declared

P0393 HIGH PREVALENCE OF COLORECTAL CANCER IN PATIENTS WITH SERRATED POLYPOSIS SYNDROME: RETROSPECTIVE TWO-CENTER COHORT STUDY

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Introduction: Serrated polyposis syndrome (SPS) is characterized by the presence of multiple serrated polyps (SP) in the colon and may represent a risk for colorectal cancer (CRC). The SPS remains to be mostly unrecognized and not-well understood among other colorectal polyposis. The CRC prevalence and clinicopathological features of SPS are not well established.

Aims & Methods

Aim: To describe clinicopathological features of patients who meet WHO SPS diagnostic criteria and to determine prevalence and predictors of CRC.

Methods: We retrieved records from two teaching Hospitals to detect individuals with high diagnostic suspicion of SPS, between February 2002 and October 2014. Patients who met 2010 WHO SPS diagnostic criteria were included. Clinical and demographic data concerning age, gender, personal and familiar history of CRC, smoking status and surgical history were collected and analyzed. Continuous and categorical variables were reported as median with interquartile ranges (IQR), and percentages, respectively. Univariate analysis determining CRC predictors was performed. A P value < 0.05 was considered to be statistically significant.
Results: In all, 64 patients met WHO diagnostic criteria for SPS;: 33 (51%) fulfilled criteria 1, 29 (45%) criteria 2 and criteria 3 was observed in only 2 (3%) patients. Median age at diagnosis was 57.9 years (IQR, 25-80) and 42 (65%) were female. Nineteen (29.7%) had familiar history of CRC in first-degree relatives. Twenty nine (45%) had smoking history. A total of 220 colonoscopies were performed; an average of two per patient was necessary to confirm SPS diagnosis. Average endoscopic follow-up was 43.7 months. At index colonoscopy, 8 patients (12.5%) had between 5-10 polyps, 19 (29.7%) between 10-20 polyps, 25 (39%) between 20-30 polyps and 12 (18.7%) more than 30 polyps. A total of 659 SP were diagnosed by pathology reports; 193 (29.3%) were sessile serrated adenomas, 372 (56.5%) microvesicular hyperplastic polyps; 85 (12.8%) caliciform or unclassified hyperplastic polyps and 9 (1.4%) were traditional serrated adenomas. Forty-one patients (64%) had at least one conventional adenoma, 19 (29.7%) had at least one advanced adenoma and 32 (50%) had at least one advanced SP. CRC was found at diagnosis or during surveillance in 9 patients (14%). No clinicopathological predictors for CRC were identified in the univariate analysis. Surgery was performed in 12 (18.5%) patients due to polyposis (n = 6), CRC (n = 4) and impossibility of SP endoscopic resection (n = 2).
Conclusion: In this two-center retrospective cohort study we found a high prevalence of CRC in SPS patients. However, we did not find clinical, endoscopic or pathological predictors for CRC. Our data suggests the need for a better detection and surveillance for CRC in SPS patients.
Disclosure of Interest: None declared

P0394 PREVALENCE OF ADVANCED COLORECTAL NEOPLASM IN LIVER TRANSPLANT RECIPIENTS

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Introduction: Liver transplant patients are at high risk of malignancy because of the prolonged immunosuppression for avoiding rejections. The aim of this study was to determine whether the prevalence of advanced colorectal neoplasms increases in liver transplant recipients and to define the appropriate duration for surveillance colonoscopy after liver transplantation.
Aims & Methods: Our study consisted of 348 liver transplant patients who underwent a colonoscopy at Seoul National University Hospital from 1991 to 2012. For each patient, two or more age-and sex-matched controls were identified from a population of asymptomatic individuals.
Results: Eighteen (5.2%) patients had advanced colonic neoplasms, including colorectal cancers (10 patients, 2.9%), after liver transplantation. A case-control study showed that the odds of advanced colonic neoplasms occurring in transplant patients were 3.8 times greater than in the matched healthy controls. Transplant patients 50 years of age or older had a 4.1-fold higher risk of developing advanced neoplasm than did the matched subjects (OR 4.127; 95% CI 1.818-9.369; P = 0.000).
Conclusion: Liver transplant patients are at an increasing risk of developing advanced colorectal neoplasms. Colonoscopy is recommended for patients before and after liver TPL, especially 50 years of age or older.

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Disclosure of Interest: None declared

P0395 IMPACT OF SUBSEQUENT SCREENING EPISODES ON THE POSITIVE PREDICTIVE VALUE FOR ADVANCED NEOPLASIA AND ON THE DISTRIBUTION OF ANATOMIC SUBSITES OF COLORECTAL CANCER: A POPULATION-BASED STUDY ON BEHALF OF THE FRENCH COLORECTAL CANCER SCREENING PROGRAM

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Introduction: The anatomic distribution of advanced colorectal neoplasia is increasingly important for choosing screening strategies and treatment options. We sought to evaluate the impact of repeated screening on the positive predictive value (PPV) for advanced colorectal neoplasia (advanced adenoma, AA, and colorectal cancer, CRC) and their distribution according to anatomic subsite distribution in average-risk adults.
Aims & Methods: The study included 98,031 men and women aged 50-74 who had a positive g-FOBT in 2010 and 2011 and underwent total colonoscopy. The PPV for detection of AA and CRC and the relative risks were determined with log-binomial models, and the distribution of anatomic subsites was estimated according to screening history.
Results: The median age was 61 years (62 years for participants with AA and 64 for those with CCR). The PPV for detection of advanced neoplasia was 24.5%, substantially higher in men than women (30.7% vs 17.7%), and it increased with age. It also fell at all screening episodes after the first. Subsequent screening episodes were associated with an increased RR for proximal AA (RR 1.13, 95%CI 1.16-1.20). Advancing age (RR 1.28, 95%CI 1.19-1.39 for every 10-year increase in age), female gender (RR 1.31, 95%CI 1.19-1.44), and subsequent screening (RR 1.15, 95%CI 1.04-1.27) were significantly and independently associated with detection of proximal adenocarcinoma. The latter was also detected at an advanced stage more often (RR, 1.24, 95%CI: 1.09-1.42). Early invasive adenocarcinoma (stages I and II) was more likely to be detected in a subsequent than an initial screening (RR 1.07, 95%CI 1.01- 1.13).
Conclusion: This study found that subsequent screening episodes using g-FOBT were associated with an increase in the detection rate of proximal AA and CCR, especially among women. The more frequent detection of CCR at an advanced stage in later screenings suggests that some of these tumors were present in earlier screenings. This potential for missed diagnoses on initial screening, together with the more modest increase in the rate of detection of invasive adenocarcinoma at early (and more curable) stages from the first to subsequent screenings, underlines the need to reinforce the population's awareness of the importance of regular consistent screening, even after negative results.
Disclosure of Interest: None declared

P0396 CHARACTERIZING THE INTERPLAY BETWEEN THE WNT SIGNALING PATHWAY AND CD24 IN INTESTINAL TUMORIGENESIS

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Introduction: CD24 is a glycosylphosphatidylinositol-linked protein that functions as an adhesion molecule and is overexpressed at an early stage of CRC (Sagiv et al., 2006). The Wnt/b-catenin signaling pathway plays an important role in CRC carcinogenesis process. A previous publication from our lab indicated that CD24 could affect the tumorigenesis process in Apc^{Min} mice (Naumov et al., 2014); Apc^{Min} mice usually develop anemia (polyp bleeding) and splenomegaly (extra-medulary hematopoiesis).
Aims & Methods: CD24's role might be, partly, through direct interaction/s with components of the Wnt pathway. Apc^{Min} and *CD24* knockout (KO) mice, both on a C57BL/6J genetic background, were crossed to generate double KO transgenic mice. Genotypes were routinely verified by analysis of DNA extracted from tail biopsies. Small and large bowel polyps were counted macroscopically following methylene blue staining and histology was verified microscopically. Colonic polyps were measured and counted using mice colonoscopy. CD24-inducible 293T-Rex cells previously developed in our lab (Shapira et al., 2011) and SW480 CRC cells stably transfected with CD24 (Naumov et al., 2014) were used to study this interaction *in vitro*.
Results: *In vitro* Western blotting analyses showed that expression of CD24 in 293T-Rex cells induced the activation of β-catenin, while down-regulation of CD24 in SW480 cells caused a decrease in the levels of active β-catenin. Depletion of *CD24* alleles in Apc^{Min} mice led to a significant reduction in the number of polyps in the small and large intestine. C57BL6/J mice carrying the Apc^{Min} mutation develop $\sim 24.3 \pm 3.7$ adenomas and several carcinomas in the small intestine by the age of 16 weeks. The $Apc^{Min}/CD24^{+/-}$ mice developed 8 ± 1.4 polyps and $Apc^{Min}/CD24^{-/-}$ (double KO) mice developed $\sim 7 \pm 1.7$ polyps ($p = 0.006$). Colonoscopy shows a significant reduction in the number and size of polyps upon depletion of *CD24* alleles. In the current study the Apc^{Min} displayed severe splenomegaly (355 ± 68 mg) compared to (205 ± 51 mg) in $Apc^{Min}/CD24^{+/-}$ mice and (141 ± 49 mg) in double KO mice similar to WT mice ($p = 0.006$). Hb level was 3.8 ± 2.5 in the Apc^{Min} significantly lower in the double KO mice (8.2 ± 0.9) and the WT ($p = 0.0009$)
Conclusion: CD24 plays a major role in intestinal tumorigenesis. Knocking down even one copy of CD24 almost completely abolished formation in vivo, and prevent anemia and splenomegaly the whole mark of intestinal blood loss seeing in the Apc^{Min}. CD24 interacts with the Wnt pathway by activating β-catenin. 4. Down regulation of CD24 maybe an important aim in the therapy of CRC.

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P0397 IDENTIFICATION OF LONG NON-CODING RNAS (LNCRNA) WITH ALTERED EXPRESSION LEVELS IN COLORECTAL ADENOMA AND CARCINOMA

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Introduction: Among several functions long non-coding RNAs (lncRNA) are known to act as crucial epigenetic regulators of cell proliferation. Their expression level alterations can lead to cancer formation. Identification of lncRNA expression profiles in colorectal adenoma and cancer (CRC) would be beneficial to expand our knowledge of CRC development.
Aims & Methods: This study aimed to identify differentially expressed long non-coding RNAs (lncRNA) in colorectal adenoma and CRC cases. Total RNA was isolated from 94 human colonic biopsy samples (27 CRCs, 29 colonic adenomas, 38 normal donors without evidence of disease) with RNeasy Mini Kit (Qiagen). Expression levels of lncRNAs were analyzed with HGU133Plus2.0 microarrays (Affymetrix). Affymetric probe sets of 2090 lncRNAs already represented on this array type were extracted with non-coding (‚NR'') Refseq IDs. Furthermore, total RNA including miRNAs was isolated from 36 independent biopsy samples (20 CRCs, 9 colonic adenomas, 7 normal donors without evidence of disease) with High Pure miRNA Isolation Kit (Roche) and expression levels of 40.914 non-protein coding transcripts were analyzed by using Human Transcriptome Array 2.0 (Affymetrix). Data were analysed using Expression Console and Transcriptome Analysis Console softwares (Affymetrix).
Results: According to HGU133Plus2.0 microarray results 3 significantly upregulated lncRNAs were identified in adenomas and 4 in CRCs, while 10 significantly downregulated lncRNAs were found in adenomas and 12 in CRC compared to the healthy controls ($p < 0.05$; $-1 \geq \log Fc \geq 1$). On the basis of the Human Transcriptome array results -analyzing broader range of non-coding RNAs- 76 upregulated lncRNAs were detected in adenomas and 154 in CRC, while 65 downregulated lncRNAs were found in adenomas and 122 in CRC compared to the healthy controls ($p < 0.05$; $-2 \geq \log Fc \geq 2$). 100% of the lncRNAs showing significant gene expression alteration on HGU133Plus2.0 arrays showed similar expression alteration tendency on Human Transcriptome arrays in the adenoma vs. normal and 94% in the CRC vs. normal comparisons. Interestingly, on HGU133Plus2.0 arrays 69% and on Human Transcriptome Arrays 73% of lncRNAs upregulated in CRC samples showed significantly elevated expression ($p < 0.05$) already in adenoma samples (e.g. upregulated CRNDE, linc-FAM75A7-18, linc-FAM135A, lincDUSP26-1 and downregulated linc-DCLK3-2, linc-AMN1, linc-SOD3-2, lincFAM55D compared to healthy controls) containing lncRNAs already associated with CRC or other types of cancer.
Conclusion: The identified lncRNAs with significantly altered expression levels can play a central role in the regulation of transcription during colorectal adenoma-carcinoma sequence. Common up- or downregulated lncRNAs in colorectal adenoma and in CRC samples can be the basis of further investigations in order to enhance early detection of the colorectal cancer development.
This study was supported by the National Research, Development and Innovation Office (KMR-12-1-2012-0216 grant).
Disclosure of Interest: None declared

P0398 NOVEL THERAPEUTIC STRATEGY FOR MICRORNA DELIVERY TO COLON CANCER CELLS – A CETUXIMAB-BASED APPROACH

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Introduction: The discovery of the deregulation of microRNA (miRNA) expression in cancer, particularly in colon cancer has demonstrated the potential therapeutic use of miRNAs. However, the biggest obstacle relies in the low miRNA delivery efficiency *in vivo*.
Aims & Methods: In this study, we aimed to develop an efficient strategy for the delivery of miRNAs to colon cancer cells. Cetuximab was used as a delivery and targeting agent.
Cetuximab was FITC-labeled using FluoReporter® FITC Protein Labeling Kit, providing a labeling ratio of ~ 11 (FITC:Cetuximab). Subsequently, we linked anti-FITC-Protamine single chain Fv (scFv) antibody conjugate to the FITC-labeled Cetuximab. Further, miRNAs were loaded onto Protamine moieties, which display high affinity for nucleic acids and have already been demonstrated effective in *in vitro* and *in vivo* delivery of siRNAs to cancer cells. We have tested the effectiveness and specificity of our delivery complex through *in vitro* evaluation of increased levels of miRNA payload in target cells.
Results: Immunofluorescence and flow cytometry results showed that Cetuximab-FITC efficiently binds to HCT116 cells, but not SW620 cells that do not express EGFR. For Cetuximab-FITC above 0.5 nM, all HCT116 cells were FITC-positive, whereas all SW620 cells were FITC-negative, as evaluated by FACS ($p < 0.05$). Further, for Cetuximab-FITC up to 50 nM, only 3% of SW620 cells were FITC-positive, demonstrating the specificity of EGFR targeting by Cetuximab-FITC. Subsequently, we confirmed by ELISA the specific binding of anti-FITC-protamine to Cetuximab-FITC ($p < 0.01$). The concentration of 3 nM Cetuximab-FITC was selected to evaluate the delivery of anti-FITC-protamine scFv at 10:1 ratio (scFV:cetuximab-FITC), and the results show specific delivery to HCT116 cells as evaluated by Western blot. Finally, we confirmed by flow cytometry and RT-PCR the increase and specific delivery of miRNAs into colon cancer cells with the developed delivery tool consisting of cetuximab-FITC:scFV:miRNA ($p < 0.05$).
Conclusion: The great enthusiastic advantage of the development of this delivery tool arises from the combination of the therapeutic agent Cetuximab already in use for colon cancer treatment together with RNA interference technology. The results obtained thus far illustrate the high potential for efficient and specific delivery of miRNAs to cancer cells, and may provide additional and novel therapeutic tools to expand current options in colon cancer management.
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Disclosure of Interest: None declared

P0399 GUT MUCOSAL MICROBIOME ACROSS STAGES OF COLORECTAL CARCINOGENESIS

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Introduction: Sustained gut microbial dysbiosis is a potential risk factor for exacerbating colorectal lesions toward carcinogenesis. However, it remains unclear whether specific members or a consortium of the gut microbes has the potential to explicate observations about tumor progression.
Aims & Methods: To catalogue the taxonomic landscape of microbial communities in colorectal carcinogenesis, we performed 16S rRNA gene sequencing on mucosal biopsies from 61 lesion-free individuals, and on paired biopsies from 47 and 52 individuals with histology-proven adenomas and carcinomas, respectively. Using the DMM models, we partitioned the relative abundance profiles into microbial community types to design tumor-stage analysis of the changes in community types and marker taxa between paired samples. The taxon abundances were also subjected to sparsity-corrected correlation analyses of occurrence relationships using the SparCC algorithm. Finally, we imputed the metagenomic content of mucosal community types associated with the disease-states using the PICRUSt algorithm and HUMAnN pipeline.
Results: We detected five robust community types, which were strongly associated with phenotypes of the colorectal mucosae ($P = 0.00007$). A community type predominated by the potentially pathogenic members of oral microbiome was primarily associated with carcinomas, whereas adenomas were assigned to a community type with high intra-cluster variabilities. Normal control mucosae were more likely to be represented by a community type enriched with members of Clostridia. We confirmed the consistent enrichments of representative taxa by real-time PCR amplification on an independent cohort of comparable size. Disease-stage analysis revealed significant patterns of change in community types at cancerous but not adenomatous sites relative to their adjacent normals. The fold changes of marker taxa were most significant in early-stage CRC. Colorectal niches of cancer- and cancer-adjacents were characterized by a markedly increased number of parasitic relationships. Adenoma-adjacents harboured co-excluding partners underlying early signs of mucosal dysbiosis. By contrast, microbial partners in normal mucosae showed strong mutualistic relationships. Furthermore, both pathological phenotypes of mucosa and the community types strongly distinguished the predicted metabolic potentials of mucosal communities.
Conclusion: Pathogenesis of CRC can be linked to the appearances of pathobiont-like microbial consortia in which protagonists interact with one another. Such polymicrobial signature predicts the statuses of colorectal lesion, the progression of which may be dependent on the processes of microbial community assembly at the mucosal interface. By interrogating the mucosal community ecology across disease-states, we gain deeper understanding of etiological factors in colorectal carcinogenesis by considering complex bacterial driver-passenger interactions.
Disclosure of Interest: None declared

P0400 ASSOCIATION OF COLORECTAL CANCER WITH PATHOGENIC ESCHERICHIA COLI: FOCUS ON MECHANISM USING OPTICAL IMAGING

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Introduction: Colorectal carcinoma (CRC) is a complex association of non neoplastic and tumoral cells and a large amount of microorganisms. *E. coli* is a consistent commensal of the human gut microbiota but some pathogenic strains have acquired the ability to produce toxins as cyclomodulins that can interfere with eukaryotic cell cycle or directly induce DNA damages. It was observed that cyclomudulin-producing-*E. coli* are more frequently detected on CRC patients and exhibit procarcinogenic properties on murine models (HCT116 xenograft, AOM/DSS; APCmin/+).
Aims & Methods: Aim of this study was to investigate some molecular or cellular mechanisms related to the infection of epithelial mucosa by cyclomudulin-producing-*E. coli* using optical in vivo imaging (IVIS spectrum; Perkin Elmer). In vivo imaging is an innovative tool for noninvasive, spatiotemporal and quantitative monitoring of carcinogenesis process in mice models. We

choose to evaluate the tumor metabolic activity using a FDG analogue as 2-DG-750 fluorescent probes and inflammation measuring myeloperoxidase (MPO) activity with a bioluminescent inflammation probe. This detection is dependent on reactive oxygen species (ROS) production. Detection and quantitation of these two signals were validated on a xenograft model of human colon adenocarcinoma epithelial cells (HCT-116) in nude mice infected with a cyclomudulin-producing-*E. coli* (11G5) and then tested on the murine CRC susceptibility model, $APC^{min/+}$.

Results: Using the 2-DG-750 probe, we observed a high and specific HCT-116 tumor uptake in correlation with tumoral volume (Pearson correlation factor: 0.9181 $p < 0.05$). Using inflammation probe, we detected a rapid systemic elimination and a strong signal in the HCT116 tumor of the 11G5 infected group 10 minutes post-probe-injection. Quantitation showed a significant increase (+1288%) of luminescent signal in the tumors of the infected group ($p < 0.05$). We confirmed this by enzyme-linked immunosorbent assay (ELISA) on tumor specimens. MPO levels (ng/ml) was significantly higher (1556 ± 313.6 vs 234.6 ± 121.6 $p = 0.001$) in xenograft infected with pathogenic *E.coli*-11G5 strain. Moreover histological examination of tumor samples confirmed the massive infiltration of HCT116-11G5 infected xenograft by neutrophils as compared to uninfected group. These data validated used of inflammation probe and showed that *E.coli* strain infection induced inflammation and ROS production in the tumor. Study of intra-digestive signal on the murine $APC^{min/+}$ models is in progress. Strong signals were co-localized with polyps.

Conclusion: Novel imaging techniques like optical imaging could be a powerful tool in translational cancer research. Bioluminescent approach can be applied to digestive tumor and seems sensitive to noninvasively monitor longitudinal tumor inflammation and oxidative stress using a commercial probe. Here we showed that *E.coli* infection induce inflammation and oxidative stress which could participate on carcinogenesis process. In vivo imaging could be an effective technology to better understood host-pathogen interactions on tumoral development.

Disclosure of Interest: None declared

P0401 EXTRACELLULAR GALECTIN-3 ENHANCES COLON CANCER CELLS MIGRATION AND INVASION RELATED TO DYNAMIC CHANGES OF EPITHELIAL GROWTH FACTOR RECEPTOR

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Introduction: Our previous study showed galectin-3 enhanced the migration of DLD-1 cells through K-Ras-Raf-Erk1/2 pathway, but extracellular galectin-3 on the migration of cancer cells and interaction with epithelial growth factor receptor (EGFR) remained unknown.

Aims & Methods: To clarify the effect of extracellular galectin-3 on the migration and invasion of colon cancer cells and relation with EGFR. Western blotting was used to analysis the secretion of galectin-3, short hairpin ribonucleic acid to stably knockdown the expression of galectin-3, wound healing and trans-well assays to evaluate the migration and invasion of colon cancer cells and immunoprecipitation /immunoblotting and proximity ligation assays for analyzing the interaction between galectin-3 and EGFR.

Results: Caco2 cells secreted more galectin-3 and migrated faster than DLD-1. The migration was inhibited by lactose and neutralizing anti-galectin-3 antibody. DLD-1 cells with knockdown of galectin-3 decreased the migration but restored by recombinant galectin-3. Blocking EGFR by EGFR antibody caused decrease of migration. DLD-1 cells with knockdown of galectin-3 decreased the invasion but recombinant galectin-3 reversed the decrease. An interaction between EGFR and galectin-3 was proven by immunoprecipitation and proximity ligation assays. Addition of recombinant galectin-3 induced an increase in phosphorylated EGFR expression within minutes, and recombinant galectin-3 enhanced entrance of EGFR from cell membrane to cytoplasma, especially under EGF stimulation. Extracellular galectin-3 increased the migration and invasion of colon cancer cells and that was correlated to its interaction with EGFR and internalization of EGFR from cell membrane to cytoplasm.

Conclusion: Targeting galectin-3 might have a synergistic effect on the EGFR targeting therapy.

Disclosure of Interest: None declared

P0403 DETECTION OF COLORECTAL CANCER AND ADVANCED ADENOMAS FOLOWING GFOBT TEST 5-6 YEARS AFTER NORMAL COLONOSCOPY IN COMPARISON TO GFOBT TEST ON THE THIRD AND FOURTH SCREENING ROUND

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Introduction: The French colorectal cancer (CCR) screening program was generalized in 2008 and is based on a biennial fecal occult blood testing (FOBT) proposed to everyone with an average risk for colorectal cancer and aged 50-74 years. Subjects from this population who undergo a normal colonoscopy are invited 5 years later for a biennial FOBT. Our data base contains information about FOBTs performed five years after colonoscopy as well as about several rounds of FOBTs. The test in use till 2015 was guaiac FOBT (gFOBT), Hemoccult II®.

Aims & Methods: Our primary aim was to compare CCR and advanced adenoma (AA) detection rates following gFOBT 5-6 years after normal colonoscopy with those observed on third and fourth rounds of screening with gFOBT. We evaluated data from 46 French districts. The study population was those aged 55-74 years and eligible for screening who had performed a gFOBT from 2008 to 2013 and qualified for one of three groups: subjects with gFOBT preceded by normal colonoscopy (COLO), subjects with gFOBT preceded by two negative gFOBTs (R3) and subjects with gFOBT preceded by three negative gFOBTs (R4). The last group had data from only 11 districts where screening existed for long enough. In R3 and R4, the intervals between all consecutive tests had to be 18-36 months. The interval between colonoscopy and gFOBT had to be 5-6 years.

Results: In total, 38 587 men and 56 957 women were included in the COLO group, 370 975 men and 469 082 women in R3 and 101 994 men and 115 090 women in R4. CCR detection rates for men were 0.7‰ in COLO, 2.0‰ in R3 and 1.6‰ in R4; it was 0.4‰, 0.9‰ and 0.8‰ respectively for women. Among men, AA detection rates were 3.2‰ in COLO, 5.9‰ in R3 and 5.8‰ in R4; it was 1.7‰, 2.6‰ and 2.3‰ respectively for women. Among men, the relative risk (RR) to detect CCR in COLO compared to R3 was 0.36 (95% Confidence Interval (95%CI) 0.25-0.52); it was 0.44 (95%CI 0.30-0.66) compared to R4. Among women, the COLO to R3 RR was 0.40 (95%CI 0.26-0.61) and the COLO to R4 RR was 0.45 (95%CI 0.28-0.72). Among men, the RR to detect AA in COLO compared to R3 was 0.55 (95%CI 0.49-0.66); it was 0.56 (95%CI 0.46-0.68) compared to R4. Among women, the COLO to R3 RR was 0.65 (95%CI 0.53-0.79) and the COLO to R4 RR was 0.74 (95%CI 0.59-0.93).

Conclusion: The risks to discover CCR or AA were lower within the group of the subjects who performed gFOBT five-six years after normal colonoscopy in comparison to those who performed a gFOBT after two or three negative gFOBTs. The observed difference was larger for CCR than AA. While French colorectal cancer screening program is changing with replacement of the guaiac based test by more sensitive fecal immunochemical test (FIT), these results support this evolution. Further analysis would be of great benefit to evaluate how several rounds of screening with high-sensitivity FIT compares to single colonoscopy and what is the number of screening rounds needed to equal colonoscopy. In France the five-year period to reintegrate into screening program subjects with a normal colonoscopy could be discussed and compared to a 10-year interval.

Disclosure of Interest: None declared

P0404 INTRA-TUMORAL (ITB) AND PERI-TUMORAL BUDDING (PTB): PREDICTORS OF TUMOR PROGRESSION, LYMPH NODE AND DISTANT METASTASES IN COLORECTAL CANCER

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Introduction: Tumor budding in colorectal cancer (CRC) is a strong, reproducible and independent prognostic factor. Whereas intra-tumoral budding (ITB) is defined as single tumor cells or a small cluster of up to 5 cells found in the tumor center, peri-tumoral budding (PTB) can be detected at the invasion front of CRC. Until now, a comparison of the clinicopathological impact of ITB and PTB by tumor region has not been performed.

Aims & Methods: The aim of the study was to validate the performance of tumor budding as a marker of tumor progression in all CRC stages independently of the cancer region.

Postoperative resections of 156 surgically treated and well-characterized stage I-IV CRC patients were systematically reviewed according to the latest UICC/AJCC classification. Collected information included patient age, gender, tumor location, TNM stage, L and V stage, tumor grade, histological subtype, perineuronal infiltration, tumor border configuration, mismatch repair status, R classification and information on adjuvant therapy. Tumor budding was optimally visualized by immunohistochemistry using pancytokeratin, a well-established marker in daily diagnostics. ITB was scored using the 1 high-power field (HPF) method to simulate the clinical scenarios in pre-operative biopsies and malignant polyps. A cut-off score of 5 buds/HPF based on Receiver Operating Characteristic (ROC) curves was used to distinguish between high and low-grade budding. Next, PTB was assessed using the 10 HPF method and the ROC based cutoff of 100 buds was identified for categorizing high and low-grade budding in postoperative CRC resections.

Results: ITB (1 HPF) and PTB (10 HPF) were strongly correlated ($r = 0.82$, $p < 0.0001$). PTB was associated with T stage ($p = 0.02$), N stage ($p = 0.04$), TNM stage ($p = 0.04$) and tumor grade ($p = 0.02$), whereas ITB significantly correlated with higher T stage ($p < 0.01$), N stage ($p = 0.03$), distant metastases ($p = 0.02$), L stage ($p < 0.01$), V stage ($p = 0.03$) and tumor border configuration ($p < 0.01$). Combined ITB and PTB scores independently correlated with poor survival outcome (HR (95%CI): 1.02, CI: 1.0002-1.04, $p = 0.03$) when adjusted for TNM-stage and adjuvant therapy.

Conclusion: Tumor budding is a strong adverse prognostic parameter independent of the cancer region (center vs front). The 10HPF/1HPF tumor budding scoring method can be applied in all CRC stages, which may be applicable to clinical scenarios including preoperative biopsies, malignant polyps and stage II CRC.

Disclosure of Interest: None declared

P0405 SERRATED ADENOMA MODEL OF THE COLON

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Introduction: Serrated adenoma is a distinct type of lesion of the colon, with potential to evolve into colorectal cancer through a different molecular pathway than the traditional adenoma-carcinoma sequence.
Aims & Methods: Establish a possibility of creating a model of colon serrated adenoma.
Proposed a novel rat model for SA caused by picrilsulfonic acid administration. 6 Wistar rats weighing 220-250 g received picrilsulfonic acid administrated into the lumen of the common bile duct in a dose of 0.03-0.05 ml, and readministrated 5-10 days after in the same dose. The control group consisted of 5 rats. A sample of colon after 3-4 months under anesthesia was taken. Histopathological examination of the tissues stained with hematoxylin and eosin was carried out.
Results: Histologically the cecum contain polypoid formations extending out of the mucous surface; dilated crypts were presented, glands with irregular outlines parallel to a broad base of muscularis mucosa were located. Crypts were lined by epithelial cells with small nuclei and light eosinophilic cytoplasm, sometimes with mild dysplasia; crypts not contained endocrine cells. The combination aserrated crypts and surface epithelial dysplasia revealed the presence of serrated adenoma.
Conclusion: Proposed model explicitly includes morphological signs of a serrated adenoma and may be used in potential screening strategies for colorectal cancer.
Disclosure of Interest: None declared

P0406 CLINICAL IMPLICATION OF AXIN-2 EXPRESSION IN COLORECTAL CANCER

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Introduction: The Wnt pathway regulates cellular homeostasis and deregulation of this pathway has been implicated in the pathogenesis of many diseases including colorectal (CRC) cancer. The Axin-2 protein plays an important role in the regulation of the stability of the Wnt signaling pathway. Although initially described as a tumor suppressor, recent findings support the presence of a pro-tumorigenic role.
Aims & Methods: The aim of this study is to investigate the association of Axin-2 mRNA and protein expression with clinicopathological parameters and survival in CRC. Fifty seven patients who were diagnosed with adenocarcinoma of the colon and rectum and underwent resection at our surgical department were included in this study. Expression of Axin-2 was investigated using quantitative PCR and immunohistochemical staining.
Results: In most cases Axin-2 immunolocalization was detectable in the cytoplasm as opposed to only one case where it was shown to be expressed in the nucleous. The positive expression rates of Axin-2 mRNA and protein were 51% (29/57) and 33% (19/57), respectively. Statistical analysis showed no association between Axin-2 mRNA/protein expression and patients' clinicopathological parameters and survival.
Conclusion: In the present study Axin-2 mRNA and protein expression failed to provide with significant prognostic information in CRC patients. These findings may reflect the complex tumorigenic role of this marker in CRC. Further studies are required to verify our results.
Disclosure of Interest: None declared

P0407 CLINICAL SIGNIFICANCE OF E-CADHERIN IN COLORECTAL ADENOCARCINOMAS

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Introduction: The epithelial–mesenchymal transition (EMT) represents a fundamentally important process during the embryonic development, but it is also recognized as a critical event in the progression and metastases of many epithelial tumors. E-cadherin is the best-characterized molecular marker of EMT and loss of expression has been linked to poorer prognosis in several cancers. To date, in patients with colorectal cancer (CRC), the correlation between E-cadherin and patient prognosis remains controversial.
Aims & Methods: The aim of this study was to investigate E-cadherin mRNA/protein expression in a series of 57 CRC patients and relate these findings with the patients' clinicopathological features and prognosis. Quantitative PCR and immunohistochemistry analyses were performed to characterize the expression of E-cadherin in CRC tissues.
Results: The positive expression rates of E-cadherin mRNA and protein were 53% (30/57) and 42% (24/57), respectively. E-cadherin immunostaining showed no correlation with the patients' clinicopathological features. There was a trend towards higher mRNA expression levels in patients with well compared to poorly differentiated tumors ($p = 0.09$). Kaplan-Meier survival curves demonstrated that patients with negative E-cadherin mRNA and protein expression, presented a significantly and marginally significantly unfavorable disease-free survival (DFS) time ($p < 0.001$ and $p = 0.05$, respectively). Patients with negative E-cadherin mRNA expression presented also a significantly unfavorable overall survival (OS) time ($p = 0.02$). Multivariable COX regression analysis adjusted for age, gender, tumor location, TNM stage and grade of differentiation, showed that E-cadherin mRNA expression is an independent prognostic factor for OS.
Conclusion: E-cadherin downregulation is an important component of disease progression in CRC patients. Gene expression levels are a strong predictor of OS and DFS.
Disclosure of Interest: None declared

P0408 EXPRESSION AND LOCALIZATION OF β-CATENIN IN COLORECTAL CANCER

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Introduction: Aberrant activation of the Wnt signaling pathway has been implicated as a key regulator of colorectal (CRC) tumorigenesis. β-catenin plays a key role in the signaling output of the Wnt cascade. There are many reports about the significance of β-catenin in CRC, yet correlations with prognosis remain highly variable and contradictory.
Aims & Methods: The aim of this study was to investigate β-catenin expression and its relationship to clinicopathological parameters and prognosis in CRC. Immunohistochemistry analyses were performed to characterize the expression of β-catenin in CRC tissues.
Results: The study included 29 female and 28 male patients with a mean age of 67 ± 10.4 years. Cytoplasmic and focal nuclear accumulation of β-catenin was observed in 88% (50/57) and 25% (14/57) of patients respectively. There was no significant association between β-catenin overexpression in the cytoplasm and the patients' clinicopathological parameters. β-catenin overexpression in the nucleus was associated with advanced N stage ($p = 0.04$). Kaplan-Meier survival curves demonstrated that patients with β-catenin overexpression in the nucleus presented a significantly unfavorable overall survival (OS) time ($p = 0.04$). Multivariable COX regression analysis adjusted for age, gender, tumor location, TNM stage and grade of differentiation, showed that β-catenin overexpression in the nucleus is an independent prognostic factor for OS. There was no significant association between β-catenin overexpression in the cytoplasm and OS.
Conclusion: The protein expression level of nucleus, rather than cytoplasmic β-catenin predicts CRC patients with worse prognosis.
Disclosure of Interest: None declared

P0409 WHICH CRITERIA TO USE TO DIFFERENTIATE BETWEEN SESSILE SERRATED ADENOMA (SSA) FROM MICROVESICULAR HYPERPLASTIC POLYPS – A 5-YEAR RETROSPECTIVE HISTOPATHOLOGICAL STUDY

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Introduction: During the past two decades sessile serrated adenomas (SSA) received considerable attention due to their increased risk of leading to colorectal carcinoma (CRC). CRCs arising from SSA have frequently been associated with interval cancers (those arising after negative colonoscopy). Diagnosis of these lesions can be challenging, as both macroscopic and microscopic features show similarities to microvesicular hyperplastic polyps (MVHP). Since in contrast to SSA, there is almost no malignant potential of MVHP, therefore it is critical to distinguish them from SSA in order to determine the appropriate follow up and prevent interval cancers.
Aims & Methods: The aims of our study were to compare the published histopathological classification criteria currently available in the literature for the diagnosis of SSAs and to use these criteria to examine the reclassification rate of MVHP to SSA. Colorectal polyps diagnosed between 2010 and 2014 at the 1st Department of Pathology and Experimental Cancer Research were searched for samples with descriptions matching serrated lesions. For the diagnosis of SSAs the criteria recommended by Rex et al. were used. The remaining serrated lesions were classified using the WHO 2010 criteria. These lesions were then reanalysed using seven major histopathological classification studies (Aust 2010, Chung 2008, Higuchi 2005, Mohammadi 2011, Rex 2012, WHO 2010, Yao 2011) and reassessed whether they met the diagnostic criteria for the diagnosis of SSA.
Results: A total of 347 serrated colonic polyps were found that included 50 (14.4%) SSAs, 143 (41.2%) MVHPs, 148 (42.7%) goblet cell rich hyperplastic polyps (GCHP) and 6 (1.7%) traditional serrated adenomas (TSAs). A significant difference for SSA diagnosis was noted between the classification studies, with results varying from 100% (Rex 2012, Higuchi 2005, Mohammadi 2011) to 20% (Chung 2008). This difference was also observed in the reclassification

rate of MVHP to SSA: ranging from 15 (10.5%) (Rex 2012) to 2 (1.4%) (Chung 2008) of all MVHPs.
Conclusion: In conclusion, we would like to emphasize the significant difference among studies differentiating colorectal serrated lesions. It seems to be clear that a universal diagnostic criteria based on prospective clinicopathological studies is needed to avoid the underdiagnosis that can result in inadequate surveillance and increased risk of CRC.
Disclosure of Interest: None declared

P0410 WHICH CRITERIA TO USE TO DIAGNOSE TRADITIONAL SERRATED ADENOMA (TSA) AND DIFFERENTIATE FROM CONVENTIONAL ADENOMA – RESULTS FROM A 3-YEAR RETROSPECTIVE HISTOPATHOLOGICAL STUDY

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Introduction: Among the recently described colorectal serrated lesions traditional serrated adenoma (TSA) is the rarest subtype. The morphologic distinction between TSA and conventional adenoma, especially villous/tubulovillous adenoma (VA/TVA), may be difficult, because there is a significant histological overlap between these lesions. According to the literature, there are three characteristic features usually present in TSAs: ectopic crypt foci (ECF), luminal serration and typical cytology with columnar epithelial cells with eosinophilic cytoplasm and elongated, centrally placed nuclei. Currently, TSA diagnosis needs at least two of the three features above with at least one present in 50% of the polyp.
Aims & Methods: The aim of our study was to evaluate the presence of these morphological features in TSAs and TVAs, and define which features are most helpful in distinguishing TSA from TVA. Colorectal polyps diagnosed as TSA ot TVA between 2012 and 2014 at the Flór Ferenc Hospital were retrieved and histologically reassessed by two pathologists.
Results: A total of 115 polyps diagnosed as TSA or TVA were reviewed and 11 polyps were selected and classified as TSA on the basis of the current diagnostic criteria. As a control group, we studied 104 TVAs and determined the same features. Both ECF and typical cytology were seen in 10 of the 11 TSAs (91%), luminal serration was present in 73%. To the extent of more than 50% of the polyp, typical cytology was noted in 7 cases (64%), ECF and luminal serration was seen in 3 TSAs (27%). Of the 104 TVAs, typical cytology was present in 35 cases (34%), ECF was found in 9% and luminal serration was noted in 20%. Typical cytological features were seen only in 3 TVAs (3%) to the extent of more than 50% of the adenoma. Luminal serration in more than half of the specimen was seen only in one TVA. The presence of all three morphological features simultaneously was observed in 6 of the 11 TSAs (55%), and only in 3 of the 104 TVAs (3%). Two TVAs showed typical TSA-like patterns to a considerable degree.
Conclusion: In conclusion, ECF proved to be the most helpful morphological feature regarding the diagnosis of TSA, although it is not specific to TSA and is not seen in every case of TSA. Luminal serration and TSA-like cytology are frequently present in TVAs, but they are only visible in extreme cases in more than 50% of the adenoma. Some polyps show a mixed morphology, with TSA-like and conventional adenoma-like areas. These cases may be regarded as mixed polyps.
Disclosure of Interest: None declared

P0411 1H HR NMR SPECTROSCOPY OF FECAL EXTRACTS ENABLES DETECTION OF ADVANCED COLORECTAL NEOPLASIA

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Introduction: Colorectal cancer (CRC) is a growing cause of mortality in developing countries warranting investigation into its etiopathogenesis and earlier diagnosis. Here, we assessed the value of fecal metabolic phenotype of patients with advanced colorectal neoplasia and controls using ^{1}H-nuclear magnetic resonance (NMR) spectroscopy.
Aims & Methods: Fecal extract samples from 55 patients with advanced colorectal neoplasia and control patients, were evaluated using ^{1}H-nuclear magnetic resonance (NMR) spectroscopy. Unsupervised (principal component analysis) and supervised (orthogonal partial least-squares discriminant analysis OPLS-DA) multivariate analyses were applied to discriminate between samples using MATLAB (v.2013a) and SIMCA-P+ (v.13.0.1) softwares. The 7-fold cross validation, a 1000 permutation testing and determination of the area under the receiver operator characteristics curves (AUROC) were applied for internal validation. Wif-1 methylation levels in stools, serum and urine and seven dominant and subdominant bacterial populations in stools were quantified and correlated to metabolic profile of each patients.
Results: The predictability of the model was 0.507 (Q2Y) and the explained variance was 0.755 (R2Y). The goodness of fit and predictive capability (Q^2) of the ^{1}H-NMR OPLS-DA model remained higher than those of the 1000 permutated models indicating that the model was statistically robust. Patients with advanced colorectal neoplasia disclosed increased signals of four short-chain fatty acids (valerate, acetate, propionate and butyrate) and decreased signals of β-Glucose, glutamine and glutamate. The predictive accuracy of the ^{1}H-NMR OPLS-DA model for predicting advanced colorectal neoplasia (AUROC = 0.94, IC95% [0.84-0.99]) was higher than FOBT (0.71, IC95% [0.56-0.83], p = 0.0001) and the serum and/or urine Wif-1 methylation test (0.81, IC95% [0.68-0.91], p = 0.03). Correlation analysis of the microbiome and metabolome data revealed strong associations between *Faecalibacterium prausnitzii* and *Clostridium leptum* species and butyrate and valerate concentration and inverse correlation between *Faecalibacterium prausnitzii* and glucose.
Conclusion: ^{1}H-NMR spectroscopy of fecal extract samples identified a specific metabolic signature that clearly distinguish patients with advanced colorectal neoplasia from the controls. These preliminary results suggest that urinary metabolomics may have a future potential role in non-invasive colorectal screening program.
Disclosure of Interest: None declared

P0412 IRON DEFICIENCY ANAEMIA; APPROPRIATE SEQUENCE OF ENDOSCOPIC INVESTIGATIONS

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Introduction: Iron deficiency anaemia (IDA) is present in 2-5% of men and postmenopausal women and is a common reason for gastroenterology referral (1, 2). British society of gastroenterology recommends an upper and lower gastrointestinal (GI) endoscopy to rule out pathology including malignant disease (2). Traditionally an oesophago-gastro-duodenoscopy (OGD) is performed first followed by colonoscopy. This retrospective study evaluates the usefulness of this strategy.
Aims & Methods: We analysed our endoscopy database to look for patients who underwent both an OGD and colonoscopy to investigate IDA over a period of one year to 31 December 2014. Further data was collected from the clinical letters and hospital pathology database. Results were evaluated using Microsoft excel.
Results: A total of 204 patients were investigated including 113 (55%) female and 91 (45%) male patients. Among these 20 (10%) patients had upper GI symptoms, 48 (23%) had lower GI symptoms and 6 (3%) had both upper and lower GI symptoms. Remaining 136 (67%) patients were asymptomatic. In the studied group, 93 (46%) had haemoglobin less than 100g/L, 54 (26%) had Haemoglobin 100-109 g/L, 31 (15%) had haemoglobin 110-120 g/L and 26 (13%) had haemoglobin more than 120g/L. Ferritin levels were less than the lab cut off in 158 (78%), less than 50 but above the lab cut off in 26 (13%), between 50 and 100 in 11 (5%) and >100 in 8 (4%). OGD was normal in 108(53%) patients. Gastritis was found in 29 (14%), Large hiatus hernia in 22 (11%), oesophagitis in 14 (7%), gastric polyp in 12 (6%) and other findings were found in 19 (9%) including 1 gastric malignancy. Duodenal biopsies were normal in 178 (87%) and not taken in 22 (11%). Coeliac was diagnosed in 1 (<1%). Colonoscopy results showed normal findings in 81 (40%), diverticulosis in 42 (21%), polyps in 33 (16%), Haemorrhoids in 31 (15%), Malignancy in 17 (8%) and others in 15 (7%). Among those with polyps adenomatous polyps were confirmed on histology in 20 (10%) and hyperplastic in 13 (6%). Caecal intubation rate was an acceptable being 91% (186) with 18 (9%) patients having completion Virtual colonogrpahy (Computerised tomography). Coeliac serology was not checked for 150 (74%). It was negative in 53 (26%) and was positive in 1 (<1%). Importantly the only one patient with gastric malignancy did not have any upper or lower GI symptoms. Among patients with colonic malignancy 3 (18%) patients had lower GI but no upper GI symptoms.
Conclusion: This study showed that 17 (8%) patients had colonic malignancy while only 1 (<1%) had upper GI malignancy. Hence we would recommend colonoscopy as the initial endoscopy procedure instead of an OGD when investigating iron deficiency anaemia both in asymptomatic patents and those who present with lower GI symptoms

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P0413 "SCORE SYSTEM" FOR CARDIOVASCULAR RISK: A TOOL TO SELECT PATIENTS AT HIGH RISK FOR COLORECTAL NEOPLASIA

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Introduction: Cardiovascular (CV) disease and colorectal cancer (CRC) are important health problems worldwide and share several risk factors. Little is known about the risk of colorectal neoplasia (adenomas or CRC) among individuals at different risk for CV disease. European Guidelines on CV disease prevention recommend the SCORE system to assess the total CV risk in apparently healthy persons.
Aims & Methods: To evaluate: 1) the prevalence of colorectal neoplasia in an average CRC risk population according to the individual CV risk, 2) the

relationship between the CV risk and type of colorectal neoplasia (non advanced adenoma, advanced adenoma [AA] and CRC).
Results: 605 patients were included in this study. The mean age was 59.7 ± 11.6 years, and there were 311 men (51.4%). 9.8% of patients were diabetic and 23.8% were smokers. 223 patients (36.9%) had 1 or more colorectal neoplasias. The prevalence of colorectal neoplasia in patients with low CV risk, intermediate CV risk and high/very high CV risk was 8.3% (9/109), 41.6% (126/303) and 45.6% (88/193), respectively ($p < 0.001$). The prevalence of advanced colorectal neoplasia (AA or CRC) was 4.6% (5/109), 24.1% (73/303) and 34.7% (67/193), respectively ($p < 0.001$). In multivariate analyses, the moderate risk group and the high/very high risk group had a significantly increased risk of colorectal neoplasia compared with the low risk group, [Odds Ratio (OR) 5.69 (95% confidence interval (CI), 2.41-13.42)] and [OR 5.62 (95% CI, 1.99-15.89)], respectively, ($p = 0.001$). The moderate risk group and the high/very high risk group had also a significantly increased risk of advanced colorectal neoplasia compared with the low risk group [OR 5.43 (95% CI, 1.86-15.88)] and [OR 8.56 (95% CI, 2.46-29.79)], respectively, ($p = 0.001$). The high/very high risk group had a non-significantly increased risk of advanced colorectal neoplasia compared with the moderate risk group [OR 1.58 (95% CI, 0. 96- 2.60), $p = 0.075$].
Conclusion: The prevalence and risk of overall and advanced colorectal neoplasia increase in parallel with the risk of death due to CV disease. The SCORE system may be used as a predictive risk model of colorectal neoplasia. Hence, patients at increased CV risk may benefit from CRC screening.
Disclosure of Interest: None declared

P0414 IS THE INFORMATION PROVIDED ON HISTOPATHOLOGY REQUEST FORMS FOR COLORECTAL CANCER ADEQUATE?

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Introduction: Surgical pathology depends heavily on the input of clinicians and surgeons. The pathologist's need for adequate clinical information before diagnosis can be made has been highlighted in the past. According to the Royal College of Pathologists' UK guidelines for reporting colorectal cancer, histopathology requests need (1) a diagram of the surgical procedure, (2) if the cancer has been detected as part of the bowel cancer screening programme, (3) the histological type of tumor if known, (4) a history of inflammatory bowel disease/ familial cancer, (5) the pre-operative stage of tumor, (6) any pre-operative therapy has been given, when it finished and its nature, (7) if open, laparoscopic or robotic surgery has been performed, the type and dissection plane of the operation.
Aims & Methods: We aimed to audit the quality of clinical information provided in colorectal cancer resection histology requests for the past 5 years in our hospital.
Data was collected for 500 patients with large bowel cancer resections between 2/12/2009 and 18/11/2014
Results: Of 498 histology request forms, only two had a diagram present (0.4%) and three (0.6%) reported that the tumor was detected in the bowel cancer screening programme. The histological type was reported in 72 out of 496 samples (14.52%) and the presence of IBD or familial cancer was reported in 2 out of 497 (0.4%). The pre-operative stage of tumor was recorded in 27 out of 496 reports (5.4%) and the pre-operative therapy given in 56 out of 496 (11.3%). Finally, the type of surgery and dissection were adequately documented in 221 out of 497 reports (44.5%).
Conclusion: Overall, the quality of reporting of clinical information in histology reports remains suboptimal. This audit identified important areas in which reporting quality needs to be improved.

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P0415 PREDICTIVE FACTORS OF PARTICIPATION IN SURVEILLANCE PATIENTS WITH HIGH-RISK ADENOMAS

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Introduction: A good adherence to surveillance programs of people with high-risk adenomas (AAR) is essential to reduce the incidence of colorectal cancer. Identifying predictors of participation could improve the efficiency of this program, through the implementation of improvement measures.
Aims & Methods
Objective: To evaluate the possible predictors of participation and non-participation in a program of colonoscopy surveillance of individuals with AAR, and to assess the impact of reminder measures.
Methods: Analysis of 627 cases from the population screening program of CCR from Ciutat Vella Sant Martí, who had been recommended to colonoscopy surveillance after 3 years because of having high-risk adenomas (advanced adenoma and / or multiplicity) in baseline colonoscopy performed at the Hospital del mar during the years 2010-2011. Individuals who did not participate received a phone call reminder.
Results: We identified a total of 627 cases, 418 men (66%) with average age 63.6± 5.2 years. After 3 years a colonoscopy surveillance was done in 407 cases (64.9%) and it was completed in 387 cases (95%). The causes of non-performing colonoscopy in 220 cases were: to be performed (scheduled or requested) in 131 (59%) cases, ignorance of the need of control in 26 (11.7%) cases, individual negative in 11 (5%) cases, contraindicated in 3 (1.4%) cases, in 3 cases (1.4%) changed place of living and deaths in 10 (4.5%) cases.
There were no significant differences in participation because of age, sex, toxic habits, place of birth or social status. The use of statins and regular exercise were independently associated with a greater involvement ($p = 0.035$ and $p = 0.007$). With regard to comorbidity, the presence of renal failure and dyslipidemia showed a trend towards greater participation, but not significant ($p = 0.089$ and $p = 0.09$). A phone call was performed in 114 cases, contacted in 86 patients who had not made the follow up colonoscopy (39.1%). This call led to a change of attitude in 45 cases (59.2%), mostly associated with the group that did not made because of ignorance (66%), compared to other reasons ($p = 0.001$). In the group of non-participation because of individual negative it made a change of attitude in 17% of cases.
Conclusion: The most frequent reason for non-participation in colonoscopy surveillance program in individuals with high-risk adenomas is ignorance. A phone call reminder produces a significant impact on their attitude.
Disclosure of Interest: None declared

P0416 PROSPECTIVE MULTICENTER STUDY OF A FLEXIBLE SELF-EXPANDABLE METALLIC STENTS FOR MALIGNANT COLORECTAL OBSTRUCTION IN JAPAN: SHORT-TERM SAFETY AND EFFICACY IN 199 PATIENTS

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Introduction: After endoscopic stenting with self-expandable metallic stent (SEMS) was covered by government medical insurance in Jan. 2012, this procedure is widely adapted in Japan. With an approval of a new flexible SEMS by insurance in July 2013, we conducted a prospective feasibility study of this SMES.
Aims & Methods: Our objectives were to estimate safety and feasibility of a new SEMS placement for malignant colorectal obstruction in general clinical practice in Japan. We conducted a prospective, observational, single-arm and multicenter clinical trial from Oct. 2013 to May. 2014. This study was registered with UMIN Clinical Trial Registry (UMIN000011304). Thirty two facilities consisted of 7 academic and 25 community hospitals participated this study. Ahead of this study, we launched a website (http://colon-stent.com/) and pronounced the standard methods based on previous published data to standardize the maneuver of SEMS placement. Each patient was treated with a Niti-S Enteral Colonic Uncovered Stent, D-type. SEMSs were deployed under fluoroscopy and endoscopy. Technical success was defined as placement of the stent across the entire length of the stricture on the first attempt. Clinical success was defined as a resolution of symptoms and radiological relief of the obstruction within 24h. Patients undergoing the stenting as a bridge to surgery (BTS) were followed until surgery, and incurable patients undergoing palliative treatment (PAL) were followed until death or 12 months, whichever came first. The following conditions were considered to be complications: stent occlusion, insufficient expansion of stent, obstruction of the other gastrointestinal site, stent migration, perforation, tenesmus, abdominal pain, pneumonia and bacteremia. Complications were categorized as early (within 7 days) or late (after 7 days). In this analysis, we estimate the early complications.
Results: We registered 205 patients. Six patients were excluded for analysis, because of loose stenosis with passed by colonoscope (2), benign stricture (1), inability to visualize the tumor (1), fistula (1), and deterioration of respiratory condition during the procedure (1). We enrolled 199 patients for a BTS (112) and PAL (87) indication for a per-protocol analysis (PPA). In PPA, technical and clinical success was 98% (BTS : 99.1%, PAL : 97.7%) and 97% (BTS : 98.2%, PAL : 95.4%). Within 7 days after SEMS placement, the overall complication rate was 4.0% (3.6% BTS, 4.6% PAL), including abdominal pain (1.5%), insufficient expansion (1.5%), stent occlusion (1.0%), obstruction of the other gastrointestinal site (1.0%), stent migration (0.5%), death (0.5%) and pneumonia (0.5%). There was no perforation.
Conclusion: This study demonstrates the feasibility of a new flexible SEMS placement for malignant colorectal obstruction. Within 7days after SEMS placement, the incidence of complications was relatively low as well as no perforation.
Disclosure of Interest: None declared

P0417 TUMOR DIAMETER IS AN EASY AND USEFUL PREDICTOR OF RECURRENCE IN STAGE II COLORECTAL CANCER

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Introduction: Adjuvant chemotherapy for stage II colorectal cancer can generally be administered to high-risk subgroups. The ASCO and ESMO have stated 9 risk factors associated with recurrence of stage II colorectal cancer. The risk factors are defined as patients with ≤ 12 sampled lymph nodes, a T4 lesion, perforation, poorly differentiated histology, vascular invasion, lymphatic vessel invasion, perineural invasion, obstruction, or a high carcinoembrionic antige level. To better identify these patients, we aimed to assess factors that affect recurrence.
Aims & Methods: In our hospital, 432 colon and 96 rectal stage II cancer patients who underwent surgical resection between 2001 and 2011 were divided into recurrence and non-recurrence groups. Age, sex, lymphatic vessel invasion, venous invasion, tumor diameter, tumor depth, histological type, preoperative carcinoembryonic antigen level, number of sampled nodes, adjuvant chemotherapy, morphology, surgical approach, anastomotic leakage, preoperative bowel obstruction, and preoperative perforation were retrospectively compared between the groups.
Results: For colon cancer, multivariate analysis revealed a significant association between tumor diameter ≥ 40 mm and recurrence ($p = 0.039$). For rectal cancer, multivariate analysis revealed that tumor diameter ≥ 50 mm ($p = 0.001$) and ≤ 12 sampled nodes ($p = 0.021$) were associated with recurrence. Tumor diameter in rectal cancer was associated with worse disease-free survival ($p = 0.026$).
Conclusion: Tumor diameter is a significant predictor of recurrence in stage II colorectal cancer. This is an important finding because tumor diameter is easy to evaluate clinically and might help to identify candidates for adjuvant chemotherapy.
Disclosure of Interest: None declared

P0418 CUMULATIVE INCIDENCE OF COLORECTAL NEOPLASIA DURING ENDOSCOPIC SURVEILLANCE IN SERRATED POLYPOSIS SYNDROME (SPS) PATIENTS: A MULTICENTER STUDY

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Introduction: Due to the increased colorectal cancer (CRC) risk in patients with Serrated Polyposis Syndrome (SPS), annual surveillance colonoscopy with polyp removal is currently advised. However, incidence of neoplastic lesions under endoscopic surveillance remains poorly studied and current recommendations are based on low-quality evidence.
Aims & Methods: We aim at describing colorectal neoplasia incidence in SPS under endoscopic surveillance. From March 2013 through April 2015, SPS patients were retrospectively recruited at eighteen Spanish centers. Data were collected from medical, endoscopy and histopathology reports. We included those patients who, after a successful clearing colonoscopy, underwent endoscopic surveillance with an interval up to 3 years. Patients with total colectomy were excluded. Cumulative incidence of neoplasia [CRC, advanced adenomas, serrated polyps (SP) with high-grade dysplasia (HGD), SP ≥10mm, proximal SP and proximal sessile serrated adenomas (SSP)] was calculated by Kaplan-Meier survival analysis. Advanced SP was defined as ≥10 mm and/or SP with HGD and/or proximal SP.
Results: In 158 SPS patients with a median follow-up time of 25.6 months (range: 6.4-129.1) a total of 321 surveillance colonoscopies were performed (median: 2, range: 1-7). Mean age at SPS diagnosis was 55.5 years (SD: 10.0) and 71 (44.9%) were female. Median time between procedures was 13.7 months (range: 6.0-35.8). Four invasive CRC were detected during surveillance (3-year cumulative risk: 3.0%). Three-year cumulative incidence of colorectal polyps was as follows: advanced adenomas, 12.4%; SP with HGD, 0.9%; SP ≥10mm, 32.5%; proximal SP, 72.8%; proximal SSP, 30.8%. The cumulative risk of advanced SP under surveillance was 74.3% and 87.9% at 3 and 5 years, respectively. During follow-up, 10 (6.3%) patients were referred for surgery due to an invasive CRC (n = 4, 2.5%) or severe polyposis (n = 6, 3.8%).
Conclusion: Whereas SPS patients under endoscopic surveillance show a considerable risk of polyp recurrence, the majority of them can be managed endoscopically. Cumulative risk of CRC under close endoscopic surveillance seems to be low. Further studies are needed to define high-risk patients in order to tailor surveillance strategy.
Disclosure of Interest: None declared

P0419 ENDOSCOPIC TREATMENT ALONE OR COMPLEMENTARY SURGERY FOR T1 COLORECTAL CANCER – IS THERE STILL ROOM FOR OPTIMIZING CURATIVE RESSECTION CRITERIA?

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Introduction: Up to 9% of colorectal polyps may conceal an adenocarcinoma with submucosal involvement (Malignant Polyp). Careful surveillance or complementary surgery after endoscopic are accepted treatment strategies. Identifying high-risk patients remains challenging, as oncologic results are a priority while unnecessary surgery should be avoided
Aims & Methods: Our objective was to evaluate oncologic results of endoscopic excision of T1 colorectal with or without complementary surgery.
A total of 121 patients were included between 2003-2007 and 2010-2014 (male patients – 74.4%; average age – 68.5 ± 10.6 years; follow-up: 30 ± 20 months). Clinical, endoscopic and histological features were analyzed. Unfavorable outcome was defined as residual lesion after endoscopic excision, regional or distant metastasis, recurrence or disease-related deaths.
Results: All 121 identified lesions were subject to endoscopic treatment. About 43.4% (53/121) of those were submitted to surgery as well. The most relevant criteria for surgical referral were the presence of lymphatic/vascular invasion ($p = 0.001$), involved margins ($p = 0.014$) and being under 65 years-old ($p = 0.02$). Residual cancer cells were identified in only 12.2% of surgical specimens (7/53) and 10.7% of patients had an unfavorable outcome. Univariate analysis revealed that incomplete or piecemeal endoscopic excision ($p = 0.046$), free margin < 1 mm ($p = 0.028$) and the need for surgical treatment ($p = 0.012$) are associated with an unfavorable prognosis.
There was no significant difference in procedure-related complications between the two groups (surgery *vs* endoscopy alone), with one death due to perforation during an endoscopic procedure.
Conclusion: Overall, we can affirm that the treatment of these lesions is safe and efficacious. However, the presence of incomplete endoscopic excision, positive margins and the need of complementary surgery is associated with worse prognosis. The large majority of surgical specimens had no residual cancerous lesion, suggesting that criteria for referral should be improved in order to avoid unnecessary surgery.
Disclosure of Interest: None declared

P0420 EASY AND DIFFICULT COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): PROSPECTIVE STUDY TO SAFELY SPEED UP WESTERN EXPERIENCE

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Introduction: Endoscopic submucosal dissection (ESD) achieves significantly higher en bloc and R0 resection rates than endoscopic mucosal resection (EMR) and represents the best technique to achieve the curative resection of gastrointestinal superficial neoplasms. Although a level of competence can be achieved in the Western world through a stepwise training, it is unclear if it is sufficient to safely adopt ESD for colorectal lesions.
Aims & Methods: Aim was to identify pre-operative patient and lesion features prognostic of successful ESD. A prospective single center study conducted by an endoscopist who achieved an initial level of competence in colorectal ESD. Inclusion criteria were: colorectal neoplasms either ≥15 or ≥20 mm associated or not to a scar, respectively; no features of SM-deep invasion (pit pattern V associated with a demarcation area). ESD was performed by the standard technique without expert supervision. The multivariate analysis was used to identify prognostic variables of successful ESD (en bloc resection). The following variables were evaluated: patient age and sex; location in different colorectal segments; location on fold; morphology; size (cm2); nodularity (>20 mm); scar of a previous resection; endoscopist experience.
Results: From March 2010 to July 2014, ESD was attempted in 106 patients (mean age 66; females 43%) for 114 lesions (median size 10 cm^2, range 1-85). Lesions were 85 (75%) in the colon, 29 (25%) in the rectum; LST-G 70 (61%), LST-NG 35 (31%), Is 9 (8%); with scar 11 (10%) and a nodule in 27 (24%).
En bloc, R0, and curative resection rates were achieved in: 92 (81%), 90 (79%), 86 (75%). SM invasion was diagnosed in 13 (11%). Perforation occurred in 5

Abstract number: P0423
Comparison between EMR-C and conventional EMR, EMR-C and ESD for all rectal neuroendocrine tumors.

Number of lesions	EMR-C (n = 34)	EMR (n = 56)	*p*-value(EMR-C Vs. EMR)	ESD(n = 32)	*p*-value(EMR-C Vs. ESD)
Lesion size, mean ± S.D. (range), mm	5.3 ± 1.6 (2–8)	5.0 ± 1.8 (2–13)	0.354	9.1 ± 2.2 (6–14)	< 0.001
En bloc resection, n (%)	34 (100)	56 (100)	NA	32 (100)	NA
Procedure time, mean ± S.D., minutes	4.2 ± 2.0	2.1 ± 1.2	0.002	19.8 ± 11.3	0.002
Histologic complete resection, n (%)	32 (94.1)	43 (76.8)	0.032	30 (93.8)	> 0.999
Intraprocedural bleeding, n (%)	3 (8.8)	0	0.051	4 (12.5)	0.705
Postprocedural bleeding, n (%)	1 (2.9)	1 (1.8)	> 0.999	1 (3.1)	> 0.999
Perforation, n (%)	0	0	NA	0	NA

(4%) without precluding a successful ESD in 3. Prognostic variables of successful ESD in colon at the multivariate analysis are reported in the Table; no significant variables were identified for rectal ESD.

	OR (95% CI)	P =
Age	1.11 (1.01-1.23)	0.037
Location in fixed looping segments	0.14 (0.02-0.78)	0.025
Size diameter > 40 mm	0.08 (0.01-0.46)	0.005
Scar presence	0.02 (0.01-0.33)	0.007

Conclusion: A level of competence in colorectal ESD is not sufficient for a widespread adoption of ESD in the colon. Superficial neoplasms at a very high level of difficulty for ESD are colonic either located in the cecum or flexures, larger than 40 mm, and associated with a scar. Western endoscopists without expert supervision should avoid ESD of very difficult lesions until an expertise level has been achieved.
Disclosure of Interest: None declared

P0421 THE THERAPEUTIC EFFECT OF IRREVERSIBLE ELECTROPORATION ABLATION IN MOUSE MODEL OF COLORECTAL CANCER

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Introduction: Irreversible electroporation (IRE) is a promising novel technique for the ablation of tumors. IRE has an advantage over other ablation techniques in its mechanism to remove undesired cells by affecting the cell membrane without thermally destructing blood vessels, nerves and the surrounding tissues. Studies regarding the clinical application of IRE have been performed in humans, as well as in animals, for organs such as the liver, kidney, prostate, etc. and IRE is now accepted as a novel anti-cancer ablation modality.
Aims & Methods: The aim of this study was to evaluate the therapeutic effect of IRE in mouse model of colorectal cancer for the first time. The Caco2 cells (ATCC) were cultured in petri-dishes. Male nude mice (Immunodeficient (CAnN.Cg-Foxn1 nu/CrljBgi) 6 weeks old, Orient inc., Korea) were introduced. Caco2 cells were each visually injected at 1.0 x 10^7 cells/ml into both flakes (one for control, the other for IRE). We performed in vivo IRE procedures in the tumors of nude mouse model. Electrical pulses were applied to the tumor of nude mouse using a DC generator at 1∼2kV/cm amplitude, 20∼50 pulses, 100 < length, with 1mm separation between two needle type electrodes. We analyzed the tissues with H&E staining and TUNEL assay immediately afterwards, and then 10 hours, 24 hours.
Results: All mice were preserved during the experiment without significant complications. There was complete cell death within the IRE lesions without intervening live cells. Variable nucleic changes-pyknosis and karyohexis, and vacuolar degeneration were observed only within the IRE lesions. The framework of extracellular matrix and blood vessels were not affected by IRE. The apoptotic area and signals were increased in IRE groups comparing control groups in tunnel assay.
Conclusion: The present study demonstrated that IRE ablated colon cancer tissue very effectively through the induction of cellular apoptosis. This study suggests that IRE is the potential use of IRE in gastrointestinal cancer patients.
Disclosure of Interest: None declared

P0422 THE EFFECT OF HMG-COA REDUCTASE INHIBITOR ON NF-E2-RELATED FACTOR 2 (NRF2) ACTIVATION IN COLON CANCER CELLS

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Introduction: Statin has been ascribed not only to their cholesterol lowering effect but also to their pleiotropic actions including anti-inflammatory and anti-oxidant effects as well as anti-neoplastic effect. Nrf2 (NF-E2-related factor 2) is a transcription factor that control the transcriptional response of cells to oxidative stress. There are little known how statins affect activation of Nrf2 and Nrf2 signaling pathway in colon cancer cells.
Aims & Methods: We investigated the effect of simvastatin on expression of Nrf2 and nuclear translocation of Nrf2 in two colon cancer cell lines, HT-29 and HCT 116 by cell proliferation assay, western blotting and immunocytochemical analysis. We also investigated which signal cascade such as ERK or PI3K pathway control nrf2 activation and whether simvastatin affects induction of antioxidant enzymes (heme oxygenase-1 (HO-1), NAD(P)H: quinine oxidoreductase 1 (NQO1), γ-glutamate-cysteine ligase catalytic subunit (GCLC)).
Results: We demonstrated simvastatin induced dose-dependent upregulation of Nrf2 expression and anti-oxidant enzymes (HO-1, NQO1, and GCLC) in HT-29 and HCT 116 cells. We demonstrated that simvastatin stimulated Nrf2 nuclear translocation. In addition, PI3K/Akt inhibitor (LY294002) and ERK inhibitor (PD98059) blocked simvastatin induced Nrf2 and HO-1 expression in both HT-29 and HCT 116 cells.
Conclusion: In this study, we show that simvastatin induces Nrf2 activation and nuclear translocation of Nrf2 and expression of anti-oxidant enzymes via ERK and PI3K/Akt pathway in colon cancer cells.
Disclosure of Interest: None declared

P0423 CAP-ASSISTED ENDOSCOPIC MUCOSAL RESECTION FOR RECTAL NEUROENDOCRINE TUMORS: COMPARISONS WITH CONVENTIONAL ENDOSCOPIC MUCOSAL RESECTION AND ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: The incidence of rectal neuroendocrine tumors (NETs) is increasing, and most rectal neuroendocrine tumors with a size < 15 mm can be treated endoscopically. Given that almost all rectal NETs involve the submucosal layer or deeper layers of the rectal wall, conventional endoscopic mucosal resection (EMR) may not be suitable for achieving high en bloc and histologic complete resection. Cap-assisted endoscopic mucosal resection (EMR-C) was suggested as an effective treatment for rectal NETs in a few studies.
Aims & Methods: We aimed to compare the outcomes of conventional endoscopic mucosal resection (EMR), EMR-C resection, and endoscopic submucosal dissection (ESD) for the treatment of rectal NETs. A total of 138 rectal NETs < 15mm in diameter were treated endoscopically by a single endoscopist at Asan Medical Center from 2009 to 2014. We retrospectively analyzed 122 rectal NETs that had been removed using EMR (n = 56), EMR-C (n = 34), or ESD (n = 32) methods.
Results: The mean size of the rectal NETs was larger in the ESD group (9.1 ± 2.2 mm; range, 6–14 mm) than in the EMR group (5.0 ± 1.8 mm; range, 2–13 mm) and the EMR-C (5.3 ± 1.6 mm; range, 2–8 mm) group ($P < 0.001$). Six (4.9%) of one hundred and twenty-two lesions were larger than 10 mm in size (five in the ESD group and one in the EMR group). The histologic complete resection rate was higher in the EMR-C group than in the EMR group (94.1% vs. 76.8%, $P = 0.032$). Intraprocedural bleeding tended to be more frequent in the EMR-C group than in the EMR group (8.8% vs. 0, $P = 0.051$). All intraprocedural bleeding was controlled easily during the endoscopic procedure. No differences in the rates of adverse events or histologic complete resections were observed between the EMR-C group and the ESD group for 6–8 mm sized NETs; however, the procedure time was significantly shorter in the EMR-C group (3.9 ± 1.1 mm) than in the ESD group (19.0 ± 12.1 minutes) ($P < 0.001$). Meanwhile, the role of EMR-C in the treatment of rectal NETs larger than 8 mm could not be clearly assessed in this study. No recurrence occurred in any of the three groups.

Conclusion: EMR-C is the most advisable technique for endoscopic resection of rectal NETs with sizes equal to or smaller than 8 mm.
Disclosure of Interest: None declared

P0424 SECOND-LOOK OPERATION FOR RECURRENT COLORECTAL CANCER BASED ON INTENSIVE SURVEILLANCE CONSISTS MAINLY OF CARCINOEMBRYONIC ANTIGEN AND COLONOSCOPY AND COMPUTED TOMOGRAPHY

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Introduction: The usefulness of postoperative carcinoembryonic antigen (CEA) monitoring and improvements in imaging techniques have renewed enthusiasm for second-look operation (SLO) as the most effective treatment for recurrent colorectal cancer by reresection following early detection. The aim of our study is to evaluate the role of CEA and imaging techniques-directed SLO.
Aims & Methods: Seven hundred fifty-six patients with Dukes stages B and C, who had undergone curative resection, were monitored postoperatively using CEA and imaging techniques. An SLO was performed on any potentially resectable recurrence, and in addition, an SLO was done when a persistently rising CEA value was detected.
Results: Recurrence developed in 18.8% (142/756) of patients, and 90.8% (129/142) of the recurrences were detected within the first 3 years following curative resection. When comparing carcinomas of the colon with that of the rectum, the former were associated with significantly more hepatic and intraabdominal recurrences, whereas the latter had significantly more locoregional and pulmonary recurrences. Seventy-two patients underwent SLO. Of these patients, 54.2% (39/72) had all of their disease resected, and 1.4% (1/72) had no detectable disease at the SLO. Among the142 patients with recurrence, 71 (50%) patients underwent SLO. The resectable group at SLO carried a significantly better survival than the unresectable recurrence group (41.3 vs. 5.2%; $P < 0.01$).
Conclusion: Complete removal of colorectal cancer recurrences by SLO, on the basis of postoperative, follow-up CEA and imaging technique findings, results in improved survival.
Disclosure of Interest: None declared

P0426 THE UTILITY OF A NOVEL EX VIVO TRAINING MODEL FOR COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION USING A BOVINE RECTUM

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Introduction: The colorectal endoscopic submucosal dissection (CR-ESD) procedure is very technically demanding because of the inherent histological and anatomical features of the human colorectum. Clinically, endoscopists should learn to perform CR-ESD on the rectum because of the lower risk of perforation and less difficulty. Training using an animal model is generally recommended before performing a CR-ESD in human. We reported the similarities of histological characteristics between the bovine rectum (B/R) and the human rectum. In light of those findings, we created a novel animal training model using B/R, which reproduces the colorectal shape and elasticity of the human colorectum. This model was made using a sponge and a B/R of appropriate length fitted in a model. The maneuverability and feeling of the ESD procedure in this model were extremely similar to that in human CR-ESD. In addition, the anatomical features of the human colorectum, including the thinner wall, the narrow lumen, the presence of angulations, and haustra folds were reproduced in this model.
Aims & Methods: Aim: To assess the utility of a new animal training model for CR-ESD.
Methods: Study1: Two endoscopists (E1, E2) without experience performing CR-ESD but with some experience in gastric ESD performed the ESD of 3-cm artificial lesions in 28 consecutive sessions using this colorectal ESD training model. The speed of the ESD procedure (s/cm^2), the injury score of the muscularis propria layer (MP) (scoring 1–4: 1, no damage; 2, injury to the surface of the MP; 3, laceration of the MP; 4, perforation), the injury score of the resected specimen (1, no damage; 2, injury to marking spot; 3, cut into the resected specimen), and the rate of perforation were recorded. We evaluated the effects of this training model by comparing the results of the first 14 sessions (former period; FP) with those of the last 14 sessions (latter period: LP). Study2: A follow-up survey was performed for the clinical outcomes of the first 5 cases of colorectal ESD carried out by those two endoscopists (E1, E2). For evaluating the technical aspects of the ESD procedure, size of the lesions, procedure time, en bloc resection rate, R0 resection rate and complications were evaluated.
Results: Study1: The speed of the ESD procedure were significantly faster in the LP compared to the FP in all endoscopists: mean procedure speed (FP/LP) (s/cm^2): E1, 397/195 ($p = 0.044$); E2, 421/302 ($p = 0.02$). The MP injury scores were significantly lower in the LP than the FP in both endoscopists ($p = 0.046$, $p = 0.0071$). The injury score of resected specimen were also significantly lower in the LP than the FP in both endoscopists ($p = 0.046$, $p = 0.0062$, respectively). Study2: The median size of the lesions were 32 (20-40) mm for E1 and 22 (12-34) mm for E2. The median procedure times were 51 (10-115) min for E1 and 57 (32-74) min for E2. En bloc resection rate were 100% (5/5) for both endoscopists, R0 resection rate were 100% (5/5) for E1 and 80% (4/5) for E2. There were no complications.
Conclusion: The utility of the novel ex vivo animal training model using B/R was demonstrated. This model has the potential to simulate CR-ESD with great similarity to that performed in humans and contribute to a safe induction of clinical colorectal ESD.
Disclosure of Interest: None declared

P0427 RESISTANCE TO GAMMA-IRRADIATION AND PPAR-GAMMA AGONISTS INDUCED APOPTOSIS IN CACO-2 COLON CANCER CELLS

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Introduction: The involvement of peroxisome proliferator-activated receptors (PPARs) in the cancer cell apoptosis is a generally accepted fact. However, some reports indicate that the activation of PPARγ might be directly responsible for carcinogenesis. It is well known that the high level of heat shock proteins (HSPs) in cancer cells is associated with metastasis, poor prognosis and the resistance to radio as well as chemotherapy. HSP70 as a part of the most important systems for maintaining the viability of the cell, is known to counteract against the apoptosis. Here we report the involvement of HSP70 in anti-apoptotic action of activated PPARγ in γ-irradiated human colon cancer cells.
Aims & Methods: We have employed undifferentiated Caco-2 cells cultures as an experimental model of human colon adenocarcinoma. In this system PPAR-γ agonists (ciglitazone 1x10-6M and retinoic acid RA, 1x10-6M) induced nuclear translocation of PPAR-γ as well as HSF-1. This translocation was followed by the increase of HSP70 mRNA and protein expression. As it had been previously shown by us, cell cultures subjected to γ-radiation (photons) using the therapeutic dose of 2.5 Gy, manifested typical for apoptosis PARP degradation pattern, presenting both the native 112 KD and digested 85 KD forms. It suggests activation of caspases 3 or 6.
Results: Stimulation of the cultures with PPARγ agonists prior to the irradiation eliminated PPAR-γ nuclear translocation and PARP degradation altogether. PPARγ was found to be sequestered in the complexes with AKT-1 in cytoplasmic as well as in nuclear pool. However γ-radiation did not affect PPAR-γ agonists stimulated HSF-1 translocation and subsequent HSP70 expression. Based on the obtained results, we would like to propose a plausible molecular mechanism of chemo- and radio- resistance of colon cancer cells. In γ-irradiated cells, nuclear translocation of PPARγ is abolished and PPARγ-AKT-1 complexes are conserved in which PPARγ remains insensitive for its agonists treatment. Most likely, at the same time PPARγ agonists directly activate HSF-1 nuclear translocation and subsequent HSP70 expression. The process seems to be undisturbed by the γ-irradiation what renders the colon cancer cells resistance to apoptosis under combined chemo- and radiotherapy treatment.
Conclusion: Our results provide evidences for the anti-apoptotic action of PPARγ agonists used simultaneously with the γ-radiation due to the formation of stable complexes of PPARγ with AKT-1 in which PPARγ was restrained in inactive form. Moreover, the up-regulated HSP70, in response to PPARγ agonists in γ-irradiated cultures promotes cell survival.
Disclosure of Interest: None declared

P0428 IS VEGETARIANISM A PROTECTIVE FACTOR FOR IRRITABLE BOWEL SYNDROME? A CASE-CONTROL STUDY

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Introduction: Diet, health and disease is one of the most frequent and less comfortable questions gastroenterologists are asked about. The role of diet in physiopathology and treatment of IBS is still under-evaluated. A predominantly vegetable diet is commonly associated with bloating and flatulence. Vegetarianism may affect gut microbiota, intestinal peristalsis and inflammation. A balanced vegetarian diet may have some health benefits, but which is its influence on IBS?
Aims & Methods: We use a case-control design; patients with IBS were selected by purposive sampling; vegetarians were recruited from gastroenterologist offices, vegetarian and health food sites, the Vegetarian Society, and from friends and relatives of participants; the control sample was randomly selected from the general population. A questionnaire was delivered to all subjects to reveal recent gastrointestinal symptoms (using GSRS), to diagnose IBS (using Rome III criteria) and to evaluate eating habits (a food frequency questionnaire based on a validated European Prospective Investigation of Cancer protocol). We conducted descriptive, bivariate, and multivariate analysis to examine the associations between food habits and IBS.
Results: We compared 47 cases of IBS patients with a control group ($n = 104$) from the same community. Among IBS patients, only 8.5% were vegetarians and

among vegetarians only 8.8% were diagnosed with IBS (OR = 0.14, 0.04-0.42, CI 95%, $p < 0.001$), since the prevalence of IBS in general population was 15.8%. Among potential risk factors in the study, age, past history of digestive disease, canned food, processed meat, whole cereals and pulses were statistically significant predictors of IBS.
Conclusion: Although some vegetable foodstuffs can exacerbate digestive symptoms, a well-balanced and customized vegetarian diet can be a protective factor for IBS.

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P0429 EXCESS MEDICAL DIAGNOSES IN FAMILIES OF PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: Previous studies have shown that IBS patients as a group have an excess of co-morbid chronic medical conditions. Past work has also indicated intergenerational transmission of illness and evidence if illness modeling and/or reinforcement in IBS. However, the general amount of chronic illness in IBS families of origin has not been well documented to date.
Aims & Methods: We aimed to test whether the frequency of chronic medical problems in IBS families of origin is elevated and whether it is related to amount of IBS co-morbidities, associated with IBS morbidity and poorer current disease coping, and whether there is evidence of illness modeling. 530 IBS patients (Rome II or III criteria+ physician diagnosis; 79.4% females; mean age = 35.8 years) and a sample of 337 demographically similar control subjects without gastrointestinal problems (78.7% females; mean age = 34.7 years) reported whether they themselves, their mother, father or siblings had ever been diagnosed with 12 chronic medical conditions (in addition to IBS and psychiatric conditions) on the validated Comorbid Medical Conditions Questionnaire – CMCQ. Subjects also completed the IBS Severity Scale Score (IBS-SSS), the IBS-QOL, the Visceral Sensitivity Index (VSI) and the Catastrophizing subscale of the Coping Strategies Inventory.
Results: IBS patients reported more medical conditions in their families than healthy subjects (Means: 2.86 vs. 1.39; $p < .0001$). Seven of the 12 medical conditions were more common in IBS families than control families (see Table). Amount of medical co-morbidities of IBS patients correlated robustly with co-morbidity amount in their mothers (Spearman's Rho = 0.42), fathers (Rho = 0.25) and siblings (Rho = 0.42); $p < 0.0001$ for all. These associations were also significant for male and female IBS patients analyzed separately. IBS patients also reported substantially higher rates of family IBS than controls: Overall 27.2% vs. 7.0%, Odds Ratio = 4.9; mothers 16.1% vs. 3.7%; fathers 6.9% vs. 1.3%; and siblings 13.8% vs. 2.6%; $p < 0.0001$ for all. The number of medical conditions in mothers and siblings of IBS patients was modestly but significantly correlated with more severe IBS (Rho = 0.15 and 0.20) and greater IBS-QOL impairment (Rho = -0.11 and -0.09) in the patients. VSI and Catastrophizing were unrelated to amount of family medical conditions.

Chronic medical diagnoses in families of IBS patients versus control subjects (* = $p < 0.05$):

	IBS families (%)	Control families (%)	Odds Ratio
Fibromyalgia	7.6*	3.0	2.64
Asthma	22.5	19.6	1.19
TMJ	14.8*	5.7	2.84
Chronic fatigue	5.3*	0.9	6.06
Migraines	38.3*	20.2	2.45
Tension Headaches	38.9*	18.5	2.81
Insomnia	27.9*	12.4	2.74
Back pain	32.7*	20.3	1.91
Chronic Pelvic Pain	3.2	1.2	2.60
Interstitial Cystitis	2.0	1.2	1.62
Prostatitis	5.3	3.0	1.79
Dysmenorrhea	5.5	2.7	2.08

Conclusion: IBS patients report an excess of chronic medical conditions in their immediate family compared to controls, and the illness amount in the family is correlated with patients' own co-morbidity load. No evidence of impact of family medical illness on maladaptive coping or visceral anxiety, nor of gender-specific modeling influences, were observed. Our findings need to be confirmed by surveying family members of IBS patients and controls directly about their medical history in future work. [Supported by grant RO1 DK31369]
Disclosure of Interest: None declared

P0430 SYSTEMATIC REVIEW WITH META-ANALYSIS: PREVALENCE OF BILE ACID MALABSORPTION IN IRRITABLE BOWEL SYNDROME WITH DIARRHOEA

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Introduction: Irritable bowel syndrome is a prevalent disorder with a marked socioeconomic burden. Previous studies support the proposal that a subset of patients with features compatible with diarrhoea predominant IBS (IBS-D) have bile acid malabsorption (BAM).
Aims & Methods: The objective of this study was to perform a systematic review and meta-analysis to assess the prevalence of BAM in patients meeting accepted criteria for IBS-D. MEDLINE and EMBASE were searched up to February 2015. Studies recruiting adults with IBS-D, defined either by the Manning, Kruis, Rome I, II or III criteria and which used 23-seleno-25-homotaurocholic acid (SeHCAT) testing for the assessment of BAM were included. BAM was defined as 7 day SeHCAT retention of < 10%. We calculated the rate of BAM and 95% confidence intervals (CI) using a random effects model. The methodological quality of included studies was evaluated using the Quality Assessment for Diagnostic Accuracy Studies (QUADAS-2).
Results: The search strategy identified 6 relevant studies comprising 908 individuals. The rate of BAM ranged from 16.9% to 35.3%, with an unadjusted rate [AF1] of 29.3%. The pooled rate was 28.1% (95% CI 22.6-34%). There was significant heterogeneity in effect sizes (Q-test $\chi^2 = 17.9$, $p < 0.004$; I^2 72.1%). The type of diagnostic criteria used or study country did not significantly modify the effect.
Conclusion: These data provide evidence that in excess of one quarter of patients meeting accepted criteria for IBS-D have BAM. This distinction has implications for the interpretation of previous studies as well as contemporaneous clinical practice and future guideline development.
Disclosure of Interest: S. Slattery: None declared, A. Ford: None declared, Q. Aziz: None declared, A. Farmer Lecture fee(s): Almirall

P0431 UNSUPERVISED SYMPTOM-BASED CLUSTERING OF PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: Despite capacious research on IBS, the pathophysiology remains unclear and therapy options are sparse. Identifying subgroups of patients with a distinct profile may improve targeted research and development of individually tailored treatment options, as has been demonstrated in functional dyspepsia [1]
Aims & Methods: We included 164 patients with IBS defined by the Rome III criteria (mean age 34, range 18-62 years, 69% female). A crossvalidated Principal Component Analysis formed the basis for hierarchical clustering of patients based on symptom profiles. To model the symptom profile the following validated questionnaires were used: Gastrointestinal Symptom Rating Scale-IBS (GSRS-IBS) (individual items), bowel-related questions of the Rome III questionnaire, pain-related questions from the IBS Symptom Severity Score (IBS-SSS), and the average stool form during two weeks measured by the Bristol Stool Form Scale. An ANOVA with post-hoc t-tests (Bonferroni corrected) was applied to compare the clusters on the following measures: Pain intensity and pain thresholds measured by a rectal barostat procedure, oroanal transit time (radiopaque markers). Severity of anxiety and depression (Hospital Anxiety and Depression Scale (HAD), chronic fatigue (Fatigue Impact Scale (FIS), IBS-related quality of life (IBSQOL) and Sense of Coherence (SOC) were also compared between the clusters.
Results: The combination of symptom-based measurements was modelled with an optimized fit of three principal components, giving an R^2 of 0.4, regarded as a very robust model for patient data. Hierarchical clustering defined three major clusters: One group (16.5%) showed low severity scores for all modelled symptoms, two groups showed distinctly higher than average scores on either

constipation (48.8%) or diarrhea (34.8%) measures. The two distinct-symptom groups showed significantly higher pain intensity and lower pain threshold measures, higher anxiety, depression and fatigue levels and lower scores for SOC and QOL when compared to the low-symptom IBS patients. The high constipation group also had significantly longer oroanal transit time than the other two, but the high diarrhea group did not differ from the low symptom group.

	Constipation group	Diarrhea group	Low symptoms group	Significance
Oroanal transit time	1.9 days^#	1.1 days*	1.0 days*	<0.0001
Pain intensity(VAS)	52 mm^	52 mm^	18 mm*#	<0.0001
Pain threshold	26 mmHg	26 mmHg^	31 mmHg#	0.05
Anxiety (HAD)	8	9^	6#	0.03
Depression (HAD)	5^	5	3*	0.03
FIS	65^	56^	31*#	0.001
SOC	131^	127^	150*#	0.01
QOL	59^	54^	79*#	<0.0001
GSRS Abd Pain	4.4^	4.7^	2.5*#	<0.0001
GSRS Bloating	4.9^	4.6^	3.2*#	<0.0001
GSRS Constipation	3.9^#	2.1^*	1.7*#	<0.0001
GSRS Diarrhea	3.2^#	5.1^*	2.5*#	<0.0001
GSRS Satiety	2.8^	2.9^	1.6*#	0.001

*vs Const, # vs Diarr, ^vs low symptoms

Conclusion: Symptom-based cluster analysis confirms previous grouping into constipation- and diarrhea-predominant groups, but also shows a low overall symptoms group, similar to what has been shown in functional dyspepsia [1]. This might reflect differences in pathophysiology and thus have impact on therapy strategies.

Reference

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Disclosure of Interest: None declared

P0432 THE OVERLAP BETWEEN CONSTIPATION PREDOMINANT IRRITABLE BOWEL SYNDROME AND FUNCTIONAL CONSTIPATION IN PATIENTS ASSESSED FOR PELVIC FLOOR DISORDERS

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Introduction: According to ROME III criteria, Pelvic floor symptoms (PFD) are incorporated into functional constipation, and strictly differed from constipation related IBS (c-IBS). However, abdominal pain was previously reported in patients reporting PFD

Aims & Methods: The aim of this study was to assess the incidence and type of IBS-related symptomatology on registration of those patients presenting with PFD and symptoms of chronic constipation.

Methods: All patients referred for the assessment and evaluation of PFD were analyzed by specific questionnaires including the Rome III criteria and the bowel component of the Birmingham Bowel and Urinary symptom questionnaire – BBUS-Q22 for IBS symptomatology. Patients were further assessed with dynamic transperineal ultrasonography or X-ray defecography, conventional station pull-through anorectal manometry and balloon expulsion test.

Results: Two hundred consecutive patients were included in the study (mean age 51.6 years, range 22-85 years).Reclassification of patients resulted in 167 patients (83.5%) being designated with IBS. Sixty six percent of patients reported regular improvement of symptoms with defecation with 55% noting symptoms associated with a change of stool form and 71% with fewer stools. There were significant differences noted in reporting of hard stools by those patients redesignated as IBS-PFD and a high percentage of reported soft stool in the FC-PFD patients. Repeated straining was more common in the IBS-PFD group as was fecal urgency, a sensation of defecation block and episodes of reported incomplete bowel emptying. The frequency of bowel movements between the groups was similar. There was no significant difference between the IBS-PFD and FC-PFD groups in the incidence of pelvic floor abnormalities. Anismus was diagnosed frequently in both groups, but was more prevalent in the IBS group (P = 0.03).

Conclusion: The key outcome of this study is that PFD can be related to IBS as well as to FC. The reclassification of the majority of patients with PFD as also having significant IBS symptomatology might have important ramifications for eatment and functional outcome.

Disclosure of Interest: None declared

P0433 CO-MORBID FUNCTIONAL DYSPEPSIA IN IBS IS ASSOCIATED WITH AN INCREASED SYMPTOM RESPONSE TO A LACTULOSE NUTRIENT CHALLENGE TEST

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Introduction: Irritable Bowel Syndrome (IBS) is associated with an increased postprandial symptom response to a 25g combined lactulose nutrient challenge test compared to healthy controls (1). Co-morbid Functional Dyspepsia (FD) is highly prevalent in IBS, but is not regularly taken into account. Our aim was to investigate the relationship between co-morbid FD status and the time course of the postprandial symptom response to this test.

Aims & Methods: 205 IBS patients (Rome III), 94 (46%) of whom had co-morbid FD (Rome III), and 83 healthy volunteers (HV) consumed a 400-ml liquid breakfast (Nutridrink, 1.5 kcal/ml, 16% proteins, 49% carbohydrates, 35% fat, gluten free, lactose < 0.025 g/100 ml) combined with 25g of lactulose after an overnight fast. They completed graded rating scales (0-20) assessing severity of five gastrointestinal (GI) symptoms (abdominal pain, bloating, nausea, gas, urgency) and overall "digestive comfort" before breakfast and every 15 minutes up to 240 minutes postprandially. The relationship between subject status (HV, IBS, IBS + FD) and the course of GI symptom scores over time was analyzed using linear mixed models. "Time" was included as a categorical within-subject effect, "group" (HV, IBS, IBS + FD) was included as categorical between-subject effect, and the group-by-time interaction effect was also included. The main effect of group and the interaction effect are the effects of interest.

Results: A significant main effect of group, indicating a significant difference between the three groups in the average symptom level over time, was found for all symptoms (all p < .0001). Post-hoc tests showed significant differences for all pairwise comparisons between the three groups (all p < .05, stepdown Bonferroni corrected), including the IBS versus IBS + FD comparison. A group-by-time interaction effect was found for pain (p = .002), bloating (p = .0008), urgency (p = 0.019), and digestive comfort (p = .002), but not for gas (p = .07) or nausea (p = .52). Planned comparisons on the significant interaction effects showed that in HV, contrary to IBS and IBS + FD, no postprandial increase in ratings was found for any of the symptoms, resulting in significant differences at all time points (all p < .0001, stepdown Bonferroni corrected) between HV on one hand and both IBS and IBS + FD on the other hand. Differences between IBS and IBS + FD were found at all time points for pain and digestive comfort (all p < .001 and p < .05, stepdown Bonferroni corrected, respectively), up to 2 hours postprandially for bloating (all p < .05, stepdown Bonferroni corrected) and at 30 minutes postprandially only for urgency (p = .005, stepdown Bonferroni corrected).

Conclusion: In IBS, co-morbid FD is associated with increased GI symptom reporting, both preprandially and after a combined lactulose nutrient challenge test, particularly for the symptoms pain, bloating, urgency, and is associated with decreased overall digestive comfort reporting. These results indicate that presence of co-morbid FD is relevant for symptom reporting in IBS.

Reference

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P0434 DIAGNOSIS AND MANAGEMENT OF MODERATE-TO-SEVERE IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C) IN EUROPE: POOLED RESULTS FROM THE IBIS-C STUDY

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Introduction: This is the first study to assess the diagnostic and therapeutic management of moderate-to-severe IBS-C in six European countries (France, Germany, Italy, Spain, Sweden and UK). Here we present the pooled results from all participating countries.

Aims & Methods: Observational study in patients diagnosed with IBS-C (Rome-III criteria) in the last five years and moderate-to-severe disease severity at inclusion (IBS-Symptom Severity Scale [IBS-SSS] score ≥175), with a 12-month follow-up (6 months retrospective and 6 months prospective), in order to assess healthcare resource utilisation (HRU) and costs prior to and after an active phase of the disease. Diagnostic procedures were collected since the onset of symptoms. The study began in April 2012; last patient last visit: January 2014.

Results: 525 patients were included (60% severe, mean age [±SD] 45.3 ± 15.8 years old, 86.9% female). Mean time since diagnosis: 3.0 ± 5.2 years; mean symptom duration: 12.8 ± 13.1 years. Diagnostic procedures since the onset of symptoms were highly variable: the most common were blood tests (71.6%; range: 88.9% Sweden– 57.6% France); colonoscopy (62.9%; range: 78.4% Germany–41.1% Italy); abdominal ultrasound (54.7%; 62.7% Germany–36.1% Sweden).

Abstract number: P0436 Table 1: Serum cytokines and mucosal mRNA expression in healthy controls and IBS patients.

Serumcytokine(pg/ml)	IBS(n = 144)	Healthy(n = 42)	*p*-value†
IL-6	0.4 (0.28-0.68)	0.34 (0.24-0.54)	0.06
IL-8	11.3 (7.51-14.41)	9.1 (6.49-13.15)	0.12
IFN-γ	8.0 (5.1-12.1)	10.9 (6-15.3)	0.07
Mucosalcytokine($2^{-\Delta Ct}$)	**IBS(n = 109)**	**Healthy(n = 36)**	***p*-value†**
IL-10	$8.6x10^{-5}$ ($6.9x10^{-5}$-$1.1x10^{-4}$)	$9.6x10^{-5}$ ($7.8x10^{-5}$-$1.3x10^{-4}$)	0.05
FOXP3	$2.5x10^{-4}$ ($1.8x10^{-4}$-$3.5x10^{-4}$)	$3.1x10^{-4}$ ($2.2x10^{-4}$-$3.7x10^{-4}$)	0.07

†Mann Whitney U test. Data shown as median (25% > 75%)

The main associated comorbidities were anxiety (34.1%), dyspepsia (31.0%), headache (28.0%), and insomnia (27.0%). 62.1% (74.1% Italy–57.6% France) of patients had an average of 4.0 ± 2.7 diagnostic tests (4.5 ± 3.0 Italy–3.4 ± 2.7 France) during follow-up and 65.3% took prescription drugs for their IBS-C (90.4% UK–41.1% Italy). The most commonly prescribed medications were laxatives (48.8%), antispasmodics (19.8%), and prokinetics (18.9%). 20.4% took other medications. Specifically, laxatives were prescribed as a monotherapy (14.1%), in combination with antispasmodics (6.3%) or with another drug that was not an antispasmodic, antidepressant, or prokinetic (10.7%). Overall, 67.2% of patients took non-prescription medication for their IBS-C (82.1% Italy–56.3% Spain) (33.0% laxatives; 24.2% pre/probiotics, 19.6% herbal medicine) and 33.0% of patients sought complementary therapies (44.4% Sweden–27.5% Germany). Overall, marginal improvement was noted in symptom severity (IBS-SSS total score ± SD) between baseline (323.2 ± 84.3) and the 6-month visit (253.9 ± 105.6, 76.1% moderate-to-severe; 85.4% France–67.3% Italy).
Conclusion: IBS-C symptoms remain undiagnosed for an average of almost 10 years and there is a high degree of variability in diagnostic and management procedures between European countries. Over half of the patients continued to undergo diagnostic tests after a diagnosis has been reached and the degree of control did not improve over time despite a high level of prescription and non-prescription medication use. At the end of the study over three quarters of patients still suffered from moderate-to-severe IBS-C.
Disclosure of Interest: J. Tack Conflict with: Grants / research support: Abbott, Novartis, Shire. Honoraria / consultancy fees: Almirall, AstraZeneca, Danone, GI Dyamics, GlaxoSmithKline, Ironwood, Janssen, Menarini, Novartis, Rhythm, Shire, Takeda, Theravance, Tsumura, Will Pharma, Zeria. Speaker fees: Abbott, Almirall, AstraZeneca, Janssen, Menarini, Novartis, Shire, Takeda, Zeria., V. Stanghellini Conflict with: Grants / research support: Alfa Wassermann, Almirall, Aptalis, Italchimici, Norgine, Shire, Takeda, Valeas. Honoraria / consultancy fees: Abbott, Alfa Wasserman, Almirall, Angelini, Aptalis, CM&D Pharma, Farmaderma, Ironwood, Norgine, Shire, Takeda, Valeas, Vibrant, Zeria., F. Mearin Conflict with: Speaker fees: Almirall., Y. Yannakou Conflict with: Grants: Shire; Medtronic. Speaker fees: Almirall; Shire; Sucampo., P. Layer Conflict with: Abbott / Solvay, Almirall, Aptalis / Axcan, Norgine, Shire., B. Coffin Conflict with: Honoraria / consultancy fees: Almirall, Mundipharma, Mayoly Spindler, Menarini., M. Simren Conflict with: Unrestricted research grants: Danone, AstraZeneca. Consultant/ Advisory Board member: Danone, Nestlé, Chr Hansen, Almirall, Albireo, Shire. Participation in a company-sponsored speaker's bureau: Almirall, Shire, Tillotts, Takeda., J. Mackinnon Conflict with: Employee of TFS Develop S.L, contracted by Almirall S.A to conduct the study., J. Bertsch Conflict with: Employee of TFS Develop S.L, contracted by Almirall S.A to conduct the study, J. Fortea Conflict with: Employee of Almirall, S.A

P0435 CLASSIFICATION OF IRRITABLE BOWEL SYNDROME – A CRITICAL EXPLORATION OF THE ROME III CRITERIA

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Introduction: The aims of this study is to explore the subtypes of irritable bowel syndrome (IBS) in a cohort three years after acute Giardia infection and in a control group with sporadic IBS. Further, to compare these subtypes according to Rome III criteria (based on stool consistency) to a classification based on stool frequency (diarrhoea or constipation).
Aims & Methods: Prospective cohort study of patients aged ≥18 years with confirmed giardiasis during a large outbreak in Bergen, Norway, in 2004 and a group of controls matched by age and gender. A postal questionnaire was mailed to all participants in 2007, three years after the acute infection. Outcomes were IBS according to Rome III criteria, and diarrhoea (defined as ≥4 bowel movements a day at least "sometimes") and constipation (defined as <3 defecations at least "sometimes").
Results: Response rates were 66% (781/1184) among exposed patients and 33% (1099/3380) among controls. The prevalence of IBS was 47% (346/781) and 14% (154/1095) respectively, with an adjusted relative risk 3.3 (95% CI 2.9 to 3.7). In the Giardia group the distribution of IBS based on stool consistency according to Rome III criteria was 38% IBS-D, 46% IBS-M, 10% IBS-C and 6% IBS-U, and in the control group 32% IBS-D, 34% IBS-M, 19% IBS-C and 14% IBS-U.
Of the IBS patients in the Giardia group 70% reported diarrhoea and 14% reported constipation, compared to 46% and 24%, respectively, in the control group. Subtyping IBS based on these characteristics yielded a different distribution than when subtyping based on stool consistency ($p < 0.001$ in both groups, Kappa-values 0.168 and 0.279). In the Giardia group 62% had IBS and diarrhoea, 7% had IBS and constipation and 7% had IBS and both, the corresponding numbers in the control group was 40%, 18% and 6%.

Table: Relationship between IBS subtyped according to Rome III criteria (based on stool consistency) and IBS subtyped by frequency of bowel movements (diarrhoea/constipation at least "sometimes") among exposed and controls three years after acute giardiasis.

		IBS with diarrhoea	IBS with constipation	IBS with diarrhoea and constipation	IBS without diarrhoea nor constipation	Total
Exposed	IBS-D	102	3	5	22	132 (38%)
	IBS-C	17	12	5	19	34 (10%)
	IBS-M	98	8	15	38	159 (46%)
	IBS-U	1	7	0	13	21 (6%)
Total		215 (62%)	24 (7%)	25 (7%)	82 (24%)	346 (100%)
Control	IBS-D	35	1	1	13	50 (32%)
	IBS-C	9	11	0	10	30 (19%)
	IBS-M	14	13	8	18	53 (34%)
	IBS-U	4	2	0	15	21 (14%)
Total		62 (40%)	27 (18%)	9 (6%)	56 (36%)	154 (100%)

Conclusion: In post-giardiasis IBS there was a larger proportion of IBS-D and IBS-M compared to sporadic IBS in the controls. Subtyping IBS based on diarrhoea and constipation, rather than on stool consistency according to Rome criteria, significantly changed how patients were classified, and the resulting changes appeared to be different in post giardiasis IBS compared to sporadic IBS. These results challenge the accuracy of the current Rome III criteria in characterizing IBS.
Disclosure of Interest: None declared

P0436 SERUM AND MUCOSAL CYTOKINE PROFILES DO NOT DISCRIMINATE BETWEEN HEALTH AND IBS, BUT INCREASED LEVELS OF PRO-INFLAMMATORY CYTOKINES CORRELATE WITH LONGER OROANAL TRANSIT TIME AND REDUCED PSYCHOLOGICAL WELL-BEING

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Introduction: Evidence suggests patients with irritable bowel syndrome (IBS) have an altered cytokine profile, although it is unclear if cytokines are associated with severity of symptoms. We therefore aimed to determine if global cytokine profiles differ between IBS and healthy and if cytokine expression is associated with IBS symptoms.
Aims & Methods: Serum from 144 IBS patients and 42 healthy subjects was analyzed for cytokine levels (IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-13, IL-17A, IFN-γ, TNF) by MSD MULTI-ARRAY analysis. Sigmoid colon biopsies from 109 IBS and 36 healthy were analyzed for mRNA expression (IL-8, IL-10, TNF, FOXP3) by qRT-PCR. Global cytokine profile of serum and mucosal cytokines was evaluated by multivariate analysis (SIMCA-P+ software). Study subjects underwent rectal sensitivity test using a barostat, and oroanal transit assessment using radiopaque markers. IBS symptom severity and psychological symptoms were assessed using Patient Health Questionnaire-15, IBS Severity Scoring System and Hospital Anxiety and Depression scale.
Results: According to multivariate discrimination analysis, global cytokine profiles of IBS patients and healthy subjects overlapped, thus not able to discriminate IBS patients from healthy. However, serum levels of pro-inflammatory cytokines IL-6 and IL-8 tended to be increased, and IFN-γ tended to be decreased in IBS patients. Mucosal mRNA expression of IL-10 and FOXP3 tended to be lower in IBS patients (Table 1). Other measured serum and mucosal cytokines did not differ between IBS and healthy subjects. Subjects (including IBS and healthy) with longer oroanal transit had increased mucosal mRNA expression of IL-8 ($r = 0.33$; $p = < 0.0001$) and TNF ($r = 0.2$; $p = 0.02$). No correlation of rectal pain threshold and cytokine expression was recorded. Subjects with a higher degree of somatization tended to have

increased serum levels of IL-6 (r = 0.2; p = 0.01), IL-8 (r = 0.18; p = 0.01) and TNF (r = 0.15; p = 0.04). Subjects reporting more anxiety tended to have lower mucosal mRNA expression of IL-10 (r = -0.16; p = 0.05). Subjects reporting higher levels of depression had increased serum levels of IFN-γ (r = 0.18; p = 0.01) and IL-6 (r = 0.15; p = 0.04). IBS symptom severity tended to correlate positively with serum levels of IL-6 in IBS patients (r = 0.17; p = 0.05).
Conclusion: Global cytokine profiles were similar between IBS patients and healthy subjects, thus cytokine profiles do not discriminate between IBS and health. Nonetheless, increased levels of pro-inflammatory cytokines were associated with longer oroanal transit and reduced psychological wellbeing in IBS and healthy subjects.
Disclosure of Interest: None declared

P0437 AN APPRAISAL OF CLINICAL PRACTICE GUIDELINES FOR IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome(IBS) is a chronic gastrointestinal disorder with an estimated prevalence of 10-20%. Many countries lack appropriate clinical practice guidelines for the diagnosis and treatment of IBS. It can be painful and debilitating, lead to feelings of anxiety and depression, and negatively affect quality of life.
Aims & Methods: To determine and assess the quality of clinical practice guidelines on IBS. Four databases (included MEDLINE and EMBASE) and some guideline websites were searched till to March 2015. Methodological quality of selected guidelines was assessed by the AGREE II instrument.
Results: From 863 citations, 17 relevant guidelines were included. The overall agreement among reviewers was moderate (Intra-class correlation coefficient = 0.81; 95% confidence interval [CI], 0.56-0.76). Overall, the guidelines performed well in the clarity and presentation domain with a mean score of 56.12%, followed by scope and purpose (58.56%) and rigor of development (50.25%). In contrast, poor scores were given for the remaining domains: stakeholder involvement (23.25%), applicability (28.14%) and editorial independence (31.54%). Four sixths domains scores were lower when compared with international level. There are 5 (22.73%) guidelines described the systematic methods for searching. And only 5 (23.81%) guidelines reported methodological expertise were included in guideline developing teams.
Conclusion: Although existing guidelines may accurately reflect agreed clinical practice, many guidelines lack proper methodological quality. Greater efforts are needed to provide high-quality guidelines that serve as a useful and reliable tool for clinical decision-making in this field.

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Disclosure of Interest: None declared

P0438 EFFECTS OF ELUXADOLINE ON ABDOMINAL PAIN IN PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH DIARRHOEA: RESULTS OF TWO PHASE 3 TRIALS

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Introduction: Eluxadoline (ELX) is a locally active, mixed mu-opioid receptor agonist and delta-opioid receptor antagonist that demonstrated improvements in the symptoms of irritable bowel syndrome with diarrhoea (IBS-D) in two Phase 3 trials.
Aims & Methods: To examine the efficacy of ELX in abdominal pain in IBS-D, additional prospective analyses were performed for two double-blind, placebo (PBO)-controlled Phase 3 trials (IBS-3001, IBS-3002). Patients (pts) meeting Rome III criteria for IBS-D were randomised to twice-daily ELX (75 or 100 mg) or PBO. Both trials had identical designs through 26 weeks (wks) of treatment. The primary endpoint was a composite response based on simultaneous daily improvement in worst abdominal pain (WAP) and stool consistency over Wks 1–12 (US Food and Drug Administration [FDA] endpoint) and Wks 1–26 (European Medicines Agency [EMA] endpoint). Additional prospective analyses of WAP (0–10 scale) included: Cochran–Mantel–Haenszel (CMH) assessments of WAP responders, defined as pts with ≥50% of days with ≥30% improvement (study level and pooled); longitudinal analyses (LA) of WAP response rates, both at specific time points and at the study level; assessment of pooled data using CMH analyses of WAP responders over the two intervals based on ≥40% and ≥50% improvements in pain; and an analysis of covariance (ANCOVA) assessment of change from baseline (CFB) in WAP daily scores of pooled data at specific time points.
Results: A total of 2428 pts with IBS-D were enrolled across both trials. A significantly greater proportion of ELX-treated pts (75 or 100 mg) were FDA and EMA composite endpoint responders compared with pts who received PBO ($p < 0.05$), with the exception of ELX 75 mg in IBS-3001 over Wks 1–26. CMH analyses of the pooled data showed no significant differences for WAP responders (ie ≥30% pain improvement for ≥50% of days; Table 1) between ELX-treated pts and those who received PBO. Significant differences were observed for ELX 100 mg over PBO for WAP responders at both the ≥40% and ≥50% pain improvement levels. Findings were similar for the pooled data ANCOVA CFB in WAP scores at Wks 12 and 26. At the study level, LA of WAP daily response rates showed significant improvement with ELX 75 mg vs PBO at Wk 26 in IBS-3001 (p = 0.016), and significant improvements for both ELX doses at Wks 12 and 26 in IBS-3002 ($p \leq 0.013$).
Table 1: Pooled WAP analyses

	Wks 1–12			Wks 1–26		
	PBO	ELX 75 mg	ELX 100 mg	PBO	ELX 75 mg	ELX 100 mg
≥30% WAP improvement*	42.3	45.0*0.261*	46.8*0.069*	44.0	46.3*0.357*	48.3*0.086*
≥40% WAP improvement*	35.8	40.1*0.078*	43.2*0.003*	37.7	41.5*0.122*	44.2*0.008*
≥50% WAP improvement*	30.0	34.7*0.047*	36.0*0.011*	32.5	36.4*0.101*	38.7*0.009*
CFB in WAP**	-2.6	-2.8*0.060*	-3.0*<0.001*	-3.0	-3.3*0.023*	-3.4*0.002*

*Percent responders and p values compared with PBO**CFB in WAP score and p value compared with PBO

Conclusion: Phase 3 trial findings demonstrated that ELX improves abdominal pain in pts with IBS-D, particularly for ELX 100 mg with ≥40% and ≥50% pain improvement definition for responders. This was further supported by LA of WAP daily response rates and ANCOVA CFB in WAP score analyses.
Disclosure of Interest: A. Lembo Consultancy: Forest Laboratories (now Actavis, Inc.), Salix Pharmaceuticals and Prometheus, L. Dove Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), D. Andrae Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), L. Turner Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), J. Davenport Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), P. Covington Consultancy: Actavis, Shareholder: Furiex Pharmaceuticals (subsidiary)

P0439 ROBUSTNESS OF ELUXADOLINE FOR THE TREATMENT OF IRRITABLE BOWEL SYNDROME WITH DIARRHOEA: RESULTS FROM PHASE 3 COMPOSITE ENDPOINT ASSESSMENTS

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Introduction: Eluxadoline (ELX), a locally active, mixed mu-opioid receptor agonist and delta-opioid receptor antagonist, has been shown to treat symptoms of irritable bowel syndrome with diarrhoea (IBS-D).
Aims & Methods: The robustness of ELX treatment was assessed by comparing the results of four composite efficacy endpoints across two double-blind, placebo (PBO)-controlled Phase 3 trials (IBS-3001, IBS-3002). Patients (pts) meeting Rome III criteria for IBS-D were randomised to twice-daily ELX (75 or 100 mg) or PBO. Efficacy was evaluated through 26 weeks (wks). Pts rated worst abdominal pain (WAP; 0–10 scale) and stool consistency (Bristol Stool Scale [BSS]) daily. The *primary efficacy* endpoint was a composite response (based on simultaneous daily improvement in WAP and stool consistency, with ≥50% of days demonstrating a response) evaluated over Wks 1–12 (Food and Drug Administration; with ≥60/84 days of diary compliance) and Wks 1–26 (European Medicines Agency; with ≥110/182 days of diary compliance). Other prospectively defined composite endpoints included: a *worst case* approach, using the same daily criteria but requiring an absolute ≥42/84 days or ≥91/182 days of response, respectively, regardless of diary compliance; weekly (wkly) *Method 1*, requiring a wkly average BSS of ≤5 if baseline average BSS ≥6, or a reduction in wkly average BSS scores of ≥1 point for pts with a baseline average BSS ≥5.5 and <6; wkly *Method 2*, requiring a ≥50% decrease in the number of days in a week when BSS was ≥6 compared with the number of days at baseline (Wk 1) when the BSS was ≥6. Both wkly methods used the same WAP criteria, ie ≥30% improvement in the wkly average of WAP scores compared with average baseline pain. Both wkly methods required improvement of WAP and BSS in the same wk for ≥6/12 wks for a pt to be considered a responder.
Results: A total of 2428 pts with IBS-D were enrolled across both trials. In general, significantly more pts receiving ELX were composite responders than those receiving PBO, regardless of the composite endpoint analysed ($p < 0.05$;

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Table 1: Prospective study-specific results

Responders (%)*p value vs PBO* PBO	ELX 75 mg	IBS-3001 ELX 100 mg	PBO	ELX 75 mg	IBS-3002 ELX 100 mg		
Daily composite endpoint ***Primary efficacy***	Wks 1–12	17.1	23.9*0.014*	25.1 *0.004*	16.2	28.9 < *0.001*	29.6 < *0.001*
Wks 1–26	19.0	23.4*0.112*	29.3 < *0.001*	20.2	30.4*0.001*	32.7 < *0.001*	
Daily composite endpoint ***Worst case***	Wks 1–12	16.6	23.4*0.013*	24.2*0.006*	13.9	28.3 < *0.001*	28.3 < *0.001*
Wks 1–26	15.9	22.7*0.012*	26.3 < *0.001*	15.7	28.9 < *0.001*	30.6 < *0.001*	
Wkly composite endpoint ***Method 1***	Wks 1–12	25.8	33.5*0.013*	36.2*0.001*	26.4	36.2*0.004*	37.7 < *0.001*
Wkly composite endpoint ***Method 2***	Wks 1–12	31.1	38.4*0.026*	41.8 *0.001*	32.7	38.6*0.091*	45.0 < *0.001*

Table 1). Comparable results for composite endpoints were seen for both ELX dose groups, although results for the 75 mg group were slightly less robust than for the 100 mg group at the study level. Data from pooled analyses showed similar findings.
Conclusion: Results from two Phase 3 trials demonstrate that ELX is an effective treatment for IBS-D based on robust results across multiple composite endpoints and across time.
Disclosure of Interest: B. Lacy Financial support for research: Participated in scientific advisory boards for Ironwood, Prometheus, Salix, and Forest (now Actavis, Inc.), L. Dove Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), D. Andrae Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), J. M. Davenport Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), L. Turner Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), R. Lopez Financial support for research: Actavis, Furiex Pharmaceuticals (subsidiary), Shareholder: Actavis, Furiex Pharmaceuticals (subsidiary), P. Covington Consultancy: Actavis, Shareholder: Furiex Pharmaceuticals (subsidiary)

P0440 ADDITION OF GLUCOSE TO FRUCTOSE REDUCES BREATH HYDROGEN BUT NOT SYMPTOMS IN FRUCTOSE MALABSORBERS WITH A FUNCTIONAL BOWEL DISORDER

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Introduction: Absorption of fructose is enhanced by the addition of equal amounts of glucose in healthy volunteers. The success of this strategy in improving absorption of fructose and in reducing abdominal symptoms when consuming free fructose or fructans in patients with functional bowel disorders is not known. This study aimed to address these issues by performing a randomised, double blind, cross-over trial.
Aims & Methods: Breath hydrogen and symptom response to six sugar solutions - glucose; sucrose; fructose; fructose + glucose; fructo-oligosaccharide (FOS); FOS + glucose – given in random order were assessed in patients with fructose malabsorption and a functional bowel disorder (Rome III). Following a 24 hour run-in period where participants consumed a diet low in fermentable carbohydrates (fibre and FODMAPs), participants collected breath samples at baseline and every 20 minutes for 4 h after consuming the sugar solution. A further 8 breath samples were collected hourly, during which only food low in FODMAPs was consumed. Breath hydrogen was calculated as area-under-the-curve. Symptom scores were recorded at the end of each day, using both 100 mm visual analogue scale and 4-point Likert scale.
Results: Of the 26 participants (3 female, aged 22-65 y), 21 had IBS, 3 functional bloating, 1 functional diarrhoea and 1 chronic constipation. Breath hydrogen response to 25 g fructose (775 ± 904 ppm.4 h (mean ± SD)) reduced during the first 4 h following the addition of 25 g glucose (84 ± 99; p = 0.012, t-test), which was similar to that after glucose alone (133 ± 175) or sucrose (155 ± 224). Breath hydrogen response to 10g FOS (3089 ± 1688) was not changed with the addition of glucose (2166 ± 1320; p = 0.559). Overall abdominal symptoms after fructose (median 15 mm, IQR 2-46) or FOS (19.2-32) were not changed with the addition of glucose (5.1-35; p = 0.236; 17.2-46, p = 0.926, respectively). Addition of glucose worsened abdominal pain when given with FOS (5.1-16 vs 13.2-18; p = 0.049) and nausea when given with fructose (1.0-2 vs 2.1-10; p = 0.018). When assessed by the Likert scale, addition of glucose to fructose increased nausea (p = 0.011) and to FOS increased nausea (p = 0.011) and wind (p = 0.027).
Conclusion: The results do not support the strategy of adding glucose to foods high in free fructose to reduce fructose malabsorption or to fructans as it does not reduce, and potentially worsens symptoms associated with consumption of these sugars in patients with functional bowel disorders.
Disclosure of Interest: None declared

P0441 TRANS-ANAL IRRIGATION THERAPY TO TREAT ADULT CHRONIC FUNCTIONAL CONSTIPATION: A SYSTEMATIC REVIEW

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Introduction: Trans-anal irrigation (TAI) is used widely to treat bowel dysfunction, although evidence for its use in adult chronic functional constipation remains unclear. Long-term outcome data are lacking, and the effectiveness of therapy in this patient group is not definitively known[1].
Aims & Methods: Evidence for effectiveness and safety was reviewed and the quality of studies was assessed. Primary research articles of patients with chronic functional constipation, treated with TAI as outpatients and published in English in indexed journals were eligible. Searching included major bibliographical databases and search terms: bowel dysfunction, defecation, constipation and irrigation. Fixed- and random-effect meta-analyses were performed.
Results: Seven eligible uncontrolled studies[1-7], including 243 patients, of retrospective or prospective design were identified. The definition of treatment response varied and was Investigator-determined. The fixed-effect pooled response rate was 50.4% (95%CI: 44.3% to 56.5%) but featured substantial heterogeneity ($I^2 = 67.1\%$). A random-effects estimate was similar: 50.9% (95%CI: 39.4% to 62.3%). Adverse events were inconsistently reported but were commonplace and minor.
Conclusion: The reported success rate of TAI is about 50%, which may be adequate for chronic constipation. Findings may vary between studies due to methodological or contextual differences. Evidence for TAI in functional constipation is weak: there is a need for well-designed prospective trials to evaluate the effectiveness of treatment.

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Disclosure of Interest: None declared

P0442 IN VITRO STUDIES ON THE ANTI-SPASMODIC AND ANTI-INFLAMMATORY POTENTIAL OF CHAMOMILE, MYRRH AND COFFEE CHARCOAL – COMPONENTS OF A TRADITIONAL HERBAL MEDICINAL PRODUCT (MYRRHINIL-INTEST®)

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Introduction: The herbal medicinal product Myrrhinil-Intest® consisting of myrrh, chamomile flower dry extract and coffee charcoal is marketed in Germany since 1959. Clinical data prove the effectiveness of this herbal

preparation for inflammatory intestinal disorders such as irritable bowel syndrome, functional diarrhea as well as inflammatory bowel disease (colitis ulcerosa) [1,2]. However, the underlying pharmacological mechanisms within the gastrointestinal system have not yet been fully elucidated.
Aims & Methods: Objective of this study was to assay the herbal components for their effect on intestinal motility and inflammation. Thus, spasmolytic activity was determined using isometric tension measurement in isolated rat small intestinal preparations. An *in vitro* TNBS inflammation model in rat small intestinal preparations was used to determine anti-inflammatory activity. Therefore, the effect of the plant extracts on TNBS induced inflammatory damage was characterised based on TNFα-gene expression analysis, isometric contraction measurement and histological analysis. Furthermore, TNFα release from LPS-stimulated THP-1 cells was assayed. Additionally, microarray gene expression analysis was performed in LPS/IFNγ stimulated native human macrophages to determine underlying mechanisms.
Results: Chamomile flower (KA) and ethanolic myrrh extract (MY) exerted a spasmolytic effect by inhibiting the acetylcholine-induced contractions to 56% (KA: IC50 = 160 µg/ml) and 10% (MY: IC50 = 158 µg/ml) respectively. Serial testing with increasing concentration of the calcium-channel agonist (BAY K8644, 10^{-10}–10^{-7} M) in the presence of different MY concentrations (0.15 - 0.35 mg/ml) demonstrated that MY acts via inhibition of L-type calcium channels.
With regard to anti-inflammatory activity, chamomile flower and aqueous myrrh extract (0.1–100 mg/ml) normalised the TNBS-induced overexpression of TNFα-mRNA as well as TNBS-induced loss of contractility and decrease in mucosa layer thickness concentration-dependently, whereas coffee charcoal (0.1-100 µg/ml) had no effect in the TNBS inflammation model. LPS-induced TNFα release from THP-1 cells was inhibited concentration-dependently by ethanolic myrrh extract (IC50 = 60.65 µg/ml), chamomile flower extract (IC50 = 439 µg/ml) and coffee charcoal extract (IC50 = 1886 µg/ml). Furthermore, chamomile flower (200 µg/ml) and coffee charcoal extract (500 µg/ml) markedly influenced the gene expression profile of LPS/IFNγ-stimulated human macrophages. Coffee charcoal inhibited the LPS/IFNγ-induced expression of genes associated with chemokine signalling.
Conclusion: The presented study demonstrates the pharmacological potential of the herbal ingredients of the fixed combination with respect to its spasmolytic and anti-inflammatory activities within a multi-target principle. Taken together, it could be demonstrated that the components are able to target gastrointestinal disorders by exerting antispasmodic and anti-inflammatory effects which reinforce the reported clinical effectiveness.

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P0443 FOUR YEARS FOLLOW UP OF GUT-DIRECTED GROUP HYPNOSIS IN PATIENTS WITH REFRACTORY IRRITABLE BOWEL SYNDROME – A LONG TERM SUCCESS

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Introduction: We previously showed that gut directed group-hypnosis (GHT) has a significant beneficial effect for patients with refractory irritable bowel syndrome (IBS).
Aims & Methods: Aim of this follow up (FU) study was to investigate long-term effects of GHT over four years. All 46 participants with GHT of our previous randomized controlled trial were invited to complete the IBS-impact scale (IBS-IS) for IBS related quality of life (higher values mean less complaints), the hospital anxiety and depression scale (HADS), visual analogue scales (VAS) for physical and psychological well-being as well as individual IBS symptoms.
Results: 30/46 patients (65%) completed all FU-questionnaires. After a mean duration of 4.13 years FU IBS-related quality of life and affective status showed a significant improvement compared to baseline (IBS-IS: 3.53 vs. 5.38 at FU, $p<.001$; HADS-depression: 6.28 vs. 4.14 at FU, $p<.05$; HADS-anxiety: 9.69 vs. 6.83 at FU, $p<.001$). Also VAS-scores for physical and psychological well-being, as well as individual symptoms revealed a significant improvement ($p<.001$, respectively $p<.01$). Gender, IBS-subtype and practising of hypnosis had no influence on this success of GHT.
Conclusion: The beneficial effects of GHT are long lasting over 4 years in patients with refractory IBS. Therefore GHT is a highly valuable therapy option and should be offered in tertiary centres.

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Disclosure of Interest: None declared

P0444 A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL OF THE EFFECT OF DIETARY FERMENTABLE CARBOHYDRATES ON THE COLON USING MAGNETIC RESONANCE IMAGING: SUPPLEMENTARY OLIGOFRUCTOSE INCREASES COLONIC VOLUME BUT SO DOES THE LOW FODMAP DIET

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Introduction: Magnetic Resonance Imaging(MRI) can be used to assess gastrointestinal (GI) function non-invasively without the use of ionising radiation. An uncontrolled pilot study (UEGW2014) found that supplementing the diet of healthy volunteers for a week with oligofructose(OF) 5g bd increased fasting colonic volume by 18%. Adoption of a diet low in fermentable oligo-, di-, mono-saccharides and polyols (FODMAPs), such as OF, has been shown to reduce symptoms of irritable bowel syndrome.
Aims & Methods
Aim: to investigate the effect of altering the amount of fermentable carbohydrate in the diet on colonic physiology and fermentation. The hypotheses were 1) starting a low FODMAP diet would reduce colonic volume, 2) supplementing the diet with OF would abolish the effect.
Methods: A parallel group, double-blind, randomised controlled trial in adult volunteers without previous GI disorders. Subjects followed their usual diet for a week. At 0800 on day 7 they swallowed 5 MRI transit markers, were counselled on the low FODMAP diet by a registered dietitian and were given a standard food package (UK diet) for the rest of the day. At 0800 on day 8 they attended fasted for MRI scan and tests of breath hydrogen (H_2) and methane (CH_4). All subjects then followed the low FODMAP diet for a week, but were randomised to take Maltodextrin (MD) or OF 7g bd. On day 7 transit markers and testing were repeated with another standard food package (low FODMAP). Supplement was continued until the night before tests.
Primary endpoint: percentage change from baseline in colonic volume. Secondary endpoints: a measure of whole gut transit, the weighted average position score of the transit markers 24h after ingestion (WAPS24); breath H_2 and breath CH_4. Food diaries were kept for both weeks preceding MRI.
Results: Data presented as mean (95%CI). 37 subjects completed the study (19OF:18MD). One subject (MD) had corrupted images and was excluded from MRI analysis. Compliance with diet and supplements was good. Contrary to our hypothesis CV increased on MD from 650mL (558–742) to 740mL (616–865) or 15.5% (2.5–28.4, $p<0.05$). The increase was greater in the OF group: from 693mL (620–765) to 803mL (732 —874) or 19.6% (6.5–32.7, $p<0.01$) but the difference between groups was not significant. Breath H_2 response of the groups diverged ($p<0.01$): on MD H_2 fell by 11ppm (3–18) but on OF H_2 rose by 16ppm (−2–35). WAPS24 and CH_4 did not change from baseline significantly in either group, with no difference between groups.
Conclusion: Fasting breath hydrogen fell on a low FODMAP diet and rose with OF use, confirming previous studies[1,2]. Contrary to the study hypothesis colonic volume increased significantly on the low FODMAP diet, an effect that may be due to the presence of replacement substrate for colonic bacteria in substituted foods (e.g. tapioca or potato). Since the low FODMAP diet did not lead to a reduction in colonic distension other mechanisms for any clinical effect, such as changes in the microbiota, may need consideration.

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Disclosure of Interest: None declared

P0445 A SINGLE-BLIND STUDY EVALUATING THE EFFECTS OF A GLUTEN-FREE DIET IN DIARRHOEA PREDOMINANT IRRITABLE BOWEL SYNDROME

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Introduction: Gluten has been shown to alter bowel barrier function in patients with diarrhoea-predominant irritable bowel syndrome (D-IBS), particularly those who are HLA-DQ2 and/or DQ8 positive.
Aims & Methods: We aimed to assess the clinical response to a gluten-free diet (GFD) in D-IBS patients previously naïve to the effects of gluten and blinded to HLA-DQ status.
We enrolled 48 D-IBS patients (24 HLA-DQ negative and 24 HLA-DQ positive) to undertake a six-week GFD following dietetic input. Both patients and dietitian were blinded to HLA-DQ status. Validated questionnaires were self-completed at baseline and at week-6. The primary end-point was mean-change in IBS-severity scoring system (IBS-SSS), with a 50-point reduction conferring clinical benefit. Secondary end-points were change in hospital anxiety and depression score (HADS), fatigue impact score (FIS), and short-form 36 (SF-36).
Results: Data from 41 patients (74.4% women, mean-age 40.3yrs) was available for per-protocol-analysis. Of these, 21 were HLA-DQ negative and 20 HLA-DQ positive; baseline characteristics were similar other than worse pain-frequency ($p=0.03$), physical-fatigue (0.04), and vitality (0.05) in the HLA-DQ positive group. Overall, a GFD reduced IBS-SSS $\geq$50 points in 71% ($n=29$). In fact,

the mean-total IBS-SSS decreased from 286 to 131 points (change -155, $p < 0.001$), which was seen similarly across both HLA-DQ groups. However, HLA-DQ negative subjects showed a greater reduction in abdominal distension in the first four weeks compared to HLA-DQ positive ($P = 0.04$), although this was non-significant by week-6. There was a marked improvement in HADS, FIS, and SF-36 amongst both groups. However, HLA-DQ positive subjects showed a greater response to depression ($p = 0.02$), fatigue (physical, $p = 0.04$; cognitive, $p = 0.07$) and vitality ($p = 0.05$) compared to HLA-DQ negative subjects. On study completion, 90% ($n = 37$) were discharged and 61% ($n = 25$) continued with a GFD.

Conclusion: A GFD is a therapeutic option for the management of D-IBS. A clinical improvement was seen in 71% of patients undertaking a six-week GFD, with 61% opting to continue with a GFD for the foreseeable future. The pathophysiological mechanism may differ according to HLA-DQ status.

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Disclosure of Interest: None declared

P0446 IS THE RESPONSE TO IBODUTANT MAINTAINED IN IBS-D FEMALE PATIENTS AFTER STOPPING TREATMENT? AN IRIS-2 EXPLORATORY ANALYSIS

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Introduction: Ibodutant, is a potent antagonist of neurokinin-2 receptors currently in phase III clinical development for Irritable Bowel Syndrome with Diarrhea (IBS-D). A phase II study (IRIS 2) tested the efficacy of 8-week oral treatment with 3 doses of ibotudant (1 mg, 3 mg, 10 mg) in 559 IBS-D patients defined by Rome III criteria. The treatment period was followed by a 2-week treatment-free withdrawal period. Based on the response to the binary question on the combined satisfactory relief of IBS symptoms and abdominal pain/discomfort a statistically and clinically relevant efficacy was demonstrated in the female subgroup ($n = 333$) at the 10 mg dose ($p = 0.003$ over placebo).

Aims & Methods: To evaluate the maintenance of treatment response in the female IBS-D population exposed to ibodutant after 2 weeks of treatment withdrawal versus placebo.

During the whole study, patients reported on a weekly basis their overall IBS symptom relief and abdominal pain/discomfort relief (binary yes/no question: "*Did you have satisfactory relief of your overall IBS symptoms during the last week?*" and "*Did you have satisfactory relief of your abdominal pain or discomfort during the last week?*"). The rate of responders (50% rule) developed during the 2-week withdrawal phase was compared versus the last two weeks of treatment to assess the maintenance of effect.

Results: The frequency of responders given at week 7 to 8 (last 2 weeks of treatment) and at the end of the withdrawal phase (week 9 to 10) is given below.

IBS-D Females (N = 333) No of Responders (%)	Ibodutant 1 mgN = 89	Ibodutant 3 mgN = 87	Ibodutant 10 mgN = 79	Placebo N = 78
Week 7-8	58 (65.2%)	52 (59.8%)	58 (73.4%)	41 (52.6%)
Week 9-10	51 (57.3%)	51 (58.6%)	47 (59.5%)	36 (46.2%)
Change %	7 (7.9%)	1 (1.2%)	11 (13.5%)	5 (6.4%)

The number of responders declined at the end of the 2-week treatment-free withdrawal phase in all treatment groups, with the maximum decline at the efficacious dose of 10 mg once daily (13.5% less patient who maintained their response during the withdrawal phase was lowest in the placebo group (approximately 6.4%)).

Conclusion: When ibodutant treatment was withdrawn and patients continued to report their IBS-symptoms the responder rates declined notably in the 10 mg treatment group, thus confirming the role of ibodutant as maintanance treatment in IBS-D. The highest decline at the 10 mg dose showing efficacy versus placebo, while comparatively well maintained response rate in the other treatment arms, gives additional evidence of the true treatment effect of ibodutant at 10 mg dose.

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P0447 ONE-YEAR FOLLOW-UP OF NURSE–ADMINISTERED GUT-DIRECTED HYPNOTHERAPY FOR PATIENTS WITH IBS

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Introduction: Gut-directed hypnotherapy is an effective treatment for patients with irritable bowel syndrome (IBS), but it is costly, time consuming and availability is a problem. We have recently reported good short-term effectiveness of nurse-administered, gut-directed hypnotherapy in a tertiary care centre (Lövdahl et al Am J Clin Hypnosis 2015).

Aims & Methods: Our aim was to determine the long-term results of nurse-administered, gut-directed hypnotherapy and to identify factors predicting treatment outcome at one-year follow-up. We included 85 patients with IBS (mean age 40 (20-70 years; 60 women) with symptoms refractory to standard management. Participants received hypnotherapy administered by a nurse once/week for 12 consecutive weeks. Response to treatment was assessed with the IBS Severity Scoring System, IBS-SSS before, during (6 weeks) and immediately after the hypnotherapy treatment period (12 weeks), as well as during follow-up at week 26 ($n = 77$) and one year ($n = 68$). Patients also completed questionnaires at baseline, week 12, 26 and one year assessing the severity of extracolonic symptoms, anxiety and depression and GI-specific anxiety.

Results: At the end of the treatment period, i.e. at week 12, 50 patients (59%) were responders (IBS-SSS score reduction ≥ 50). At follow-up (week 26 and one year), 86 and 79%, respectively, of responders at week 12, were still responders; in total the responder rate at both week 26 and one year was 62%. Compared to baseline, at the one-year follow-up patients reported marked improvement of IBS symptoms (IBS-SSS: 335 (253,384) vs. 212 (147,287) (median, (IQR); $p < 0.0001$) as well as of extra-colonic symptoms ($p < 0.0001$), GI-specific anxiety ($p < 0.0001$), general anxiety ($p < 0.0001$) and depression ($p < 0.001$) Responder status already at week 6 could predict the responder status of the patients at week 26 ($p < 0.0001$) and at one year ($p = 0.003$), but no baseline variables could predict the one-year outcome. Being a responder at the one-year follow-up based on IBS symptom improvement (IBS-SSS score reduction ≥ 50 vs baseline) was also associated with a greater improvement in depression ($p = 0.01$), GI-specific anxiety ($p < 0.0001$) and extra-colonic symptoms ($p = 0.002$).

Conclusion: Nurse-administered gut-directed hypnotherapy is an effective treatment option with good long-term results for patients with IBS symptoms refractory to other treatments. A rapid clinical response during hypnotherapy predicts good long-term results, and the IBS symptom improvement at one year is associated with improvement also in psychological and bodily symptoms.

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P0448 LARGEST REPORTED PROSPECTIVE EVALUATION OF A LOW FODMAP DIET IN IBS PATIENTS IN A REGIONAL HOSPITAL

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Introduction: The irritable bowel syndrome (IBS) is a highly prevalent condition with unclear underlying pathophysiology and for which no standard effective therapy is established. A number of recent studies have shown that fermentable oligo-, di-, mono-saccharides and polyols (FODMAPS) alter intestinal physiology and can trigger gastrointestinal symptoms, while a low FODMAP diet improves symptoms in tertiary care IBS patients.

Aims & Methods: Our aim was to perform a prospective study to determine whether a low FODMAP diet improves symptoms in IBS patients in the setting of a regional hospital in Belgium.

Consecutive IBS patients, seen at the gastroenterology outpatient clinic, were instructed how to take a low FODMAP diet by an experienced dietician. All patients were asked to score their symptom severity before and 8 weeks after the implementation of a low FODMAP diet. The intensity of 5 symptoms (bloating, abdominal cramps, borborygmi, stool disturbances, fatigue) was evaluated using 0 to 100 mm visual analogue scales (VAS). The global effect of the low FODMAP diet was also evaluated by means of a VAS (0mm = no improvement to 100mm = complete symptom resolution). VAS are reported as mean+/-standard deviation. Responses were compared using the Wilcoxon signed rank test. Results were considered significant if $p < 0.001$.

Results: Eighty-two patients with IBS according to Rome III criteria, 83% females, mean age 39 ± 12 years, were included in this prospective study. After 8 weeks of low FODMAP diet, we found a significant reduction of global symptom score (sum of all evaluated symptoms) (318 ± 61 vs. 131 ± 61; $p < 0.001$). An improvement of $>50\%$ of the global symptom score was observed in 65% of the patients. The low FODMAP diet also improved all cardinal IBS symptoms (abdominal pain, 63 ± 21 vs. 29 ± 20 mm; bloating 58 ± 20 vs. 30 ± 22mm; flatulence 69 ± 18 vs. 30 ± 20 mm and stool disturbances (64 ± 20 vs. 30 ± 20mm) (all $p < 0.001$). In addition, fatigue was significantly less with a low FODMAP diet (63 ± 20 vs. 41 ± 26mm, $p < 0.001$). The

global efficacy rating was 65 ± 24mm on the VAS. Of the 82 patients, 21 had a result of >90mm, these patients can be considered as complete responders.
Conclusion: A diet low in FODMAPs effectively reduces IBS symptoms and fatigue in secondary care practice. Robust symptom improvement occurs with a strict low FODMAP diet. To our knowledge, this prospective study is the largest reported trial in a regional hospital and confirms the results obtained in tertiary care centers. The results support the use of dietary intervention in IBS in general clinical practice.
Disclosure of Interest: None declared

P0449 LOW FODMAP ADVICE FOR PATIENTS WITH IRRITABLE BOWEL SYNDROME: LONG-TERM OUTCOMES FOR SYMPTOMS AND DIETARY INTAKE

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Introduction: Short chain fermentable carbohydrate (FODMAP) restriction reduces symptoms of irritable bowel syndrome (IBS) and is routinely used in clinical practice. Comprehensive FODMAP education incorporates a low FODMAP exclusion diet for 4-8 weeks followed by FODMAP reintroduction to test individual tolerance. Patients are empowered to self-manage their diet and symptoms, however whether this approach is effective in the long term is unknown. Previous research has indicated that after 4 weeks of FODMAP exclusion, calcium intakes are low.
Aims & Methods: This study aimed to assess the long-term effectiveness of the low FODMAP diet and the impact on dietary intake in patients with IBS.
Patients with IBS (n = 375) from primary and secondary care were invited to take part in a prospective questionnaire study after completion of comprehensive FODMAP education from a dietitian as described above. Symptoms were assessed at baseline before FODMAP education, following FODMAP exclusion (4-8 weeks) and following FODMAP reintroduction (6-18 months) using the global symptom question "Do you currently have satisfactory relief of your gut symptoms?" and the Gastrointestinal Symptom Rating Scale. Dietary adherence to long-term FODMAP restriction was assessed using a Likert scale and dietary intake was measured using a validated FODMAP FFQ and compared to UK dietary reference values (DRVs). Statistical analyses used the chi-squared test.
Results: Questionnaires from 103 patients were received (age: mean ± sd; 48 ± 15 years, female: n = 76). Following FODMAP exclusion, 63 (61%) patients reported satisfactory relief. Of these, 44/63 (70%) continued to report satisfactory relief following FODMAP reintroduction in the long term. Of those who had satisfactory relief on initial FODMAP exclusion, significantly more reported absent or mild abdominal pain (n = 52 vs n = 20; P < 0.001), bloating (n = 46 vs n = 19; P = 0.009), flatulence (n = 45 vs n = 12; P < 0.001), borborygmi (n = 49 vs n = 21; P = 0.007), urgency (n = 48 vs n = 17; P = 0.001), sensation of incomplete evacuation (n = 49 vs n = 21; P = 0.007) and lethargy (n = 46 vs n = 20; P = 0.018) over the long term, than those who did not have satisfactory relief on initial FODMAP exclusion. In the long term, 78 patients continued to follow an adapted low FODMAP diet and their total mean ± sd FODMAP intake was 20.9g ± 15.1 compared to 29.4g ± 22.9 for 19 patients following a normal diet. The mean ± sd calcium and iron intakes for the whole group (n = 103) were 1130mg ± 682 and 13.7mg ± 4.6 respectively. Of the 78 who continued to follow an adapted low FODMAP diet, 59 (76%) and 55 (71%) patients met the calcium and iron DRVs.
Conclusion: The majority of patients who achieve satisfactory relief of symptoms following FODMAP exclusion continue to have satisfactory relief in the long term indicating that FODMAP education is useful for long-term symptom control and self-management. The majority of patients continue to follow an adapted low FODMAP diet and approximately three-quarters meet their calcium and iron requirements in the long term.
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P0450 GUT-DIRECTED HYPNOTHERAPY IS NOT INFERIOR TO THE LOW-FODMAP DIET IN REDUCING SYMPTOMS ASSOCIATED WITH IRRITABLE BOWEL SYNDROME: A RANDOMISED CLINICAL STUDY

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Introduction: Obtaining high-quality evidence for efficacy of gut-directed hypnotherapy (GDH) in patients with irritable bowel syndrome (IBS) is constrained by the difficulty in designing a blinded placebo. An alternative is to compare GDH to a therapy with proven efficacy, such as the low FODMAP diet (LFD), which benefited 70% of such patients in a recent randomised, controlled trial[1]
Aims & Methods: This study aims to determine if GDH is non-inferior in efficacy to the LFD and to assess whether they have additive effects. A randomised controlled trial was performed in IBS patients (Rome-III) comparing (a) LFD: education at the beginning of week 1, review at week 6; (b) GDH: six weekly one-hour hypnosis sessions for 6 weeks; (c) a combination of both. The primary endpoint was the change in overall gastrointestinal (GI) symptoms as evaluated using a 100 mm visual-analogue-scale from baseline to week 6. Secondary endpoints were the change overall GI symptoms from baseline to 6-months post-treatment and the change in individual gastrointestinal symptoms (abdominal pain, bloating, wind, satisfaction with stool consistency and nausea), psychological indices including anxiety and depression as assessed by the Hospital Anxiety and Depression Scale (HADS) and IBS-related Quality Of Life (QOL) from baseline to week 6 and 6-months post treatment.
Results: Of 74 participants (mean age 40, SD 14 y; 14 male), 25 received GDH, 24 the LFD, and 25 combination therapy. The groups were well matched. Overall GI symptoms improved from baseline to week 6 by mean [95% CI] of 33 [25, 41], 30 [19, 42] and 36 [27, 45] mm, respectively (all $p < .0001$) with no differences across the groups ($p = .67$; one-way-between-groups ANOVA). Improvement (≥20 mm reduction) was achieved in 72% who received GDH, 71% LFD and 72% combined treatment. Overall symptoms remained improved from baseline to 6 months by 38 [27, 50], 30 [16, 43] and 27 [14, 40] mm ($p < .0001$). 74% receiving GDH, 82% LFD and 54% combined treatment maintained their response. Significant reductions in abdominal pain, bloating, wind and stool consistency, but not nausea were observed from baseline to week 6 and 6 months. No differences in improvement were observed for individual GI symptoms across treatment groups at either timepoint. Anxiety significantly reduced at week 6 and was maintained 6 months post-treatment in those who received GDH and LFD. Long-term improvement for depression was only observed following GDH. IBS-QOL significantly improved in all treatment groups from baseline to week 6 but was only maintained 6-months post-treatment for those who received the combined treatment. No difference in any psychological index was observed across treatment groups from baseline to week 6 or 6-months.
Conclusion: Efficacy of GDH is not inferior to that of LFD for relief of GI symptoms in IBS patients, but they do not show additive effects. Improvement in in psychological status was in general independent of the mode of treatment. GDH is an effective alternative to the LFD, but the lack of additive effect is unexplained.

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Disclosure of Interest: P. Gibson Conflict with: Published book on diet in IBS, S. Peters: None declared, C. Yao: None declared, S. Shepherd Conflict with: Published books on diet in IBS and coeliac disease, H. Philpott: None declared, G. Yelland: None declared, J. Muir: None declared

P0451 GENDER RELATED DIFFERENTIAL EFFECT OF TACHYKININ NK2 RECEPTOR-MEDIATED VISCERAL HYPERALGESIA IN GUINEA PIG COLON

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Introduction: The tachykinin NK_2 receptor antagonist ibodutant is currently under clinical investigation for treating irritable bowel syndrome (IBS) with diarrhea, having shown a greater efficacy in female gender (Tack et al., 2013).
Aims & Methods: Aim of this study was to investigate the NK_2 receptor-related gender specificity in a model of colon visceral hyperalgesia. Colitis was induced by rectal instillation of TNBS (0.5 ml, 30 mg/ml in 30% ethanol) in female and male guinea pigs. Electromiographic visceromotor responses (VMR) to colorectal distension (CRD, 0.5-1-1.5-2 ml) was evaluated 3 days after. Ibodutant was evaluated at the doses of 0.33, 0.65, 1.9, and 6.5 mg/kg (s.c., 30 min before CRD) both in inflamed and control animals. The release of neurokinin A (NKA) following treatment (15 min superfusion) of KCl (80 mM) or capsaicin (10 μM) was measured by EIA in both mucosal and smooth muscle dissected distal colon tissues of control and inflamed animals. Pharmacokinetic parameters of ibodutant following a single s.c. administration (0.73 or 2.1 mg/kg .) were measured in the plasma (0-24h).
Results: Ibodutant did not affect VMR following CRD in control animals at any of the used doses. After TNBS-induced colitis ibodutant inhibited the increased visceral hypersensitivity (evident at the lower CRD volume) in female animals by 55 ± 15% at 0.33 mg/kg dose, and the inhibition was total at the higher doses. In male animals the ibodutant 0.65 mg/kg dose was uneffective, and the 1.9 mg/kg inhibited the VMR by 79 ± 9%. Ibodutant pharmacokinetic parameters did not differ between females and males at both tested doses (0.73 and 2.1 mg/kg). NKA was released following KCl and capsaicin treatment and it was generally greater in smooth muscle than in mucosal specimens. Differences dependent on the animal gender were evident in the release from distal colon and especially in the mucosal preparations: the NKA release induced by KCl in control males was 3.9-fold greater than in female preparations (P = 0.0469).
Conclusion: Present results indicate that ibodutant is effective in preventing abdominal pain in a model of visceral hypersensitivity in guinea pigs with a greater efficacy in females. The differences observed in mucosal nerve activation may reflect its participation in colonic visceral hypersensitivity (Hoffman, 2012), and possibly gender related differences.

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controlled, parallel-group phase II study (the IRIS-2). No. 520; *Digestive Disease Week*, 2013.

Disclosure of Interest: None declared

P0452 EFFECTIVENESS AND TOLERABILITY OF LINACLOTIDE IN THE TREATMENT OF IBS-C IN A REAL-WORLD SETTING: RESULTS FROM A GERMAN NON-INTERVENTIONAL STUDY

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Introduction: Recent studies suggest that symptom control of IBS-C is only rarely achieved with medications traditionally used for this disorder[1]. Linaclotide is the first compound licensed by the EMA for the treatment of moderate to severe IBS-C. In two phase 3 clinical trials, linaclotide has been shown to significantly improve major symptoms of IBS-C including abdominal pain/discomfort, bloating and constipation[2]. How clinical efficacy translates into effectiveness in a european real world setting, however, has not been investigated.

Aims & Methods: This study sought to elucidate the effectiveness and tolerability of linaclotide in the treatment of IBS-C in everyday clinical practice in Germany. The study was designed as a multicentre, non-interventional, prospective study, scheduled over 12 months. Patients included, were $\geq$18 years old and suffered from moderate to severe IBS-C. The decision for treatment with linaclotide was taken solely by the attending physician prior to study initiation. Data was recorded during regular patient visits (approx. 0, 4, 12, 24 weeks after start of treatment and in week 52 or at the end of treatment). Endpoints for measuring effectiveness include among others abdominal pain and bloating (11-NRS) and number of bowel movements. Tolerability was assessed recording the frequency and severity of adverse Events (AE) as well as the physician's evaluation of tolerability.

Results: 79 centers participated in the study, 375 patients were enrolled. The average time of observation was 4.4 months (median 5 months). Abdominal pain [11-NRS] improved by more than 50% compared to baseline (4.9 points at baseline vs. 2.4 points at 12 months (LOCF); $p < 0.0001$). Intensity of bloating [11-NRS] improved to a similar degree (5.3 points at baseline vs. 2.7 points at 12 months (LOCF); $p < 0.0001$). Bowel movements increased from 2.7 per week at baseline to 4.4 at 12 months (LOCF), $p < 0.0001$. A subgroup analysis revealed, that patients who had failed to receive symptom relief when taking a traditional IBS-C medication prior to study initiation, showed a similarly pronounced treatment response to linaclotide as the overall study population. More than 90% of physicians assessed the tolerability at 6 months as either excellent or good. 50 adverse events (AE) occurred in 27 patients. Three AE in two patients were reported as serious (diarrhea and abdominal cramps). Upon cessation of treatment both patients recovered within one day.

Conclusion: Linaclotide proved to be safe and effective in reducing major symptoms of IBS-C in everyday clinical practice. Further, this study indicated, that patients with a history of failed treatment attempts for IBS-C, alike may benefit from Linaclotide. The improvement of IBS-C symptoms in response to linaclotide, as found in this study, was comparable to that seen in clinical trials.

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P0453 INCIDENCE OF COLON CANCER AFTER TREATMENT OF ACUTE COLONIC DIVERTICULITIS IN JAPAN

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Introduction: Although a few studies have reported the relation between colon cancer and acute colonic diverticulitis (ACD) in western countries, it had not yet been examined in Japan.

Aims & Methods: The purpose of this study was to determine the relationship between ACD and colon cancer in Japan. This study protocol was approved by the ethics committee at Tokyo Saiseikai Central Hospital (TSCH). Between January 1998 and January 2009, 420 ACD patients were diagnosed and treated in TSCH. ACD diagnosis was established by US and/or CT. Patients were treated conservatively and/or surgically. In tracking the patients, questionnaires were sent in order to obtain information on the development of colon cancer. The Cox proportional hazards model was performed to identify risk factors for colon cancer using information about family history of colon cancer, polyps, BMI (body mass index), physical exercise, dietary preferences (meat intake, fiber intake, etc.) smoking habits and alcohol consumption.

Results: One hundred and eleven patients answered the questionnaires, and their median (intraquarter range) follow-up periods were 9.3 (5.3) years. Nineteen patients had a history of recurrent ACD. The patient characteristics are summarized in Table 1. Three cases (2.7%) after treating ACD developed colon cancer. In this study, the incidence rate was calculated to be 276.3/year*-million (mean age 55.5 years-old), while the recent incidence rate of colon cancer among 55 to 60-year-old Japanese is estimated to be 90.975/year*million. Case 1: a 68-year-old male without a history of ACD was diagnosed with colon cancer and surgically treated 5 months after being treated for ACD. The severity of ACD was moderate and had been treated conservatively. Case 2: a 60-year-old female without a history of ACD was diagnosed with colon cancer and surgically treated a month after being treated for ACD. The patient's ACD was complicated by a small abscess and was treated conservatively. Colon cancer was not identified through a CT at admission, but was diagnosed by colonoscopy a month after ACD treatment. Case 3: a 68-year-old female with a history of ACD was diagnosed with colon cancer and surgically treated 43 months after being treated for ACD. She was also treated for colon polyps at the same time. The severity of ACD was moderate and treated conservatively.**Table1:** Patients Characteristics

Presenting features	n = 111
Mean (range) age (yr)	55.4 (18-91)
Gender (M/F)	72/39
Location of ACD (Rt/Lt)	75/36
Hx. of recurrent ACD	19
Complicated ACD	9
Treatment of ACD (conservative/surgery)	107/4
Family Hx. of colon cancer	9
Family Hx. of colon polyp	8
Occurrence of colon cancer	3
Occurrence of colon polyps	27

Conclusion: We found three cases of colon cancer post ACD. The incidence rate seems to be higher than that in the general population, but we are not able to conclude the relationship between ACD and colon cancer because of the small number of cases and the short duration of tracking time.

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Disclosure of Interest: None declared

P0454 SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE OF THE COLON DOES NOT SHOW ALTERATION OF FECAL MICROBIOTA

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Introduction: Data on fecal microbiota in symptomatic uncomplicated diverticular disease (SUDD) of the colon are lacking. We assessed therefore fecal microbiota in SUDD, comparing it with patients with asymptomatic diverticulosis and with healthy people.

Aims & Methods: Seventeen female patients with SUDD (median age 64.5 ± 4.7 yrs, range 56-68 yrs), 16 female patients with asymptomatic diverticulosis (median age 61.6 ± 4.0 yrs, range 52-70 yrs) and 19 healthy women (median age 59.0 ± 5.0 yrs, range 563-69 yrs) were analysed. Patients came from the same residence area.

Stool samples were collected at least 4 weeks after colonoscopy. Real-time PCR was used to quantify targeted microorganisms using the Applied Biosystems 7500 Real-Time PCR instrument. *Bifidobacterium* genus, *Clostridium coccoides* group, *Bacteroides-Prevotella* group, *Escherichia* subgroup, *Lactobacillus* genus and *Akkermansia muciniphila* were assessed for the qualitative analysis.

Results: There were no differences in the demographic characteristics among the three groups. The overall bacterial quantity did not differ among the three groups. Thus, a colonic bacterial overgrowth was absent in SUDD ($p = 0.449$). The quantitative analysis of bacterial populations in feces assessed by real-time PCR showed no difference in the numbers of rRNA gene copies neither for the total bacteria nor for the different types analysed in the stool samples in the three study groups (*Akkermansia*: $p = 0.298$; *Bacterioides*: $p = 0.354$; *Bifidobacterium*: $p = 0.876$; *Clostridium*: $p = 0.463$; *Escherichia*: $p = 0.728$; *Lactobacillus*: $p = 0.633$).

Conclusion: SUDD does not show colonic bacterial overgrowth nor any significant qualitative alteration of the fecal microbiota. Further studies are requested to investigate whether bacterial imbalance involving other bacterial strains may be detected in those patients.

Disclosure of Interest: None declared

P0455 THE ROLE OF ENDOSCOPIC THERAPY IN THE MANAGEMENT OF ACUTE COLONIC DIVERTICULAR BLEEDING

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Introduction: Colonic diverticular bleeding (CDB) may require endoscopic therapy in the acute setting to stop the hemorrhage and avoid surgery. However identification of the bleeding diverticula with endoscopic hemostasis is not always feasible.
Aims & Methods: The aim is to evaluate the efficacy of endoscopic hemostasis in acute CDB in a period of 5 years. We performed a retrospective observational study of patients who underwent endoscopic therapy in CDB between January 2010 and December 2014.
Results: 156 admissions with CDB in this period were identified. In 15.4% of cases the bleeding diverticula was identified and endoscopic treatment was attempted in all of them. 79.1% were male patients with mean age 78.4 ± 7.3 years. Hemostatic modalities employed: combination of adrenaline injection plus hemoclips in 54.2%, hemoclips in 20.8%, adrenaline in 16.7% and argon plasma coagulation in 8.3%. The rate of rebleeding was in 12.5% within the first 72 hours. Endoscopic hemostasis was attempted again in all cases of bleeding recurrence and it was well succeeded in 66.7%. However, 33.3% (n = 1) needed urgent surgical treatment.
Conclusion: Endoscopic therapy in CDB is safe and has a high success rate. The choice of endoscopic technique did not appear to influence the success of therapy.
Disclosure of Interest: None declared

P0456 NATURAL HISTORY OF ACUTE COLONIC DIVERTICULAR BLEEDING

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Introduction: Colonic diverticular bleeding (CDB) is a common cause of lower gastrointestinal bleeding. Treatment measures may include endoscopic, radiological and surgical options.
Aims & Methods: The aim is to characterize epidemiological, clinical and endoscopic features of patients with CDB in a period of 5 years. We performed a retrospective observational study of patients with CDB admitted in a Gastroenterology unit between January/2010-December/2014.
Results: We included 126 patients with a total of 156 admissions. 59.6% were men and the mean age was 78.7 years (range 51 – 96). The average length of stay in the gastroenterology unit was 5 days. 30.1% required blood transfusion with a mean of 2.7 units of packed red blood cell units per transfused patient. 33.4% were under anti-platelets or non-steroidal anti-inflammatory drugs (NSAIDs) and 12.1% under anticoagulant therapy. Bleeding location was identified in 15.4% patients and endoscopic treatment attempted in these cases. Rebleeding rate was 29.5% with only 32.7% of these rebleeding in the first 30 days. Mortality rate was 1.9%.
Conclusion: CDB is usually self-limited and tipically managed with conservative treatment. Rebleeding is frequent although global morbidity/mortality is low. Many patients with CDB are under anticoagulantor antiplatelet therapy.
Disclosure of Interest: None declared

P0457 MUCOSAL IMMUNE ACTIVATION AND NERVE FIBER SPROUTING IN PATIENTS WITH SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE

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Introduction: The pathogenesis of diverticular disease is still uncertain but it is thought to be multifactorial, involving environmental, colonic sensory-motor and structural factors. Symptomatic uncomplicated diverticular disease (SUDD) is a syndrome characterized by recurrent irritable bowel syndrome (IBS)-like symptoms attributed to diverticula in the absence of other macroscopically evident alterations. We hypothesized that colonic immune activation plays a role in symptom generation in patients with SUDD.
Aims & Methods: Thus, we characterized immune cells, nerve density and sprouting in patients with SUDD, diverticulosis and healthy controls (HC). For this, a total of 38 subjects were enrolled, of which 14 as HC, 16 with colonic diverticulosis, and 10 with SUDD. In patients with diverticula, mucosal biopsies were obtained close to diverticula and at least 20 cm from the last observed diverticula (normal mucosa). In HC, biopsies were performed at sigmoid and at descending colon. The expression of tryptase (mast cell marker), CD3 (T cell marker), CD68 (macrophage marker), neuronal specific enolase (NSE) [nerve marker], and growth-associated protein 43 (GAP-43) [neuronal outgrowth marker] was assessed by quantitative immunohistochemistry. IBS-like symptom severity and frequency were graded from 0 to 4, by means of validated symptomatic questionnaires.
Results: Mast cells were significantly increased in the peridiverticular mucosa of patients fulfilling the Roma III criteria for IBS, in comparison with HC (5.9 ± 0.7% vs 3.6 ± 0.5%; $P < 0.05$), but not in patients with SUDD as compared to diverticulosis or HC. No differences were detected in the T cell counts among the three groups. Macrophages were significantly increased in patients with SUDD and diverticulosis as compared to HC, both in the peridiverticular (5.8 ± 0.4%, 6.9 ± 0.6%, 4.9 ± 0.4%, respectively; $P < 0.05$) and in normal mucosa (7.1 ± 0.7%, 6.6 ± 0.4%, 4.0 ± 0.3%, respectively; $P < 0.001$). Similarly, the percentage of NSE+ fibers over lamina propria area was significantly enhanced in patients with SUDD and diverticulosis in comparison with HC (5.1 ± 0.7%, 5.5 ± 0.8%, 3.4 ± 0.4%, respectively; $P < 0.05$). Interestingly, GAP-43 immunoreactivity was significantly increased only in patients with SUDD as compared to HC (5 ± 0.6% vs 2.4 ± 0.7%, respectively; $P < 0.05$).
Conclusion: Mucosal immune activation, characterized mainly by macrophages, is a common characteristic of patients with diverticula regardless bowel symtpoms. Mast cells are increased only in patients with SUDD fulfilling Roma III criteria for IBS. Interestingly, nerve fiber sprouting is significantly increased only in patients with SUDD. Neuro-immune activation and sprouting may play a key role in symptom generation in patients with SUDD.
Disclosure of Interest: None declared

P0458 COLONIC DIVERTICULOSIS AND METABOLIC SYNDROME: A THREATENING ASSOCIATION?

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Introduction: Colonic diverticulosis (CD) has been related with advanced age and lacking of diet fiber. Recently, several studies have shown that metabolic syndrome (MS) is also implicated in its etiopathogenesis.
Aims & Methods: This study aimed to assess the association between MS, obesity and CD. Prospective study within 1 year. Definition of MS according to NCEP-ATP III. Collection of demographic data, risk factors for MS and endoscopic findings of patients who underwent total colonoscopy in our department. Obesity was defined as BMI > 30 kg/m2. Informed consent was obtained. Local Ethic Committee and National Data Protection Committee approved the study. Statistical analysis was done with SPSS 21 and statistical significance was defined as $p < 0.05$.
Results: Two hundred and three patients, 95 males, mean age 65.5 years. CD was diagnosed in 30.5%. Right-sided diverticulosis was found in 3%, left-sided diverticulosis in 79% and pancolonic diverticulosis in 18%. Hypertension was present in 84%, dyslipidemia in 84%, diabetes mellitus (DM) in 47%, MS in 71.9%; 66.8% had increased waist circumference and 43% were obese. A significant association was found between CD and age ($p = 0$), hypertension ($P = 0.02$), dyslipidemia ($p = 0.046$), increased waist circumference ($p = 0.033$) and MS ($p = 0.003$). There was no association with gender ($p = 0.76$), obesity ($p = 0.47$) or DM ($p = 0.836$). There was no higher prevalence of adenoma or adenocarcinoma in patients with CD, in comparison with patients without CD.
Conclusion: In our series, MS was significantly associated with CD. The identification of risk groups is important since diverticulosis can have serious and potentially fatal complications. From our knowledge, this is the first European prospective study evaluating the association between MS and CD.
Disclosure of Interest: None declared

P0459 LOW PREVALENCE OF COLONIC DIVERTICULOSIS IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Acquired colonic diverticulum is very common in developed countries and its prevalence increase with age. Colonic diverticulosis is associated with high intracolonic pressure and a weakened bowel wall. Chronic colitis is characterized by liquid stools with low intracolonic pressure and thickened bowel wall. And recently, several studies repoted mesalazine seems to be effective in preventing recurrence of acute uncomplicated diverticulitis.
Aims & Methods: The aim of this study was to assess the prevalence of colonic diverticulosis in inflammatory bowel disease patients, and to assess the prevalence of colonic diverticulosis in mesalazine-based treatment inflammatory bowel disease patients. We investigated that colonoscopy results (colonic diverticulosis) of patients with ulcerative colitis (UC) and Crohn's disease (CD) older than 30 years were retrospectively evaluated and compared with those of patients who underwent screening colonoscopy (control group) from April 2008 to April 2015 in our institution. And the prevalence of colonic diverticulosis was detected in the mesalazine-based treatment UC patients and CD patients compared with no mesalazine-based treatment UC and CD patients.
Results: UC patients were composed of 72 men and 68 women, with a mean age 51.3 years. CD patients were 30 men and 16 women, with a mean age 47.8 years. And control group were composed of 72 men and 68 women, with a mean age 52.3 years. The prevalence of colonic diverticulosis in UC patients was 20/140 (14%) and in CD patients was 3/46 (6%). And the prevalence of colonic diverticulosis in control group was 56/140 (40%). A significantly lower rate of colonic diverticulosis was detected in the UC patients and CD patients compared with the control group ($p < 0.001$). But, no significant difference in the prevalence of colonic diverticulosis was detected between the UC patients and the CD patients ($p < 0.14$). Next, the prevalence of colonic diverticulosis in mesalazine-based treatments UC patients was 14/120 (12%), no mesalazine-based treatments UC patients was 6/20 (30%). Mesalazine-based treatment UC patients was significantly lower percent of colonic diverticulosis was detected compared with no mesalazine-based treatments UC patients ($p = 0.01$). But, the prevalence of colonic diverticulosis in mesalazine-based treatment CD patients was 2/38 (5%), no mesalazine-based treatment CD patients was 1/8 (13%). No significant difference

in the prevalence of colonic diverticulosis was detected between the mesalazine-based and no-mesalazine treatment CD patients (p = 0.49).
Conclusion: Inflammatory bowel disease (UC and CD) patients were lower prevalence of colonic diverticulosis. And in UC patients, we suggested that mesalazine can prevent occurrence of colonic diverticulosis.

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Disclosure of Interest: None declared

P0460 DIFFERENT ABNORMALITIES IN LONGITUDINAL AND CIRCULAR MUSCULAR FUNCTION IN HUMAN COLONIC DIVERTICULAR DISEASE

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Introduction: The pathogenesis of diverticular disease (DD) is multifactorial. Although several aetiological cofactors have been implicated in its pathogenesis, a relevant role seems to be played by an abnormal neuromuscular function. Derangement of enteric innervation has been described consisting in a decrease in cholinergic nerves and nitric oxide content, reduced density of interstitial cells of Cajal and enteric glial cells. Extensive structural changes in the muscle layer have also been reported with thickening, increased collagen and elastin deposition. However data on muscle function are scarce.
Aims & Methods: The aim of this study was to investigate the morpho-functional and molecular alterations inherent to the sigmoid colonic muscle of patients affected by DD. Longitudinal and circular smooth muscle cells (SMC) and strips were isolated separately from surgical colon specimen of 9 patients (58 affected by sigmoid DD and 9 patients (61 surgery for colon cancer. Contractile effects for muscarinic agonist acetylcholine (Ach 1μM) for cells and Carbachol (0.01-1000 μM) for strips, were tested. Relaxant effects were tested in response to vasoactive intestinal peptide (VIP 1μM). qPCR analysis was performed for transcription of muscarinic M3, VIP (VPAC1/VPAC2), Natriuretic Peptide Clearance (NPR-C) receptors and endothelial nitric oxide synthase (eNOS). qPCR data were normalized to β-actin mRNA. Data are expressed as mean ± SE, $p < 0.05$ considered significant.
Results: In DD, an impairment in cholinergic-induced contraction was observed on longitudinal smooth muscle. A significant decrease contractile response was observed both on muscle cells (9.8%±1.4 *vs* 16.8%±1.8) and strips (830 ± 54 *vs* 1644 ± 173 mN/cm^2) and resulted associated to a significant decrease of transcripts for M3 receptors compared to control (6.8 ± 0.18 *vs* 7.98 ± 0.45). No alterations between normal and DD circular SMC were instead observed in contractile responses and cholinergic receptors expression. Relaxation in turn was impaired in circular, but not in longitudinal muscle. DD circular SMC presented a significant decrease in VIP-induced relaxation (33.3%±8.3) in respect to control (93.2%±1.4) that was associated to a significant decrease of transcripts for: VPAC1 (8.7 ± 4.4 *vs* 15.6 ± 0.1), VPAC2 (9.0 ± 0.4 *vs* 13.2 ± 1.0), NPRC (9.5 ± 0.03 *vs* 15.2 ± 0.3) and eNOS (10.3 ± 0.9 *vs* 14.7 ± 0.2).
Conclusion: Different molecular alterations occur in sigmoid longitudinal and circular muscle in DD that impair SMC response to enteric neurotransmitters. These myogenic alterations likely contribute to neuromuscular disorders in DD.
Disclosure of Interest: None declared

P0461 EVALUATION OF THE EFFECTS OF MESALAMINE AND PROBIOTICS ON FAECAL CALPROTECTIN LEVELS IN PATIENTS WITH SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE

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Introduction: Recent observations suggest that symptomatic uncomplicated diverticular disease (SUDD) is related to change in the colonic microflora and to low-grade inflammation. Faecal calprotectin (FC) levels are related to intestinal inflammation. Mesalamine can improve symptoms and reduce FC levels to a normal range in many patients, but in some FC may persist elevated. The management of these patients is presently unknown.
Aims & Methods: Evaluate the effects of the combined use of mesalazine and probiotis or the increase of mesalamine dose in SUDD patients with persistent elevated FC after mesalamine treatment. One hundred and ten patients (18 y or more) were selected after a clinical interview, colonoscopy, abdominal CT and FC test > 150 microgr/gr. Patients with intestinal neoplasia, previous intestinal surgery, use of antinflammatory drugs and concomitant disease with intestinal inflammation were excluded. The patients were medicated with mesalamine 800 mg b.i.d. for 60 days, and another FC test was done. Patients that presented FC > 150 microgr/gr (32, 2 pts excluded) were divided in two groups – 1) Mp Group – 15 patients that used mesalamine 800mg b.i.d. and a mix of probiotics (*L. acidophilus, L.casei, L. lactis, B. lactis, B. bifidum*) b.i.d. for 8 days; 2) M3 Group – 15 patients that used mesalamine 800 mg t.i.d for 8 days, and another FC test was done. Paired t test was used for statistical analysis.
Results: After 60 days of treatment with mesalazine 800 mg b.i.d, 78/110 (71%) patients presented FC < 150 microgr/gr and 32/110 (29%) FC > 150 microgr/gr. There was a statistically significant decrease (51.8%) in FC levels after combined treatment (Mp Group) (309.70 ± 121.80 x150.80 ± 104.23, $p < 0.002$). There was also a statistically significant decrease in FC levels (42.2%) after treatment with higher dose of mesalazine (M3 Group) (455.40 ± 264.17 x 261.50 ± 209.16; $p < 0.01$). FC levels reduced more (51.8%) in Mp than in M3 group (42.2%), but no statistically significant differences in post treatment FC levels were seen when Mp and M3 groups were compared.
Conclusion: FC decrease to normal range in most SUDD patients after treatment with mesalamine 1.6g. The combined use of mesalamine and probiotics or increasing the dose of mesalamine to 2.4 g may decrease FC in SUDD patients that persisted with FC elevated.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 09:00–17:00
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS I – HALL 7

P0462 PROTEASE-ACTIVATED RECEPTOR-1 SIGNALING DEEPLY PARTICIPATES IN THE ABILITY OF TUMORIGENESIS BY CONTROLLING HIPPO-YAP PATHWAY

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Introduction: Control of cell number is important in animal development and tissue homeostasis, and its dysregulation may result in tumor formation or organ degeneration. The Hippo pathway plays crucial roles in organ size control and tumorigenesis. The activity of YAP/TAZ, a transducer of the Hippo pathway, is required to sustain self-renewal and tumor-initiation capacities in cancer stem-like cells (CSCs). But, upstream signals that control the mammalian Hippo pathway have not been well understand. Here, we reveal that the connection between Protease-activated receptor 1 (PAR1) signaling pathway and the Hippo-YAP pathway in gastric cancer.
Aims & Methods: MKN45 cells stably expressing PAR1 (MKN45/PAR1) were established in our laboratory(1). siRNA against PAR1 was synthesized. We studied the change in fraction of side population cell, compared the tumorgenesis in nude mice, and increased dephosphorylated YAP protein levels in nucleus, when PAR1-expressing cell line (MKN45/PAR1 and MKN74), PAR1-null expressing cell line MKN45 (control cell) and inhibited PAR1-expressing cell line MKN74 by PAR1 siRNA were treated with PAR1 agonist TFLLR-NH_2 or PAR1 agonist plus PAR1 selective antagonist SCH79797.
Results: The activity of PAR1 induces increase of the fraction of Side population cells which is enriched with CSCs. But the fraction of side population cells were not increased, when inhibited PAR1 activity. The statistical analysis of the ratios of tumor weight over total situs weight proved that PAR1 activated gastric cancer cell by TFLLR-NH_2 resulted in a significant increase of tumor burden (MKN45/PAR1 and MKN74 cells treated by TFLLR-NH_2 versus control, $P < 0.05$). The peritoneal dissemination tumor weight of MKN45/PAR1 and MKN74 cells treated by TFLLR-NH_2 plus SCH79797 were small as compared to MKN45/PAR1 and MKN74 treated by TFLLR-NH_2 alone. A TFLLR-NH_2 inhibits the Hippo-YAP pathway kinase Lats via Rho GTPase, thereby activates YAP by decreasing phosphorylation and makes YAP increased in nucleus localization.
Conclusion: Our research identifies that PAR1 signaling deeply participates in the ability of tumorigenesis by controlling Hippo-YAP pathway signaling in gastric cancer stem cell. We presume that inhibited YAP will be a new target to treat human gastric cancer invasion and metastasis by dysregulated PAR1 or its agonists.

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Disclosure of Interest: None declared

P0463 INCREASED EXPRESSION OF STEMNESS GENES IN HUMAN ADIPOSE TISSUE-DERIVED STEM CELLS (ADSCS) TREATED WITH PERITUMORAL ADIPOSE TISSUE CONDITIONED MEDIUM

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Introduction: Obesity is associated with an increased risk of cancer and it has been hypothesized that the action of adipokines may influence tumor

microenvironment in esophageal adenocarcinoma (EAC) [1]. Moreover, the adipose tissue stromal vascular fraction is a reservoir of adipose tissue-derived stem cells (ADSCs): a mesenchimal multipotent cell population able to express genes considered as "stemness" markers.
Aims & Methods: Our aim is to investigate if peritumoral adipose tissue may play a direct role by altering the expression of stemness genes in human adipose derived stem cells (ADSCs).
Human ADSCs were isolated from obese patients undergoing bariatric surgery and were cultured with conditioned medium (CM) derived from adipose tissue fragments of peritumoral and distal depots of 15 patients with EAC, undergoing surgical resection. After 48h we measured mRNA levels of CD34, CD90, OCT-4 and nucelostemin (NSTM) in ADSCs using Real Time quantitative PCR.
Results: Gene expression CD34, CD90, OCT-4 and NSTM was significantly increased in ADSCs cultured with CM, compared to control untreated cells. In particular, expression of CD34, OCT-4 and NSTM was significantly higher in ADSCs cells cultured with CM of peritumoral depot, in comparison with ADSCs cultured with CM of distal depot. Moreover, the mRNA expression of CD34, OCT-4 and NSTM was increased in cells cultured with CM of peritumoral depot derived from patients with lymph node involvement (N+), compared to peritumoral CM of patients without lymph node involvement (N-).
Conclusion: Our results suggest that peritumoral adipose tissue may directly influence ADSCs through the action of secreted factors. In particular, the mRNA expression of CD34, OCT-4 and NSTM is up-regulated in ADSCs cultured with CM of peritumoral depot derived from patients with lymph node involvement. These observations lead us to hypothesize that adipose tissue may influence stemness of peritumoral adipocytes by a local paracrine signaling, thus creating a more permissive microenvironment for tumor invasiveness.

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Disclosure of Interest: None declared

P0464 ALTERED APOB48 EXPRESSION CAN BE A MARKER OF SEVERE PANENTERIC DYSMOTILITY

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Introduction: Severe panenteric dysmotility, mainly in the clinical phenotype of chronic intestinal pseudo-obstruction (CIPO), is a severe gut dysmotility characterized by recurrent sub-occlusion episodes with no evidence of any mechanical obstruction. CIPO is a heterogeneous term as it can be applied to a variety of patients for whom a diagnostic biomarker is still unavailable. The diagnosis of CIPO would certainly benefit from the identification of a biomarker. We recently showed an altered expression of APOB in familial CIPO patients carrying a novel RAD21 mutation and in a few sporadic CIPO patients. The aim of this study was to identify whether an altered APOB expression can be a possible biomarker for familial and / or sporadic CIPO by comparing CIPO patients to those with other conditions, e.g. Hirschsprung disease (HSCR, characterized by enteric neuron aganglionosis), irritable bowel syndrome (IBS) and motility unrelated disorders (i.e. celiac disease and non-celiac gluten sensitivity).
Aims & Methods: Sera and ileal biopsies of CIPO patients (n = 28; 18 F, age range: 17 - 67 years) and healthy controls (n = 10; 5 F, age range: 25-38) were used for western blot and quantitative immunohistochemistry. Sera from patients with HSCR, IBS and motility unrelated disorders (celiac disease and non-celiac gluten sensitivity, NCGS) (n = 40 each group) served as disease controls.
Results: Sera from idiopathic CIPO patients showed an elevated expression of APOB48, compared to healthy controls and to sera from patients with HSCR, IBS, celiac disease as well as NCGS. Consistently, the APOB48 signal was markedly increased at tissue level in ileum biopsies of CIPO cases compared to healthy controls and IBS ($32.9 \pm 9.2\%$ vs $7.2 \pm 2.5\%$ cases vs controls; $p = 0.0012$, Student' t test; $32.9 \pm 9.2\%$ vs $5.6 \pm 1.5\%$ CIPO cases vs IBS; $p = 0.0008$). Quantitative analysis performed in gut biopsies revealed also a significant reduction in the number of neuron specific enolase (NSE)- labeled myenteric ganglion cell bodies / ganglion in CIPO compared to control specimens ($p = 0.0039$).
Conclusion: APOB48 expression at serum and tissue level was homogeneously increased in sporadic CIPO highlighting a potential convergent mechanism on a gut-specific APOB isoform. The increased APOB48 can be exploited as possible biomarker to better differentiate CIPO from other diseases.
Disclosure of Interest: None declared

P0465 DIGITAL MICROSCOPY IS A VALID ALTERNATIVE TO CONVENTIONAL MICROSCOPY FOR DIAGNOSING BARRETT'S ESOPHAGUS

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Introduction: Management of Barrett esophagus (BE) relies heavily on the histopathological assessment of biopsies. This assessment is subjective and associated with significant intra- and inter-observer variation. Most guidelines recommend review of biopsies by expert pathologists in case of low-grade or high-grade dysplasia (LGD/HGD). Conventional review of microscopy slides, however, is impractical and does not allow intercollegiate conferences or annotations of relevant findings in images for feedback. A digital revision platform would overcome these practical limitations.
Aims & Methods: In preparation of a national BE digital revision platform we compared the diagnostic accuracy of conventional and digital microscopy for diagnosing BE+/-dysplasia by a panel of expert pathologists. Sixty BE biopsy slides (NDBE; n = 25, LGD; n = 20; HGD; n = 15) were scanned at x20 magnification. Five expert BE pathologists independently assessed all slides four times in 2 alternating rounds of digital and conventional microscopy. Assessments were supervised by a research fellow and the order of rounds as well as the order of the slides was randomized. Pathologists were blinded for the original diagnosis and identifying slide features. Intra-observer and pairwise inter-observer agreement were calculated using custom weighted Cohen's kappa in four categories (NDBE; IND; LGD; HGD). Kappa scores were expressed as fraction of maximum possible kappa score for each cross table.
Results: The mean intra-observer agreement was 0.63 for the 2 rounds of digital assessment and 0.74 for the two rounds of conventional assessment. Mean pairwise inter-observer agreement was 0.61 and 0.64 for first and second round of digital microscopy, respectively. For the two rounds of conventional microscopy, mean pairwise inter-observer agreement was 0.62 and 0.66 respectively. In 48/60 (80%) of digital and in 50/60 (83%) of conventional microscopy reviews a majority diagnosis was reached after the first reading.
Conclusion: Diagnostic agreement of digital microscopy is comparable to conventional microscopy in the setting of an expert pathology platform for BE histology. This study validates the use of digital histopathological assessment of BE biopsies and will be used as the underlying infrastructure for a nationwide, web-based BE revision platform in the near future. This will overcome many logistical and practical issues concerned with conventional histologic review by multiple pathologists.
Disclosure of Interest: None declared

P0466 INHIBITION OF BMP2 AND BMP4 BY A NOVEL LLAMA-DERIVED NANOBODY SUSTAINS INTESTINAL STEM CELLS IN ORGANOID CULTURES

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Introduction: "Intestinal organoids" are structures that mirror the intestinal crypt-villus units. They recapitulate the complete intestinal stem cell differentiation hierarchy and therefore are powerful therapeutic tools in which to study human disease models.
Inhibition of BMP activity is one of the requirements to maintain intestinal stem cells in these *ex vivo* cultures, and is usually provided by the addition of the natural BMP-inhibitor Noggin to the media. Noggin inhibits several BMPs, including BMP2,4 and 7. It is therefore not clear which BMPs are expressed by the intestinal organoid cultures and which need to be inhibited to sustain the stem cell culture.
Aims & Methods: Since BMPs have diverse and opposing roles understanding their specific function in the intestine is of great importance. Here, we set out to investigate which BMPs are required to maintain and culture organoids.
Results: We first tested which of our newly generated and highly specific aBMP nanobodies (VHHs) were able to maintain *ex vivo* stem cell organoid cultures. The three unique llama-derived VHHs with different specificities to BMPs: anti-BMP4 (C4); anti-BMP2,4 (C8); and anti-BMP2,4,5,6 (E7), were used. Addition of these VHHs to the organoid cultures resulted in a decrease in the total BMP activity. Whereas specific BMP4 inhibition (by C4) resulted in a partial decrease in the BMP activity, concomitant inhibition of BMP2 and BMP4 (by C8) was sufficient to result in an almost complete blockage of BMP signaling, to the same level as Noggin and E7. This indicated that the intestinal organoids mainly secrete BMP2 and BMP4. Consequently, inhibition of BMP2 and BMP4, but not BMP4 alone, was enough to sustain self-renewal of crypts as organoids cultured with C8 presented the same morphological characteristics as the ones cultured with Noggin, manifested by the presence of several crypt-like budding structures. Inhibition of BMP2,4,5,6 by E7 did not provide superior growth advantage to the cultures when compared to C8, suggesting that BMP5 and BMP6 are redundant in these cultures.
Conclusion: These results have important implications. First, inhibition of both endogenous BMP2 and BMP4 is enough to sustain self-renewal of small intestine stem cells *in vitro* and this can effectively and selectively be provided by C8, our BMP2,4-specific VHH. Since recombinant Noggin is expensive, C8 offers an easy accessible and cheaper alternative for these cultures. Second, specific inhibition of BMP4 alone does not affect stem cell proliferation. Therefore, C4 antibodies

display important potential for therapeutic use in BMP4-mediated diseases, such as gastric cancer; as they would avoid the deleterious side effects of unchecked cancer stem cell proliferation observed by Noggin and other unselective inhibitors. Since inhibition of BMP5,6 is not required for intestinal stem cell cultures, future *in vivo* application of C8, would prevent detrimental effects of Noggin on for instance bone structures.
Disclosure of Interest: None declared

P0467 THROMBIN INDUCES HUMAN GASTRIC CANCER CELL TO EPITHELIAL-MESENCHYMAL TRANSITION THROUGH PAR1 ACTIVATION

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Introduction: Human α-thrombin, as a serine protease, catalyzes much coagulation-related reactions, and also promotes the activation of protease-activated receptors (PARs), a kind of G protein-coupled receptor, on the cell. We reported by using an immunohistochemical approach that PAR1 is expressing in the gastric cancer tissues, related poorer prognosis of patients, and its activation induces gastric cancer cells proliferation and invasion in vivo. Epithelial-mesenchymal transition (EMT) is defined as the process in which epithelial cells lose their cell-cell adhesion, and gain migratory and invasive properties to become mesenchymal stem cells, and plays a momentus role in cancer metastasis. These above facts underline the relevance of EMT and PAR1 acytivity to gastric cancer, but there are few reports on the role of PAR1 in EMT. This study investigates the role of PAR1 activity in EMT.
Aims & Methods: we investigated the expression levels of epithelial markers (Ecadherin and βcatenins) and mesenchymal markers (vimentin and fibronectin) by western blotting in the gastric cancer cells; pcDNA3.1 transfected MKN45 (MKN45/Mock), pcDNA3.1-PAR1 transfected MKN45 (MKN45/PAR1), and MKN74, stimulated by α-thrombin or α-thrombin with SCH79797, specific antagonist for PAR1. We observed that α-thrombin induced morphological changes, and immunofluorescence of E-cadherin and fibronectin expression in MKN45/PAR1 and MKN74 cells. We extracted these cells nuclear proteins and examined the binding of E-cadherin transcriptional factors to E-boxes (E1, E2 and E3) by means of EMSA and western blotting.
Results: Western blotting showed, epithelial and mesenchymal markers expression remains the same in MKN45/mock cells treated with α-thrombin for 24 h. But we observed the decreasing of epithelial markers expression and gain of mesenchymal markers expression in MKN45/PAR1 and MKN74 cells treated with α-thrombin. Furthermore, in MKN45/PAR1 and MKN74 cells, treated with α-thrombin and SCH79797, the decreasing of epithelial markers expression and gain of mesenchymal markers expression were suppressed. The morphological changes were observed from round- or epithelial-like to a spindle-like shape phenotype, and immunofluorescence showed the reduction of expression in E-cadherin and the gain of expression in fibronectin. EMSA showed the higher levels of Ebox13 protein complex bands in the MKN45/PAR1 and MKN74 cells treated a-thrombin, and in these cells treated with α-thrombin and SCH79797 showed suppressed levels of E-box complexes bands. We observed significant increase in nuclear levels of the Snail, one of the transcriptional factors of E-cadherin, by western blotting.
Conclusion: We found that α-thrombin induces PAR1 activation and undergo specifically EMT in gastric cancer cell lines. Inhibition of PAR1 signaling pathway may be a new strategy to prevent tumor invasion and metastasis.
Disclosure of Interest: None declared

P0468 EFFECTS OF PGP AND N-ACETYL-PGP AND CYTOKINE PRODUCTION IN SERUM ON THE DEVELOPMENT AND HEALING OF ACETATE ULCERS

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Introduction: Glyprolines are family of regulatory peptides. PGP reduces ulcer formation and accelerates ulcer healing by altering cytokine gene expression of blood mononuclear cells. Cytokines are important regulators of inflammation.
Aims & Methods: To study the effect of Pro-Gly-Pro (PGP) and N-acetyl-Pro-Gly-Pro (AcPGP) on the cytokine level in the serum after the acetate ulceration with/without systemic inflammation. Experiments were carried out on male white outbred rats (250-300g). In the first series of experiments, acetate ulcer was caused by applique of acetic acid on the serosa of the stomach by the method of Okabe, in the second series - intraperitoneal injection of LPS and the acetate ulceration. Intranasal injection of peptides (3.7 μmol/kg/40μl, i/n) or saline solution was added during 1-3^{d} or 4-6th days after the acetate ulceration. Blood was collected from the jugular vein of the rats to determine the production of IL-1α, -17α, -4, IFNγ, MCP-1 and TNFα in the serum by means of flow cytometry.
Results: The area of ulcers (AU) on the 4th and 7th days in the first control group averaged 89.8 ± 15.1 mm^2 and 39.2 ± 6.4 mm^2, respectively. PGP reduced the AU significantly on the 4th and the 7th days namely by 80.9% and 87.5%, respectively. The antiulcer effect of AcPGP on the 7th day was equal to 76.0%. The AU on the 4th and 7th days was 33.8 ± 6.5 mm^2 and 42.7 ± 4.3 mm^2 in the second control group. PGP reduced the ulcers by 57.7% and 41.2% to the 4th and the 7th days, respectively. AcPGP had only the tendency to reduce it.
The concentrations of IL-1α and MCP-1 in the serum of the first intact group were 61.9 ± 15.1 pg/ml and 537.2 ± 82.2 pg/ml, respectively. In the second intact group the concentrations of IL-1α and MCP-1 were 718.7 ± 26.0 pg/ml and 803.9 ± 4.6 pg/ml. Other cytokines (CK) in rats of both groups were in minimum quantities (< 10 pg): TNFα, IFNg and IL-17α.
The acetate ulceration in the first control group has induced a significant increase of IL-1α and MCP-1 on the 4th day in the serum in 2.2 and 13.5 times, respectively. The level of the other CK has not changed. On the 7th day the concentration of IL-1α and MCP-1 has been increased. PGP has not affected on the level of elevated cytokines by the acetate ulceration the in the serum of rats. AcPGP has reduced the value of IL-1α in the serum of 37.2% and 41.7% on the 4th and 7th day after the acetate ulceration, respectively, and on the 4th day MCP-1 by 20.4% *vs* control.
The acetate ulceration in the serum of the second control group on the 4th and 7th days, on the contrary, has caused a significant decrease in IL-1α in 2.9 and 2.6 times, respectively. The level of the other CK has not changed. The peptides, PGP and AcPGP have reduced the production of IL-1α by 58.1% and 64.2% on the 4th day *vs* control, respectively. On the 7th day the changes were minor. The content of MCP-1 in the serum of all groups has remained high.
Conclusion: 1. Development of the acetate-induced ulcers in rats is accompanied by a significant increase in serum IL-1α and MCP-1. AcPGP inhibits IL-1α and MCP-1 in the serum on the 4th day and on the 7th day only IL-1α.
2. PGP and AcPGP reduce the production IL-1α on the background of systemic inflammation and acetate ulceration to the 4th day.
Disclosure of Interest: None declared

P0469 OXYNTIC GASTRIC ATROPHY IN AUTOIMMUNE GASTRITIS COMPARED TO *HELICOBACTER PYLORI* GASTRITIS

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Introduction: Severe oxyntic gastric atrophy (OGA) is the classical phenotype of autoimmune gastritis (AIG) and occurs in a small subset of patients with *H. pylori* gastritis as well.
Aims & Methods: To assess characteristics of advanced (moderate to severe) OGA in AIG compared to advanced OGA as a consequence of *H. pylori* infection. Patients presenting for esophagogastroduodenoscopy (EGD) from July 2011 to October 2014 were prospectively included (N = 452). Gastric biopsies were obtained for histological analysis and *H. pylori* testing. Serum gastrin-17 (G17), pepsinogen (PG) I, PGII and antibodies against *H. pylori* and CagA were determined in all patients. In patients with advanced OGA, antibodies against parietal cells and intrinsic factor were also determined. Demographics, medical history, and current medication were recorded. Areas under the curves (AUCs) were calculated for serum biomarkers and compared to histology.
Results: Overall, 34 patients had advanced OGA by histology (22 women, age 61 ± 15, range 23-86). Current or past *H. pylori* infection and AIG were present in 14/34 and 22/34 patients, respectively. *H. pylori*-negative AIG patients (N = 18) were more likely to have another autoimmune disease (OR 18.8; 95%CI 2.0-173.9), severe corpus atrophy (OR 10.3; 95%CI 1.8-60.5), and corpus intestinal metaplasia (OR 37.4; 95%CI 3.8-364.6). The performance of G17, PG I and PGI/II was outstanding for AIG patients (AUC = 0.81, 0.95 and 0.96, respectively), but average for *H. pylori* positive patients with advanced OGA (AUC = 0.68, 0.77 and 0.73, respectively).
Conclusion: *H. pylori*-negative AIG has a distinct clinical, morphological and serological expression compared to advanced OGA in *H. pylori* gastritis.
Disclosure of Interest: None declared

P0470 EFFECT OF PGP AND N-ACETYL-PGP ON CON A-STIMULATED CYTOKINE PRODUCTION BY LYMPH NODES GASTRICUS CAUDALIS CELLS IN RATS ON THE BACKGROUND OF SYSTEMIC INFLAMMATION AND ACETATE ULCERATION

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Introduction: Lymphocytes of regional lymph nodes are the main sources of cytokines which are involved in inflammation. Lymph node gastricus caudalis (*ln. gastricus caudalis)* is adjacent to gastroepiploic vein and drains the rat stomach through lymph vessels. Collagen hydrolysis in inflammation leads to the formation of glycine- and proline-containing peptides. PGP reduces the development and accelerates healing of the acetate ulcer.
Aims & Methods: The aims of this study were to examine the effects of Pro-Gly-Pro (PGP) and N-acetyl-Pro-Gly-Pro (AcPGP) on Con A-stimulated cytokine secretion by cells of *ln. gastricus caudalis* in rats on the background of systemic inflammation (SI) and acetate-induced ulceration. Acetate ulcer (AU) caused by the S. Okabe method with modifications (1971). To create SI in rats with/without ulcer was used i.p. injection LPS. Cells of *ln. gastricus caudalis* (10^6/well) were cultured in the presence of the mitogen Con A and peptide PGP/

AcPGP (10^{-5} M). The supernatant was collected after 24 and 48 hours after cell seeding and the cytokines was determined by flow cytometry.
Results: The peak values of IL-1α, MCP-1, IL-17α, IFNg, IL-4 and TNFα accounted for 48 h and were equal in intact cells *ln. gastricus caudalis* 23.8 ± 4.4, 6.0 ± 1.1, 500.8 ± 85.3; 566.0 ± 139.8, 55.6 ± 6.5, 59.2 ± 15.7 pg/ml respectively. On the background of SI secretion IL-1α, MCP-1, IL-17α, IFNg and IL-4 was 1.8, 1.5, 2.0, 1.5 and 12 times less respectively, TNFα was not detected.
On the 4th day after AU induction with SI cells of *ln.gastricus caudalis* produced IL-1α, IFNγ, IL-4 in 2.2, 2.5, 1.4 times more and MCP-1, IL-17α in 1.7, 1.5 times less respectively, than the same cells but without ulcers. It should be noted that in these cells the secretion of IL-1α, IL-17α, IFNγ was respectively in 2.3, 1.8, 4.6 times greater, and MCP-1 was less in 1.9 times than comparison with cells after AU formation, but without SI. On the 7th day after AU induction with SI secretion of MCP-1 and IL-17α increased almost 4.0 times. The values of IL-1α and IFNγ have not changed. IL-4, on the contrary, decreased by 1.7 times. TNFα production was very low.
On the 4th day of AU with SI the PGP reduced production of IFNγ and IL-4 respectively in 3.3 and 3.1 times *vs* control. The AcPGP reduced production on the 7th day IFNg and IL-4 respectively in 2.1 and 2.2 times *vs* control. Both peptides significantly reduced IL-17α production. IL-1α and MCP-1 showed no significant changes.
Conclusion: On the 4th day after the AU induction with SI increased secretion of IL-1α, IFNγ, IL-4 and reduced IL-17α and MCP-1 by cells of *ln. gastricus caudalis* was observed. While AU formation without SI was accompanied by an acute shortage of all these cytokines. PGP reduces AU formation and cell *ln.gastricus caudalis* production of IFNγ, IL-4 on the background of SI. On the 7th day after the AU on the background of SI there was significant increase of MCP-1 and IL-17α and decreased production of IL-4, which is accompanied by an even greater development of ulceration, whereas without SI on the 7th day usually there was a gradual ulcer healing. PGP accelerated ulcer healing by modulation of IL-17α.
Disclosure of Interest: None declared

P0471 THE RISK OF GASTROINTESTINGAL BLEEDING WITH NOVEL ORAL ANTICOAGULANTS IN A LARGE COHORT OF PATIENTS AT A DISTRICT GENERAL HOSPITAL

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Introduction: Rivaroxaban, apixaban and dabigatran are novel oral anticoagulants (NOAC). NOACs have been used as first line treatment for atrial fibrillation since November 2012 and for VTE since December 2013. The trial data regarding the risk of gastrointestinal (GI) bleeding has been conflicting, although a meta-analysis found an increased risk of GI bleeding with NOACs as opposed to warfarin (2.3% versus 1.3%)[1]. However, little is known about the incidence of GI bleeding in the real-world setting. We aimed to evaluate the incidence of GI bleeding, endoscopic findings, time of onset of bleeding and the need for intervention in patients taking NOACs in our institution.
Aims & Methods: We performed a retrospective review of all patients at Russells Hall Hospital who received NOACs. These patients were identified from the anticoagulation database and cross-referenced with the GI database and patient notes. Basic demographic, clinical and laboratory data and endoscopic findings were collated.
Results: A total of 2490 patients were identified to be on NOACs, of which 64 were found to have an episode of GI bleeding. In this cohort of patients, this gives an incidence of 2.57%. 57 of 2337 patients were on rivaroxaban, 3 of 77 on apixaban and 4 of 76 on dabigatran with an incidence of GI bleeding of 2.4%, 3.9% and 5.3% respectively. There was a greater incidence found with females than males (55% vs. 45%) with the median age 79.6 years (range 53-95). The 30-day mortality rate was 10.9% (n = 11). The causes of death were stated as metastatic carcinoma (3), sepsis (3), pneumonia (2), and unknown (3).
Of these 64 patients, clinically 33 (51.6%) had an upper GI bleed (UGIB) and 31 (48.4%) had a lower GI bleed (LGIB). The median time from starting NOAC to having a GI bleed was 6.7 months (range 2 days-19.7 months). Endoscopy results were varied with the most common findings being haemorrhoids (15%), diverticular disease (14%), normal findings (11.8%), polyps (10.8%), peptic ulcer disease (9.7%), gastritis (8.6%), and other (30.1%). 9 patients (14%) required endoscopic intervention and 23 patients (35.9%) required the use of blood products. As compared to LGIB patients, UGIB patients required greater frequency of endoscopic intervention (15% versus 12.9%), were more likely to be inpatients (97% versus 35%) with a greater drop in haemoglobin (median Hb at presentation: 82 g/L versus 105 g/L) and increased use of blood products (55% versus 16%).
Conclusion: Although the results from our cohort of patients show a higher incidence of GI bleeding of 2.57% as compared to that observed in previous studies (2.3%), there were no deaths directly related to the bleeds, only 14% required endoscopic intervention and the use of blood products was relatively low at 35.9%. Whilst the incidence of GI bleeding is lower for rivaroxaban than apixaban and dabigatran, the data for the latter two is much smaller and thus further studies are needed to make a true comparison between the three NOACs.

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P0472 ENDOSCOPIC VARICEAL LIGATION FOLLOWED BY ARGON PLASMA COAGULATION VERSUS ENDOSCOPIC VARICEAL LIGATION ALONE: A RANDOMIZED CONTROLLED TRIAL

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Introduction: After the first attack of acute variceal hemorrhage patients have a very high risk of recurrent variceal bleeding and death. Rebleeding rates after endoscopic variceal ligation (EVL) are high, thus current recommendation is to combine non selective beta-blockers (NSBB) to EVL but side effects and relative contraindications to NSBB are common and hinder treatment or require discontinuation in 15-20% of cirrhotic patients. Induction of fibrosis of distal esophageal mucosa using argon plasma coagulation (APC) may suppress capillary proliferation and invasion of perforating veins thus decreasing esophageal varices (EV) recurrence.
Aims & Methods: This study included 40 subjects with post viral liver cirrhosis and previous history of upper gastrointestinal bleeding. They were submitted for EVL and obliteration of varices. Then patients were randomly assigned to either APC (group 1) or just observation (group 2).
Results: During 2 years follow up 20% of subjects in group 1 experienced EV recurrence but no one needed rebanding. In group 2, 68.4% experienced EV recurrence ($p = 0.002$) and 63.2% underwent rebanding ($P < 0.001$). (Figure) No subject in group 1 experienced rebleeding during the 2 year follow up, while 10.5% of subjects in group 2 experienced rebleeding from EV ($p = 0.231$). No subject in both groups showed development of gastric varices. 3 subjects in group 1 and 4 subjects in group 2 showed development of new severe portal hypertensive gastropathy ($p = 0.695$). One subject in group 2 (5.3%) experienced bleeding from severe portal hypertensive gastropathy during the 2 year follow up while no subject in group 1 experienced this ($p = 0.487$).
Conclusion: APC can decrease the risk of recurrence, the need for rebanding of EV and the frequency of endoscopic follow up after EVL. APC after EVL may be recommended in secondary prophylaxis against esophageal variceal bleeding especially in those who have contraindications, intolerant or incompliant to NSBB.
Disclosure of Interest: None declared

P0473 USEFULNESS OF THE NASOGASTRIC LAVAGE BEFORE EMERGENCY ENDOSCOPY IN THE PATIENTS WITH NON-VARICEAL UPPER GI BLEEDING

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Introduction: Before treating emergency department patients with hematochezia, melena or hematemesis, it is important to predict the presence and location of a bleeding source. Moreover, fine visual field is necessary to find a bleeding point and achieve prompt hemostasis in emergency endoscopy. In Japanese clinical practice, nasogastric lavage is often performed before emergency endoscopy for gastrointestinal hemorrhage. However, it is not clear whether nasogastric lavage before emergency endoscopy is useful.
Aims & Methods: We estimate the validity of nasogastric lavage before endoscopy in emergency department patients with non-variceal upper GI bleeding. From May 2011 to January 2014, 92 patients with hematochezia, melena or hematemesis underwent emergency endoscopy (within 24 hours from onset) in Kyorin University Hospital. In 60 patients nasogastric lavage was performed (500-2000ml) before endoscopy (group A), and in 32 patients nasogastric lavage was not performed (group B). We retrospectively reviewed their medical records to analyze the following factors: age, sex distribution, systolic blood pressure and interval from onset to endoscopy, nasogastric lavage findings (bloody, "coffee ground", clear/bile), a vision score of the endoscopic field (1: No need to wash, 2: The fold of gastric greater curvature hidden, 3: Gastric fundus full of residue and blood, 4: Gastric angle not visible), detection of bleeding points, procedural time for treatment, duration of hospitalization, the success rate of endoscopic hemostasis, rebleeding rate and complications associated with nasogastric lavage.
Results: Between group A and B, there was no significant difference in mean age, sex distribution, systolic blood pressure and interval from onset to endoscopy. And the blood test of hemoglobin, serum albumin level and blood urea nitrogen on admission were also no significant difference between group A and B.
There were 48 bleeding points in group A (60) and 26 in group B (32), and the rate of bleeding point was the same (80%). In group (A), 35 bleeding points (97.2%) were detected out of 36 bloody lavage findings, and 8 bleeding points (88.9%) were detected out of 9 "coffee ground" lavage findings. On the other hand, only 5 lesions (33.3%:1 angioectasia/4 duodenal ulcer) were detected out of the 15 patients with clear/bile lavage findings.
An average of vision score (1.85 vs 1.88, $p = 0.89$) and the success rate of endoscopic hemostasis (91.7% vs 96.2% $p = 0.80$) was not significantly different between the two groups. The rate of rebleeding or conversion to transcatheter embolization were not significantly different between the two groups (rebleeding 4.2% vs 3.8% $p = 0.52$, transcatheter embolization 4.2% vs 0.0% $p = 0.76$). And the duration of hospitalization also did not differ between the two groups (19.7days vs 22.3 days $p = 0.70$). There was no complication associated with nasogastric lavage.
Conclusion: Nasogastric lavage before emergency endoscopy may be useful in predicting the presence of bleeding resources. However, it did not lead to the improvement of clinical outcomes, such as the success rate of endoscopic

hemostasis, and the rate of rebleeding or conversion to transcatheter embolization and the duration of hospitalization.
Disclosure of Interest: None declared

P0474 PREDICTION OF CLINICAL OUTCOME OF ACUTE VARICEAL BLEEDING. DO WE NEED A RISK SCORING SYSTEM?

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Introduction: Variceal bleeding is the most common cause of acute upper gastrointestinal bleeding in Egypt and its management represents a significant economic burden. There are only few inconsistent reports on the incidence and prediction of outcome of acute variceal bleeding in Egypt. Admission Rockall Score (RS), full RS, and Glasgow-Blatchford Score (GBS) can all be used to stratify the risk but to our knowledge no studies were done to compare between them in prediction of outcome in variceal bleeding in our country.
Aims & Methods: To compare both admission and full RS and GBS in predicting outcomes in variceal bleeding patients in Upper Egypt. A total of 120 patients with variceal bleeding were enrolled in the study.
Patients were followed up 30 days after admission to emergency department to determine cases of rebleeding or death during this period. By using areas under the curve (AUC), we compared the 3 scores in terms of identifying the most predictive score of unfavourable outcome
Results: Rebleeding rate was 15% (18 patients), mortality rate was 14.7% (17 patients), transfusion was needed in 72 patients (60%). For prediction of rebleeding Blatchford score had the highest specificity 68.6% and the highest sensitivity 72.2% (AUC, 0.71) and it was superior to both the full RS (AUC, 0.67), and admission Rockall score (AUC, 0.60). Full Rockall score had the highest specificity 87.5%, (AUC, 0.79)in prediction of death and it was superior to both the admission RS (AUC, 0.72), and Blatchford score (AUC, 0.66). GBS had the highest specificity 75.0% and the highest sensitivity 66.7% (AUC, 0.76) in detecting patients who needed transfusion, it was superior to both the full RS (AUC, 0.57), and admission RS (AUC, 0.55).
Conclusion: Galasgow Blatchford score can be used to predict rebleeding and need for transfusion in patients with variceal bleeding while Full Rockall score was the most accurate score that predicted mortality risk in these patients

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Disclosure of Interest: None declared

P0475 COMPARISON OF RISK SCORING SYSTEMS IN PREDICTING CLINICAL OUTCOME OF UPPER GASTROINTESTINAL BLEEDING SECONDARY TO PEPTIC ULCER DISEASE

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Introduction: Upper gastrointestinal bleeding (UGIB) secondary to peptic ulcer disease (PUD) is still a life-threatening condition and one of the greatest challenges in Gastroenterology. Different scoring systems have been developed to identify the patients with higher risk of adverse outcomes.
Aims & Methods: To assess the effectiveness of different scoring systems - Glasgow-Blatchford-Score (GBS), the Baylor College Score (BCS), Rockall Score (RS), Almela Score (AS), Cedars Sinai Score (CSS) – at predicting rebleeding, need for surgery and mortality.
Retrospective review of all UGIB admissions secondary to PUD that required hospitalization, from January 2010 to December 2014. We recorded demographic, clinical and laboratory data and we assessed the different scores and compared them by using areas under the curve (AUCs).
Results: We identified 377 patients, 249 males, with a mean age of 70 years. Duodenum ulcers (57%) were more frequent then gastric ulcers. When analyzed the predictors of recurrent bleeding: 47 patients (13%) presented gastric ulcers along the lesser curvature or duodenal ulcers along the posterior wall of the duodenal bulb; 67% had endoscopic high-risk stigmata for recurrent bleeding (≥Forrest IIB); 54% were described as Large ulcers (> 1 cm) on endoscopy. Rebleeding occurred in 20% of patients, need for surgery in 7% and mortality was 7%.
For the prediction of rebleeding, the scores that showed more discriminating power were AS (AUC: 0.811), CSS (AUC: 0.802) and RS (AUC: 0.743); although AS and CS weren't statistically different, they were both statistically superior to RS (respectively, $p = 0.010$ and $p = 0.031$).
For the prediction of mortality, the scores that demonstrated better discriminating power were RS (AUC: 0.874), the CSS (AUC: 0.869) and the GBS (AUC: 0.856), without statistically significant differences, when compared.
Given the need for surgery, the scores that revealed the highest discriminating power, were AS (AUC: 0.771), the RS (AUC: 0.707) and the CSS (AUC: 0.696); no statistically significant differences were observed when compared.
Conclusion: The set of our results favor the use of CSS and the RS, instead of the other scores, in the prediction of rebleeding, need for surgery, and mortality during hospitalization, with superiority of CSS in the prediction of rebleeding risk.
Disclosure of Interest: None declared

P0476 COMPARISON OF THREE DIFFERENT SCORING SYSTEMS FOR RISK STRATIFICATION IN GERIATRIC PATIENTS WITH ACUTE UPPER GASTROINTESTINAL BLEEDING

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Introduction: Acute gastrointestinal bleeding is a potentially life-threatening condition which requires rapid assessment and dynamic management. Several scoring systems have been established to predict mortality and rebleeding.
Aims & Methods: The aim of this study was to compare three different scoring systems in order to predict short-term mortality, rebleeding rate, duration of hospitalization and need for blood transfusion in elderly patients with upper gastrointestinal bleeding. A retrospective analysis was undertaken in 335 elderly patients with upeer gastrointestinal bleeding. The pre and post endoscopic Rockall, Glasgow-Blatchford and AIMS65 scores were calculated, and the association between these scoring systems and patient outcomes such as rebleeding, mortality, and need for blood transfusion were assessed. The area under the receiver operating characteristic curve was calculated to assess the validity of scoring systems in predicting mortality, rebleeding, and duration of hospitalization.
Results: Pre (4.5) and post-endocopic (7.5) Rockall were superior to Glasgow-Blatchford (12.5) in terms of predicting mortality ($p = 0.006$, $p = 0.015$). Likewise, pre (4.5) and post-endoscopic Rockall were superior to Glasgow-Blatchford in terms of predicting rebleeding ($p = 0.013$, $p = 0.03$). There was an association between prolonged hospitalization and mortality. 94% of patients with an average 5 days of hospitalization were alive, while the percentage reduced to 56.1% for 20 days and 20.2% for 40 days.
Conclusion: The Rockall score is clinically useful in predicting mortality and rebleeding compared to Glasgow-Blatchford and AIMS65 systems. However, in predicting duration of hospitalization and need for blood transfusion, Glasgow-Blatchford scoring system was superior to Rockall and AIMS65 in elderly patients with upper gastrointestinal bleeding.
Disclosure of Interest: None declared

P0477 EFFICACY OF ENDOSCOPIC HEMOSTASIS WITH THE ENDOSCOPIC SUBMUCOSAL DISSECTION TECHNIQUE FOR UPPER GASTROINTESTINAL BLEEDING OVER A 12-YEAR PERIOD

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Introduction: The endoscopic submucosal dissection (ESD) technique was introduced to obtain en bloc specimens of early gastric cancer. Endoscopic high-frequency soft coagulation is used to manage visible bleeding or nonbleeding vessels during ESD. Upper gastrointestinal bleeding (UGIB) is the most common gastroenterological emergency, and has a considerable morbidity and mortality. Recently, endoscopic high-frequency soft coagulation has been used to establish endoscopic hemostasis in patients with nonvariceal UGIB. This study aimed to compare the aetiology and clinical outcome of nonvariceal UGIB between two periods during the last 12 years.
Aims & Methods: We retrospectively investigated the medical records of 568 patients who underwent emergency endoscopy for nonvariceal UGIB from September 2002 to August 2014. The patients were divided into two periods: the first period was from September 2002 to August 2008 and the second period was from September 2008 to September 2014. We examined the characteristics of these patients and compared the efficacy of endoscopic hemostasis by soft coagulation using the ESD technique and hemoclips. We also compared the rate of endoscopic hemostasis by specialists and by trainees The specialists already had the fundamental skills and knowledge needed for ESD, and each specialist assisted in 40 gastric ESD procedures.
Results: Among the 568 patients with UGIB, 230 were in the first period and 338 patients were in the second period. The ratio of *Helicobacter pylori* infection was significantly lower in the second period than in the first period (62.8% vs. 77.4%, $p < 0.001$). The proportion of patients who took antithrombotics did not change between the two periods. Peptic ulcer lesions were the main cause of bleeding (85.2%) during the study period, but bleeding from other lesions, such as esophagitis, increased significantly in the second period ($p < 0.001$). Endoscopic hemostasis was successfully carried out in 220/230 (95.6%) patients in the first period and in 321/338 (95.0%) patients in the second period, with no significant difference between the periods. There were no differences in the incidence of rebleeding (13.0% vs. 9.1%) and mortality

(0.9% vs. 2.7%) between the two periods. In the modality of endoscopic hemostasis, the rate of endoscopic hemostasis by soft coagulation using the ESD technique was significantly higher in the second period than in the first period (77.9% vs. 10.6%, $p < 0.001$). The rate of endoscopic hemostasis by trainees was significantly higher in the second period than in the first period (75.7% vs. 56.1%, $p < 0.001$).
Conclusion: Endoscopic hemostasis by soft coagulation using the ESD technique is safe for trainees and effective with UGIB.
Disclosure of Interest: None declared

P0478 EARLY ENDOSCOPY VS URGENT ENDOSCOPY ON EVOLUTION OF PATIENTS WITH PEPTIC ULCER BLEEDING

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Introduction: Acute upper gastrointestinal bleeding is a common medical emergency worldwide and its major cause is peptic ulcer bleeding (PUB). Most therapeutic guidelines recommend performing endoscopy within the first 24 hours (early endoscopy).
Aims & Methods: The aim of the study is to evaluate the influence of time interval to perform endoscopy (endoscopy timing) on mortality rate, re-bleeding rate, needs of surgery, needs of transfusions and hospitalization time.
It is a prospective study done in a tertiary medical service with permanent access to Endoscopy Department, for 8 months interval (between November 2012 and July 2013). 201 patients with peptic ulcer bleeding were included in the study. The endoscopy was performed within the first 24 hours in all patients. The patients were followed the whole duration of hospitalization. Based on endoscopy timing the patients were divided into 2 groups: urgent endoscopy (UE) (within 3 hours) and early endoscopy (EE) (3-24 hours).
Results: In the studied group of 201 patients, 112 of them had UE (55.7%), while 89 had EE (44.3%). The mean age was 62.6 years (min 19 years, max 94 years), with a predominance of male patients (68.7%).
Mortality rate was 9.5%, it was 11.6% in patients with UE compared with 6.7% in patients with EE ($p = 0.35$).
Re-bleeding occured in 8% of the paientes, it was more frequent in UE group compared to EE patients (11.6% vs 3.4%), but the difference was without statistical difference ($p = 0.06$).
Surgery was needed in 4% of the patients, with a higher rate in patients with UE than patients with EE (6.3% vs 1.1%) ($p = 0.14$).
The average need of transfusions was higher in UE group compared to EE group (2.29 vs 1.69 blood units), without statistical significance ($p = 0.08$).
Even the hospitalization period is slighty prolonged in patients with EE vs UE group (8.26 days vs 7.27 days), this was not significantly influenced by the endoscopy timing ($p = 0.33$).
Conclusion: Urgent endoscopy compared to early endoscopy has not been significantly superior regarding the mortality rate, re-bleeding episodes, needs for surgery, needs of transfusions and hospitalization period in patients with UGIB.
Disclosure of Interest: None declared

P0479 PROLONGED GASTROINTESTINAL TRANSIT IS PRESENT IN TYPE 1 DIABETES MELLITUS PRIOR TO THE DEVELOPMENT OF SYMPTOMS

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Introduction: The wireless motility capsule (WMC) is a minimally invasive ambulatory technology that concurrently measures intraluminal pH, temperature and pressure as it traverses the gastrointestinal (GI) tract. Knowledge gaps remain concerning regional GI transit times with type 1 diabetes mellitus (T1DM) with established sensory neuropathy. Moreover, pH drop across the ileocaecal valve (ICV) has been recently proposed as a surrogate biomarker for bacterial fermentation in the caecum.
Aims & Methods: 24 patients with T1DM (17 male, mean age 54 years, range 36-66), with confirmed sensory neuropathy but no GI symptoms, and 22 healthy controls (17 male, mean age 54 years, range 38-72) ingested a WMC together with a standardized meal. Gastric emptying time (GET), small bowel transit time (SBTT), colon transit time (CTT) and whole gut transit time (WGTT) and pH drop across the ICV were calculated using the WMC.
Results: In patients with T1DM, GET (350 minutes $\pm$65.8 vs. 206 $\pm$11.8, $p = 0.05$), CTT (2188 minutes $\pm$235 vs. 1302 $\pm$155, $p = 0.004$) and WGTT (2831 minutes $\pm$271 vs. 1893 $\pm$199, $p = 0.009$) was longer in comparison to healthy controls. pH drop across the ICV was higher in T1DM patients when compared to controls (-1.73 ± 0.4 vs. -1.3 ± 0.5, $p = 0.005$) and was associated slower CTT ($r = -0.6$, $p = 0.002$). Multivariate linear regression, controlling for age, gender and glycaemic control were not associated with changes in regional or whole gut transit times.
Conclusion: In patients with T1DM with sensory neuropathy, but without GI symptoms, GET, CTT and WGTT are prolonged in comparison to controls and had a larger pH drop across the ileocaecal valve suggesting heightened caecal fermentation. Whether changes in the microbiota contribute to such changes in transit times in T1DM warrants further study as it may represent a potential therapeutic target prior to the development of symptomatic dysmotility.
Disclosure of Interest: None declared

P0480 ACHALASIA IN CHILDREN: COMPARISON BETWEEN THE IDIOPATHIC AND THE GENETIC FORM

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Introduction: Achalasia is a primary esophageal motor disorder rarely observed in children. It is most often isolated and called idiopathic achalasia or exceptionally associated with a genetic disorder.
Aims & Methods: To compare the epidemiological, clinical and paraclinical characteristics in the two entity.
This is a prospective study of 116 consecutive children (M : 62 (53%), F :54 (47%), mean age :10 $\pm$ 4 yrs ; range : 3 months -16 years) enrolled over a period of 24 years (1992-2014). All children underwent a complete clinical check up, an ophthalmologic check up with a Schirmer test, an adrenal hormone balance, an esophageal barium swallow, an upper endoscopy and an esophageal manometry. a neurological examination and EMG were performed in case of suspicion of Allgrove syndrome.
Results: Achalasia was isolated (group I) in 64 cases, it was associated to Allgrove syndrome (group II) in 52 cases. 3A syndrome (alacrima, achalasia, adrenal insufficiency) was observed in 36 cases, 2A syndrome (alacrima, achalasia) in 13 cases and 4 A syndrome (alacrima, achalasia, adrenal insufficiency, autonomic neuropathy) in 3 cases. The comparison between the two groups (Table 1) showed a significant differences between children in both groups. Two (4%) deaths, caused by acute adrenal insufficiency, were recorded in group II.

Table-1

	Isolated achalasia Group I : (n = 64)	Allgrove syndrome Group II : (n = 52)	P
Mean age (year)	11 $\pm$ 4.2	8 $\pm$ 5	<0.001
Consanguinity	0%	75%	-
Backwardness	13%	35%	<0.001
Chest pain	23%	0%	<0.01
Familial achalasia	0%	43%	<0.001
Growth retardation	13%	65%	<0.001

Conclusion: Achalasia in children is frequently associated with Allgrove syndrome. Consanguinity, backwardness, growth retardation and familial form are almost found in Allgrove syndrome. Prognosis is related to the acute adrenal insufficiency.
Disclosure of Interest: None declared

P0481 RELIABILITY OF A SINGLE MULTIPLE RAPID SWALLOWING SEQUENCE DURING HIGH RESOLUTION MANOMETRY

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Introduction: Low (10ml) and/or high (200ml) volume multiple rapid swallowing (MRS) have been proposed as additional tests during oesophageal high resolution manometry (HRM) in order to assess pathophysiological alterations of clinical significance. Reproducibility of these tests has however been little explored, although, for low volume MRS, one report has suggested that a single sequence provides reliable information[1].
Aims & Methods: To assess concordance of two sequences of both 10 and 200 ml MRS in patients referred for HRM. Achalasia patients were excluded. One hundred and nine consecutive patients performed the two sequences for both tests, however only 91 of them (35 men, 48; 28-74 yrs) performed them adequately and were included in the study. Nineteen healthy volunteers (7 men, 28;23-33 yrs) provided the normal range of the following MRS related variables, which have been evaluated: 1) presence of motor inhibition, i.e. no pressure wave $>$ 20mmHg in the distal oesophageal body during MRS; 2) oesophago-gastric pressure gradient (OGPG) in the last 5s of MRS, as a measure of resistance to outflow; 3) 4s integrated relaxation pressure (4sIRP); 4) presence of after contraction, i.e. wave of $>$ 20 mmHg in the distal oesophageal body; 5) ratio between the distal contractile integral (DCI) of the identified after-contraction and the mean DCI of 10 single water swallows (MRS/SS DCI ratio), as a measure of motor reserve.
Results: Descriptive data and concordance between values of the two sequences, evaluated with Lin concordance correlation coefficient[2], are shown in table 1*. Concordance of the two sequences as to being inside or outside of our normal range was evaluated with kappa coefficient and was moderate to substantial for presence of motor inhibition, OGPG and 4s IRP during 10 ml MRS (k: 0.50, 0.78, 0.77 respectively) and 200 ml MRS (k: 0.52, 0.56, 0.63 respectively), but was disappointingly low for presence of after contraction wave and MRS/SS DCI ratio after 10 ml MRS (k: 0.28, 0.10 respectively) and 200 ml MRS (k: 0.31, 0.20 respectively).
* Lin coefficient not applicable for presence/absence of motor inhibition and after contraction as they are a nominal variable.

Table. 1: Descriptive data expressed as Median (IQ range) and Lin concordance correlation coefficient between the first and the second multiple rapid swallowing (MRS).

	10 ml MRS		Lin	200 ml MRS		Lin
	1st	2nd		1st	2nd	
OGPG (mmHg)	1 (−1 to 4)	1 (−1 to 4)	0.81	2 (1 to 5)	2 (0 to 4)	0.75
4s IRP (mmHg)	2.5 (0.6-5.2)	2.1 (0.6-4.7)	0.89	2.5 (0.7 – 5.2)	2.4 (0.2 – 5.0)	0.81
MRS/SS DCI ratio	1.3 (0.8 – 1.9)	1.4 (0.6 – 2.1)	0.54	0.7 (0.4-1.2)	1.0 (0.4 – 1.8)	0.01

Oesophago-gastric pressure gradient (OGPG), 4 second Integrated Relaxation Pressure (4s IRP), Multiple rapid swallowing/single swallow Distal Contractile Integral (MRS/SS DCI).

Conclusion: Inhibitory and resistance variables during low and high-volume MRS are reproducible, whereas strength of the after contraction is not. One sequence of MRS is not enough in order to evaluate the motor reserve; the optimal number of sequences needs to be determined.

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P0482 MANOMETRIC CHANGES ASSESSED BY HIGH RESOLUTION MANOMETRY BEFORE AND AFTER LUNG TRANSPLANTATION

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Introduction: Lung transplantation (LTx) is a good choice in most patients with end-stage lung diseases. Gastroesophageal reflux (GER) is associated with LTx rejection and can also impair the esophageal motility. However, is not very well known if other esophageal motor disorders (EMD) can also be contributed to LTx rejection. High resolution manometry (HRM) allowed a better characterization of EMD, upper esophageal sphincter (UES) and esophagogastric junction (EGJ).

Aims & Methods: To determine pre-transplant EMD and changes in esophageal motility observed after LTx. Observational cross-sectional study. 47 consecutive patients in which HRM (Manoscan; Given) was performed prior to LTx and six month after.

Results: Patients' characteristics and manometric parameters are expressed in the table. EMD were found in 36.2% and 44.7% of the patients before and after LTx respectively. There were no differences between lung disease, EGJ abnormalities and EMD before LTx ($p = 0.189$ and $p = 0.372$; respectively). Neither between lung disease and EGJ diagnosis after LTx ($p = 0.664$) but more esophageal dysmotility was observed after LTx ($p = 0.021$). There were no differences between the LTx type and EGJ abnormalities ($p = 0.064$) and EMD ($p = 0.994$). No differences were found in the EGJ diagnosis before and after LTx ($p = 0.387$), although EGJ morphology changed pre and post LTx ($p = 0.025$) as 38.3% had EGJ disruption before LTx compared to 17% after. Although there was no significant change in esophageal diagnosis pre and post LTx ($p = 0.082$), more EMD was observed after LTx at the expense of hypercontractile esophagus (1 (2.1%) pre LTx and 9 (19.1%) post LTx). There were no differences in the UES ($p = 0.506$).

Conclusion: Patients who are candidates for LTx had a high frequency of esophageal motor dysfunction. HRM changes were observed after LTx presenting more frequently higher LES pressure and hypercontractile disorder. These findings might be caused by indirect vagal nerve injury within the surgery.

Disclosure of Interest: None declared

P0483 EFFECT OF AZITHROMYCIN ON ESOPHAGEAL HYPOMOTILITY (EH) AND PREDICTION OF RESPONSE BY OESOPHAGEAL STIMULATIONS TESTS DURING HIGH RESOLUTION MANOMETRY

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Introduction: Patients with ineffective esophageal contractions and/or fragmented peristalsis during HRM are considered to have esophageal hypomotility (EH). Esophageal hypomotility is due to neural and/or muscular function impairment. In healthy subjects, esophageal stimulation tests like Multiple Rapid Swallows (MRS), increased outlet resistance at GEJ with abdominal compression (AC) and bread swallows (BS) trigger higher amplitude esophageal contractions, unravelling a "contractile reserve capacity" in the esophageal body. The response to these tests in patients with significant EH is unknown, and probably depends on severity and reversibility of neuro-muscular dysfunction. Prokinetic drugs have been used to treat HH with inconsistent results. Azithromycin (AZI) is a macrolide antibiotic with similar prokinetic effects as erythromycin, with fewer side effects and less tachyphylaxia.

Aims & Methods: We aimed to assess the effect of AZI in patients with EH and

Abstract number: P0482

Clinical data	Before LTx	After LTx	
Age	53.6 (50.6-56.6)	55 (51.9-58.1)	P < 0.001
Sex (Male)	30 (63.8%)	30 (63.8%)	
BMI	24.3 (23.2-25.4)	23.7(22.6-24.9)	0.101
Abdominal perimeter	93.8 (89.1-98.5)	92.5 (87.8-97.2)	0.089
LTx indication	3 (6.4%)		
COPD	12 (25.5%)		
Emphysema	3 (6.4%)		
Cystic fibrosis	1 (2.1%)		
Scleroderma	7 (14.9%)		
Pulmonary hypertension	1 (2.1%)		
Bronchiectasis	3 (6.4%)		
Fibro emphysema	13 (27.7%)		
Idiopathic pulmonary fibrosis	1 (2.1%)		
Histiocytosis	3 (6.4%)		
Other			
LTx type	30 (63.8%)		
Bilateral	12 (25.5%)		
Right lung	5 (10.6%)		
Left lung			
LTx rejection		34 (72.3%)	
NoAcute		9 (19.1%)	
Chronic		4 (8.6%)	
HRM Parameter	**Before LTx**	**After LTx**	**p-value**
LES pressure (mmHg)	13.4 (10.8-15.9)	18.4 (15.1-21.6)	0.001
IRP-4s (mmHg)	8.2 (6.3-10.1)	7.9 (6.4-9.4)	0.808
EGJ total length	3.9 (3.7-4.2)	3.7 (3.5-3.8)	0.011
EGJ abdominal length	2.1 (1.9-2.3)	2.2 (2.1-2.4)	0.582
EGJ thoracic length	1.8 (1.6-2)	1.4 (1.3-1.6)	0.003
esophageal length	24.9 (23.8-26)	25.1 (24.6-25.7)	0.642
DCI	1945.7 (1483.9-2407.5)	3907.4 (2715.4-5099.3)	< 0.001
CFV	4.5 (3.8-5.2)	6.6 (2.4-10.8)	0.349
Distal latency	6.2 (5.6-6.8)	6.9 (6.6-7.3)	0.036
IBP	19 (14.3-23.7)	20.7 (17.2-24.1)	0.116
UES pressure	74.7 (66.5-82.9)	62.4 (54.6-70.3)	0.011

the ability of stimulation tests to predict the response to AZI. In a placebo-controlled, parallel designed trial we studied 26 patients with esophageal hypomotility defined in the Chicago Classification V3.0 as 1) > 50% ineffective swallows with DCI < 450 mmHg-s-cm and/or 2) > 50% swallows with fragmented peristalsis. Patients underwent HRM pre and post treatment with AZI 250mg or placebo. Each HRM included MRS (5 water swallows), AC (10 water swallows during abdominal compression) and BS (10 bread swallows). DCI was used to assess strength of baseline contractions and during stimulation tests.
Results: AZI normalised EH in 5/9 patients with abnormal DCI and in 7/13 patients with fragmented peristalsis whilst placebo did not normalized EH. AZI increased DCI from 337.7 ± 286.2 mmHg.cm.s to 617.8 ± 384 mmHg.cm.s (P = 0.01). The % increase of DCI by AZI was 162.9 ± 361.2 and by placebo was 64.5 ± 92.8. DCI ratio (after MRS/baseline) > 1.2 segregated responders to AZI with a sensitivity of 78%, specificity 75%, PPV 87.5%, NPV 60% and LR of 3.11. A DCI after MRS of ≥395 mmHg.cm.s segregated responders to AZI with a sensitivity of 80%, specificity 75%, PPV was 80%, NPV 75% and LR 3.2. Combining the criteria for DCI after MRS and DCI during abdominal compression further increased sensitivity and negative predictive value. DCI during bread swallows could not predict response to AZI.
Conclusion: AZI but not placebo improved esophageal contractions in a subgroup of patients with significant esophageal hypomotility. Pre-treatment stimulation tests (MRS and AC) could identify with moderate accuracy those patients more likely to respond to AZI therapy.
Disclosure of Interest: None declared

P0484 ASSESSMENT OF ESOPHAGEAL CONTRACTILE PATTERN AND BOLUS TRANSIT BY USING DIFFERENT BOLUS CONSISTENCIES IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE (GERD)

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Introduction: Conventional manometry protocol using ten 5 ml liquid swallows has been standardized for the diagnosis of peristaltic abnormalities being the basis for current classification of esophageal motor disorders. Recently, there are reports using multiple rapid swallowing and different bolus consistencies in order to detect more esophageal contractile abnormalities.
Aims & Methods
Aim: To investigate peristaltic contractility patterns and bolus transit (BT) by comparing different bolus consistencies in patients with GERD.
Methods: Patients with GERD were recruited consecutively and grouped as follows: Group 1, Erosive GERD (positive upper endoscopy and pHmetry) and group 2, non-erosive reflux disease (negative upper endoscopy and positive pHmetry). High Resolution Manometry (HRM, MMS, Netherlands with 22 sensors, water-perfused) in supine position was used and multichannel intraluminal impedance-pHmetry (MII-pH) with 6 impedance sensors (3,5,7,9,15,17 cm) and 1 pH sensor (5 cm above lower esophageal sphincter) was used (Given Imaging) to assess BT. Study protocol included: ten 5 ml liquid swallows (LS), three 5 ml applesauce swallows (AS) and three 7.5 grs of sliced-bread (SB), were provided during HRM and at the beginning of MII-pH recording separately. Peristaltic abnormalities were classified as follows: Small breaks (> 2 but < 5 cm gap), Large breaks (> 5 cm gap) and failed (< 3 cm wave integrity). A transit time > 8 s was defined as delayed and an incomplete bolus transit if exit from distal impedance sensor was not detected for each of the bolus consistencies. Data is summarized using median and ranges. Statistical analysis compared contractile patterns and BT between groups and after different bolus consistencies using non-parametric test.
Results: 38 patients were recruited, median age 45 (28-63), 18 Erosive (F 67%), and 20 non-erosive (F 75%). Overall, there were no differences in any of the manometric parameters between groups. However, there were significantly more peristaltic abnormalities (large breaks p = 0.03 SB; small breaks $p = 0.01$ AS and $p = 0.008$ SB) in non-erosive patients (small breaks$p = 0.01$ SB) and in erosive patients when comparing with LS. In addition, more incomplete BT occurred with AS ($p = 0.0001$) and SB ($p = 0.007$) when compared with LS in non-erosive group. Prolonged transit time was observed in AS ($p = 0.0001$) and SB ($p = 0.0001$) in non-erosive but not in erosive group.
Conclusion: Our data suggest that assessment of esophageal contractility and BT with different bolus consistencies may yield more abnormalities when compared with conventional protocol. Whether these findings are relevant for functional outcomes requires further study.
Disclosure of Interest: None declared

P0485 GASTROINTESTINAL SYMPTOM BURDEN IN A SWEDISH POPULATION BASED COHORT WITH INSULIN DEPENDENT DIABETES MELLITUS

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Introduction: Long-standing diabetes mellitus (DM) is afflicted with a wide variety of complications that may cause symptoms from multiple organ systems including the gastrointestinal (GI) tract. Data from other centers have claimed that as many as 75% of patients attending DM clinics report significant GI symptoms.
Aims & Methods: The aim of our study was to understand the extent to which a defined cohort of Swedish patients with DM suffers from GI symptoms. Patients with insulin dependent DM type 1 (IDDM1) and type 2 (IDDM2) who attended the diabetic outpatient clinics at two county hospitals were included in the study. They were sent the Patient Assessment of upper GastroIntestinal Symptom Severity Index (PAGI-SYM) questionnaire for assessment of GI symptom severity which consists of 20 questions answered by use of a six-point Likert response scale, ranging from 0 (none) to 5 (very severe). The Gastroparesis Cardinal Symptom Index (GCSI) was calculated for nausea/vomiting, postprandial fullness/early satiety and bloating. Hospital anxiety and depression (HAD) scale was used for psychological assessment and the short form (SF) 36 questionnaire summary measures for physical and mental health. For those who answered the questionnaires, clinical information was retrieved from medical records regarding complications related to long-standing DM.
Results: We included 754 patients (mean age 48 years, range18-82 years). The questionnaires were answered by 434 patients (response rate 57.8%), and 363 (83.3%) of these had IDDM1 and 73 (16.7%) had IDDM2. The duration of insulin treatment was 21 ± 13 years. Ratings of individual symptoms are given in table 1. The mean GCSI total score in the cohort was 0.7 ± 0.8. Females with IDDM had significantly higher GCSI total score (0.853 vs. .622; p = 0.003), GCSI nausea/vomiting score (0.42 vs. 0.28; p = 0.019) and GCSI bloating score (1.2 vs. 0.81; p = 0.001) compared to males. There was a strong correlation (p = 0.001) between SF-36/HAD and the GCSI total, nausea/vomiting and bloating scores. There was no significant difference in GCSI scores comparing patients with IDDM1 and IDDM2, also not within sexes. Patients with one or more complications related to long-standing DM reported GI symptoms to the same extent as those with no complications and more complications was not associated with higher GCSI scores.**Table 1:** Proportion of patients reporting no (0), mild-moderate (1-3) or severe (4-5) intensity of individual symptoms included in the GCSI score.

PAGI-SYM (n = 434)	Non(%)	Mild-moderaten(%)	Severen(%)
Nausea	323 (75)	98 (23)	11 (2)
Retching	358 (83)	69 (16)	6 (1)
Vomiting	398 (92)	32 (7)	4 (1)
Stomach fullness	179 (41)	242 (56)	13 (3)
Unable to finish a normal-sized meal	329 (76)	96 (22)	9 (2)
Feeling excessively full after meals	244 (56)	167 (39)	23 (5)
Loss of appetite	296 (68)	140 (29)	15 (3)
Bloating	234 (54)	175 (40)	24 (6)
Stomach visibly larger	250 (58)	153 (35)	31(7)

Conclusion: Females with IDDM reported more GI symptoms compared with males. Although the total GI symptom burden in our study corresponded to "very mild" there was a highly significant correlation between the GCSI subscores; total, nausea/vomiting, bloating and mental and physical health and anxiety and depression. Furthermore it appears that the number complications to long standing DM do not per se imply an increase in reported GI symptoms.
Disclosure of Interest: None declared

P0486 POSTPRANDIAL PROXIMAL GASTRIC ACID POCKET IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE IN CHINA

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Introduction: The postprandial proximal gastric acid pocket (PPGAP) is an unbuffered area which escapes neutralization by food and the pH is lower than 4 of the proximal stomach between nonacid segments distally (food) and proximally (lower esophageal sphincter or distal esophagus). It has been noticed in normal individuals and patients with gastroesophageal reflux disease (GERD). The PPGAP is believed to play an important role in GERD. However, it is still poorly understood.
Aims & Methods
Aims: In this study,we analyze the differences of PPGAP between patients with GERD and normal individuals in China.
Methods: 17 normal individuals and 20 patients with GERD participated in this study. All the subjects underwent a high-resolution manometry in a fasting state to identify the location of the lower border of the lower esophageal sphincter (LBLES).Then a station pull-through pH monitoring was performed from 5 cm below the LBLES to the esophagus in increments of 1 cm in a fasting state and 10 min after a standardized meal. The PPGAP was defined by the presence of acid reading (pH < 4) in a segment of the proximal stomach between non-acid segments distally (food) and proximally (lower esophageal sphincter or distal esophagus). The appearing time,disappearing time, length and pH of PPGAP were recorded.
Results: Our results show that a PPGAP is present in 100% of the patients with GERD and normal individuals. Compared to the normal individuals,the disappearing time of PPGAP in patients with GERD was significantly later (132.65 ± 45.22min vs 74.53 ± 30.64min, p < 0.01), the lasting time of PPGAP was significantly longer (118.50 ± 49.70min vs 55.59 ± 34.25min, p < 0.01), the length of PPGAP was significantly longer (5.00 ± 2.34cm vs 1.88 ± 1.11cm, p < 0.01), the lowest pH of PPGAP was significantly lower (1.01 ± 0.40 vs 1.67 ± 0.49, p < 0.01), and the mean pH of PPGAP was significantly lower (1.29 ± 0.47 vs 2.03 ± 0.43, p < 0.01). While there was no significant difference

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	EGJ-CI cut-off value 13 (sens% > spec%)	EGJ-CI cut-off value 10 (sens% > spec%)	EGJ-CI cut-off value 5 (sens% > spec%)
Patients with GERD	**64% - 46%**	**74% - 54%**	**89% - 63%**
Patients with abnormal NRE	**63% - 24%**	**72% - 29%**	**79% - 51%**
Patients with abnormal AET	**66% - 35%**	**74% - 42%**	**87% - 54%**
Patients with positive symptom association	**58% - 48%**	**70% - 53%**	**87% - 61%**

in the appearing time of PPGAP between the patients with GERD and the normal individuals (14.25 ± 9.72min vs 18.47 ± 10.74min, $p = 0.218$).
Conclusion: The PPGAP is present generally in normal individuals and the patients with GERD. Compared to the normal individuals, in the patients with GERD, the lasting time of PPGAP is longer, the length of PPGAP is longer and the pH of PPGAP is lower. The PPGAP may be the reservoir from which acid reflux events originate. It may plays an important role in GERD. So in the future, the PPGAP may be an attractive target for GERD therapy.

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P0487 ESOPHAGEAL MOTILITY IN MORBIDLY OBESE PATIENTS WITH TYPE 2 DIABETES

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Introduction: There is a scarcity of studies of motility disorders in morbidly obese patients with diabetes.
Aims & Methods: We aimed to assess esophageal motility in this group of patients. Patients with BMI ≥ 35 kg/m^2 and type 2 diabetes eligible for bariatric surgery were included from 01.01.2013 to 30.03.2015. All patients were recruited from a tertiary care obesity centre in Southern Norway. Gastrointestinal Symptom Rating Scale (GSRS) was applied to measure self-reported upper GI symptoms. High-resolution multichannel manometry was used to study esophageal motility.
Results: A total of 51 patients were included, mean age 47 years (range 32-61) and mean BMI 43 (range 35-58) kg/m^2. Esophageal manometry revealed dysmotility in 17 patients (33%), involving the esophageal body in 10 patients, with an abnormal mean DCI (distal contractile integral) in the range of 5000-8000 mmHg*sec*cm. Lower esophageal sphincter (LES) residual pressure was normal. The remaining 7 patients had ineffective esophageal motility (IEM) defined by at least 30% ineffective contractions out of 10 wet swallows. No patients reported difficulty with swallowing or chest pain according to GSRS.
Conclusion: Esophageal dysmotility was found in 1 out of 3 morbidly obese patients with type 2 diabetes, and the most prevalent finding was abnormal high DCI, consistent with the nutcracker esophagus, which was found in about 1 out of 5 (18%). None of the patients reported relevant symptoms. The present results demonstrate a high prevalence of asymptomatic dysmotility of the esophagus in morbidly obese patients with diabetes mellitus. A study of this patient group before and after bariatric surgery is indicated to elucidate the influence of change in body weight on esophageal dysmotility and related symptoms.
Disclosure of Interest: None declared

P0488 ARE THERE ANY EFFECTS AND CONCOMITANT FACTORS OF GERD WITH OBSTRUCTIVE SLEEP APNEA SYNDROME ?

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Introduction: OSAS is one of the sleep disturbances in the society which has a prevalance of 1-5% and has various risk factors. General risk factors related to OSAS: age, gender, obesity, snoring, drugs, genetics, etc. Our objective was to study the OSAS cases which is concomitant with obesity and questioning other contributing factors.
Aims & Methods: We classified 62 patients (Female: 6, Male: 56) after GERD questioning into two groups: Patients having Reflux disease and the patients without reflux disease. We also questioned patients BMI scores, waist circumferance, smoking and alcohol consumption, reflux score, BECK anxiety and depressing score, sleep quality (good, medium, bad). We recorded Apnea and Hypopnea index and the mean O_2 saturation values of the patients. The Patients are divided into two groups as patients with reflux disease and the without reflux disease. We compared the data of the two groups.
Results: There was no difference between Reflux (+) and Reflux (-) patients mean ages ($p = 0.424$), mean BMI's ($p = 0.136$), mean waist circuference ($p = 0.343$), mean neck circumference ($p = 0.359$), mean Epworth Scale ($p = 0.107$), mean Apnea Hypopnea index ($p = 0.908$), mean Oxygen saturation ($p = 0.326$), alcohol consumption ($p = 0.620$), smoking ($p = 0.966$) .
There was significant difference in sleep quality between two groups (Reflux+, and Reflux -)($p = 0.037$). The bad and very bad sleep quality answer is higher in the reflux + group (56%) than reflux – group (27%).
There was no statistically significant correlation between Reflux Score, Epworth Scale, Apnea Hypopnea index and 0_2 saturation ($p > 0.05$).
There was significantly positive correlation between Reflux Score, BECK Anxiety Scale, and Beck Depression Scale ($r = 0.382$ $p = 0.002$, $r = 0.254$ $p = 0.046$ respectively).
Conclusion: The Apnea and Hypopnea index and Mean O_2 saturation is not affected in patients with reflux disease. Reflux disease worsens the sleep quality. Increased reflux score leads increased BECK anxiety and depression scores. The intensity of reflux is associated with anxiety and depression.
Disclosure of Interest: None declared

P0489 ESOPHAGOGASTRIC JUNCTION CONTRACTILE INTEGRAL VALUES CORRELATE WITH OBJECTIVE EVIDENCE OF GERD AT IMPEDANCE-PH MONITORING AND UPPER ENDOSCOPY

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Introduction: The esophagogastric junction (EGJ) has been shown to play a major role as defensive mechanism against gastro-esophageal reflux. In keeping, a new metric, termed the EGJ-contractile integral (EGJ-CI), which can be assessed by high resolution manometry (HRM), has been validated in distinguishing proton pump inhibitors (PPIs) refractory patients with functional heartburn from those with PPI resistant gastro-esophageal reflux disease (GERD). However, data correlating EGJ-CI values with objective evidence of GERD is lacking.
Aims & Methods: We aimed to correlate the EGJ-CI values with impedance-pH and endoscopic findings in patients with GERD. Consecutive patients with typical GERD symptoms were enrolled. All patients underwent upper endoscopy, HRM and impedance-pH testing off-PPI therapy. EGJ-CI was calculated using the distal contractile integral tool box during three consecutive respiratory cycles. The value was then divided by the duration of these cycles. A value below 13 mmHg*s*cm was considered as a defective EGJ-CI according to medical literature (the 5th percentile measured in 75 healthy volunteers). We assessed esophageal acid exposure time (AET), number of reflux episodes (NRE) and symptom association analysis (SAA) using both symptom association probability (SAP+ if $\geq 95\%$) and symptom index (SI+ if $\geq 50\%$). A positive impedance-pH monitoring was considered in case of abnormal AET and/or NRE and/or positive SAA. Finally, we analyzed three different cut-off values of EGJ-CI (13 mmHg*s*cm, as the 5th percentile in healthy volunteers, 10 and 5 mmHg*s*cm, arbitrary set) with receiver operating characteristic (ROC) curve in order to provide the optimal balance between diagnostic sensitivity and specificity for impedance-pH detected GERD diagnosis, abnormal number of reflux, pathologic AET and positive symptom association.

Results: Among 130 [65M/65F; median age 53 (21-76)] prospectively enrolled patients, 91 had GERD (abnormal AET and/or elevated NRE and/or positive SAA) and 39 had functional heartburn (FH) (negative endoscopy, normal AET, normal NRE and negative SAA). GERD patients had a lower median value of EGJ-CI [11 (3.1-20.7) vs. 22 (9.9-41), $p < 0.02$] compared to FH patients. Patients with a defective EGJ-CI (<13 mmHg*s*cm) had more frequently a positive impedance-pH monitoring or esophageal mucosal lesions at upper endoscopy ($p < 0.05$ and $p < 0.05$, respectively) than patients with a normal EGJ-CI. As shown in the Table, an EGJ-CI cut-off value of 5 mmHg*s*cm yielded the best performance in identifying GERD at impedance-pH (sensitivity 89%, specificity 63%).
Conclusion: A defective EGJ-CI at HRM is associated with objective evidence of GERD at upper endoscopy and/or impedance-pH monitoring. An EGJ-CI cut-off value of 5 mmHg*s*cm yielded the best performance in diagnosing GERD at impedance-pH monitoring.
Disclosure of Interest: S. Tolone: None declared, N. de Bortoli: None declared, E. Marabotto: None declared, C. de Cassan: None declared, S. Roman: None declared, M. Furnari: None declared, V. Savarino: None declared, L. Docimo: None declared, E. Savarino Lecture fee(s): Given Imaging

P0490 CORRELATION BETWEEN ESOPHAGOGASTRIC JUNCTION CONTRACTILE INTEGRAL AND GERD: A STUDY USING HIGH RESOLUTION MANOMETRY AND GERDQ QUESTIONNAIRE

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Introduction: Recently, a new high resolution manometry (HRM) metric, termed the EGJ-contractile integral (EGJ-CI), has been introduced in order to better identify a defective EGJ function and to distinguish proton pump inhibitors (PPIs) refractory patients with functional heartburn from those with PPI resistant gastro-esophageal reflux disease (GERD). To date, data correlating EGJ-CI values with reflux symptoms and HRM features is lacking.
Aims & Methods: We aimed to correlate the EGJ-CI values with symptoms and HRM features in suspected GERD patients. Consecutive patients with typical reflux symptoms were enrolled. Patients were invited to define their symptoms using the validated GerdQ questionnaire[1]. A positive GerdQ was considered when equal or >9 (range 0-18). Further, all patients underwent upper endoscopy, HRM and impedance-pH testing off-PPI therapy. EGJ-CI was calculated using the distal contractile integral tool box during three consecutive respiratory cycles. The value was then divided by the duration of these cycles. A value below 13 mmHg*s*cm was considered as a defective EGJ-CI according to medical literature (the 5th percentile measured in 75 healthy volunteers). Three morphological types of EGJ were defined based on the presence of axial cranial separation between lower esophageal sphincter (LES) and crural diaphragm (CD): Type I, no separation; Type II, minimal separation (>1 and <2 cm); Type III, >2 cm of separation. Manometric pattern was defined according to the Chicago Classification v. 3.0.
Results: We prospectively enrolled 130 [65M/65F; median age 53 (21-76)] patients. Sixty-four (49.2%) patients had a defective EGJ-CI (<13 mmHg*s*cm), whereas 66 (50.8%) had a normal value. Mean GerdQ score was greater in patients with a defective EGJ-CI compared to those with a normal EGJ-CI (15 vs. 8, $p < 0.02$). Moreover, a positive GerdQ (equal or >9) was more common in patients with a defective than normal EGJ-CI (54.9% vs. 35.9%, $p < 0.05$). At HRM, the study of LES-CD position allowed us to classify as Type I EGJ 60 (46.2%) patients, as Type II EGJ 50 (38.5%) patients and as Type III EGJ 20 (15.4%) patients. Type I EGJ showed the higher median value of EGJ-CI [20 (12.5-36) vs. 10.6 (3.9-17.9), $p < 0.001$, vs. 2.95 (0.2-8.4), $p < 0.001$] than Type II and III EGJ. A significant difference was also recorded between these latter two groups ($p < 0.008$). As to the motility pattern, patients with a defective EGJ-CI showed a lower frequency of normal motility (57.7%) in favor of ineffective esophageal motility (32.3%), whereas outflow obstruction pattern was present only in normative EGJ-CI patients. However, significant differences were not reached among the various groups.
Conclusion: A defective EGJ-CI at HRM is associated with the presence of more frequent and severe reflux symptoms and GERD-related HRM features (i.e. type II or III EGJ and ineffective esophageal motility pattern) compared to a normal EGJ-CI. Thus, our data suggest that a defective EGJ-CI plays a major role in GERD pathogenesis.

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P0491 ACID-HYPERSENSITIVE OESOPHAGUS REFRACTORY TO PPI: RELEVANCE OF GAS-RELATED REFLUX EVENTS AND HYPERVIGILANCE

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Introduction: Amongst patients who are refractory to PPI therapy who undergo reflux monitoring, there is a subgroup classified as having acid hypersensitive oesophagus. Hypersensitive oesophagus (HO) is defined as typical symptomatic perception of reflux events in the context of physiological levels of gastro-oesophageal reflux.
Within patients with acid hypersensitive oesophagus there are likely to be patients who have predominantly gas-related reflux episodes (supra-gastric belches/gastric belches) and those who have predominantly liquid only reflux episodes. There may also be those who are truly hyper-*sensitive*, and others who are more hyper-*vigilant* to reflux events. We anticipated that those patients with gas-related reflux events (particularly supragastric belching related) may be more hyper-vigilant, and that this may manifest as a shorter delay to pushing the symptom marker button after reflux events during 24 hour reflux monitoring.
Aims & Methods: Our aim was to assess the prevalence of gas-related and liquid only reflux events in patients with HO, and to assess time to symptom marker button press for these events.
36 consecutive patients with HO as defined as normal oesophageal acid exposure (<4.2%) with typical symptoms of heartburn or regurgitation and positive symptom-reflux association (SI >50% and/or SAP >95%) were identified. Reflux events related to symptoms were manually examined and the nature of the reflux event was characterised. Time from onset of reflux event to event marker press was measured in seconds.
Each patient was categorised as to the predominant reflux type (suprgastric belch, gastric belch or liquid only).
Relfux parameters were also measured in a comparison group of 50 consecutive patients *pathological* oesophageal acid exposure.
Results: 417 symptomatic reflux episodes were recorded by the 36 patients. The prevalence of gas related reflux events was 64% and liquid reflux events was 36%. Of the gas-related events, 139/267 (33% of total) were related to supragastric belches and 128/267 were related to gastric belches. Time to perception for liquid, supragastric belch, gastric belch, and liquid-related reflux events were not different.
10 patients (28%) had predominantly supragastric belch related reflux events, 10 had predominantly gastric belch related reflux, and 11 (30%) had predominantly liquid only reflux events. 5 patients had a mixed picture.
In the group of 50 patients with *pathological* oesophageal acid exposure, only 12% had predominant supragastric belching related reflux.
When time to recording of symptoms was analyzed on a per patient basis, no difference was seen.
Conclusion: In patients with acid hypersensitive oesophagus, the presence of gas associated reflux events related to symptoms accounted for 63% of total reflux events. Contrary to our expectation we could not see a difference in time to perception between liquid, supragastric belch and gastric belch related reflux events. It is possible that there is not a hypervigilant subset in these patients, or that the method used cannot distinguish them.
It was noteworthy that supragastric belching related reflux events accounted for nearly a third of all reflux events in patients with oesophageal hypersensitivity. This may present an opportunity for management of a subset of patients with refractory HO with behavioural therapy to reduce supragastric belching.
Disclosure of Interest: None declared

P0492 THE COMBINATION OF ACID SENSING ION CHANNELS AND 5-HYDROXYTRYPTAMINE RECEPTORS MAY BE INVOLVED IN PAIN SENSING IN GASTRO-ESOPHAGEAL REFLUX DISEASE

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Introduction: We had earlier demonstrated that STW-5 and omeprazole affect multiple chemokine families on genome and proteome level and involve G-protein coupled receptor and MAP-kinase signaling to reduce inflammation in the esophageal tissue in our rat model for gastro-esophageal reflux disease (GERD)[1,2]. Pain is a prominent symptom of GERD and commonly related to acidic reflux. The mechanisms of acid induced activation of esophageal afferent nerves are not well understood. Recently it was shown that serotonin, which is the ligand for 5-hydroxytryptamine receptors, can also activate acid sensing ion channels[3].
Aims & Methods: We analysed in our subchronic refluxesophagitis (RE) rat model the transcript modulation of acid sensing ion channels and of 5-hydroxytryptamine (5-HTR) subtypes in the esophageal tissue.
Methods: Rats were pretreated with either STW 5 (0.5 or 2ml/kg) a multicomponent herbal preparation, or the PPI omeprazole (O) (30mg/kg) for 7 days. Esophagitis was induced surgically followed by a further 10d treatment. On day 10 animals were sacrificed. RNA was isolated from defined tissue areas of the esophagi for Agilent whole genome microarray (rat). Data were analysed by Ingenuity.
Results: Tissues of animals suffering from RE showed a small, but significant increase in the expression of the ASIC-subtype 4 (3.8f, $p < 0.001$) and of 5-HTR2A (3fold), 5-HTR2B (6.6f), and 5-HTR7 (9.3f) (<0.001) compared to sham. Thus, both – ASICs and distinct 5-HTR subtypes- were up-regulated

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Table 1: Dietary pattern of GERD patients in Russia.

	Protein, g/dayM ± m	Total fat, g/dayM ± m	Total carbohydrates, g/dayM ± m	Dietary fiber, g/day,M ± m	Mono/disaccharides, g/dayM ± m	Starchg/dayM ± m
GERD (n = 124)	97.5 ± 4.0*	135.2 ± 5.6†	249.8 ± 9.5	7.19 ± 0.4‡	124.6 ± 5.7	113.8 ± 8.5
Controls (n = 41)	77.7 ± 4.0*	103.3 ± 5.1†	223.7 ± 14.1	11.4 ± 0.8‡	126.2 ± 9.6	97.7 ± 8.2

Note: *, †,‡ - $p < 0.05$

during the inflammatory process in our rat model. The higher expression of ASIC4 was not found in tissues of animals treated with either STW-5 (2ml/kg) or with O (30mg/kg). Minor differences, especially in the magnitude of down regulation, were seen for the 5-HTR subtypes after treatment with STW 5 and O. Interestingly serotonin is not only the ligand for 5-HTR subtypes, but also an inflammatory mediator which can activate ASICs in peripheral nerve tissue to activate a central pain response[2].

Conclusion: Acid-sensing ion channels and 5-hydroxytryptamine receptors may form a communication network involved in pain sensing and signaling in gastro-esophageal reflux disease. The down-regulation of ASIC4 and 5-HTR-subtypes in the esophageal mucosa may be responsible for the fast pain relief in responders to PPIs and to STW-5.

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P0493 POSTURAL CHANGES INDUCE TRANSIENT LOWER ESOPHAGEAL SPHINCTER RELAXATIONS

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Introduction: Transient lower esophageal sphincter (LES) relaxations (TLESR) constitute the major mechanism of physiological gastroesophageal reflux (GER). They are also responsible for 65% of reflux episodes in patients with mild esophagitis and they facilitate belching. They appear mainly after meals and are produced by a reflex mechanism triggered by distension of gastric fundus. They are easily detected by high-resolution manometry.

Aims & Methods: The aim of the study was to determine whether postural changes, without the effect of meals, facilitate the occurrence of TLESR.

Records of 143 patients (77 M, 66 M) (mean age 53 SD 15.8, range:18 to 90 years) referred to our Motility unit for assessment of dysphagia or GERD were retrospectively analyzed. All patients underwent high-resolution manometry (ManoScan, Sierra Scientifics). After fasting for at least 8 hours studies were conducted randomly in supine, right side, left side and seated position. The TLESR were identified as a decrease in LES resting pressure to the level of gastric pressure, inhibition of diaphragmatic crura and unrelated to swallowing.

Results: TLESR were recorded in 68 patients (47.55%) (35 M, mean age 55 SD 15 y. and 33 F, mean age 54 SD 15.8 y.). In 12 cases (8 M) esophageal shortening was appreciated. In the remaining 63 patients (40 F, 23 M) no modifications of the esophagogastric junction were observed except for variations in LES resting pressure referred to the gastric pressure. A total of 94 TLESR: 40 in the sitting position, 34 in the right lateral decubitus, 15 in the left lateral decubitus and 5 in the supine position were recorded. Most of TLESR occurred in the change from supine to a seated position or from supine or right lateral to left lateral decubitus.

Conclusion: TLESR are often triggered by postural changes, regardless of meals and may be associated with GER when the patient change their body position like going to bed, getting up or during movements lying down.

Disclosure of Interest: None declared

P0494 NUTRITIONAL PATTERN OF RUSSIAN GASTROESOPHAGEAL REFLUX DISEASE PATIENTS

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Introduction: There is a lot of controversies about probable influence of dietary patterns on the disease progression and success of treatment in GERD. Nutritional pattern of GERD patients in Russia have not been studied yet.

Aims & Methods: The **aim** of the study was to assess the nutritional pattern of GERD patients in Russia compared to healthy controls.

Methods: One hundred twenty-four GERD patients (54 men, 70 women, age (M ± m) 46 ± 17.7 yrs; BMI (M ± m) 28.5 ± 0.6 kg/m^2) and 41 controls (8 men, 33 women, age (M ± m) 42 ± 12.4yrs; BMI (M ± m) 28.3 ± 1.3 kg/m^2) were examined using validated [1] food frequency questionnaire. Diagnosis of GERD was confirmed by typical symptoms and validated GerdQ questionnaire. Non-parametric statistics (Statistica 10, StatSoft Inc, USA) was used to investigate the difference between dietary patterns in GERD patients and controls.

Results: The studied and the control group did not differ on BMI, age and sex distribution ($p > 0.05$).

Main studied parameters of dietary patterns are shown in the table 1. It was found that average total fat and protein intake was higher in GERD group compared to controls. In contrast, average total fiber intake was significantly higher in controls, but both groups consumed less fibers, then it generally recommended (20 g or more/day). There was no difference between two groups on the carbohydrates, starch and mono/disaccharides intake.

Conclusion: Nutritional pattern of Russian GERD patients are characterized by higher fat and protein intake compared to controls and insufficient consumption of dietary fiber that may influence pathogenesis of the disease.

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Disclosure of Interest: None declared

P0495 LARYNGOPHARYNGEAL REFLUX AND COUGH REFLEX SENSITIVITY

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Introduction: Cough reflex sensitivity to inhaled irritants is thought to be related to the functional state of cough-triggering afferent nerve terminals in the larynx and large airways. Laryngopharyngeal reflux (LPR) causes larynx and potentially large airways irritation. However, the relationship between the cough reflex sensitivity and the LPR is not completely understood.

Aims & Methods: We hypothesized that the cough reflex sensitivity is positively correlated with the LPR. Our hypothesis predicts that patients with more frequent LPR will have lower cough reflex threshold. Consecutive patients referred by ENT physician for suspected LPR were evaluated. Laryngopharyngeal reflux was quantified by 24h pH-impedance monitoring using Given Imaging system. Proximal pH sensor was placed1 cm above upper esophageal sphincter as detected by high resolution manometry.

Cough reflex sensitivity was determined by single breath capsaicin inhalation challenge of doubling concentrations of capsaicin (0.49-500μmol/l) using KoKo PFT system. Cough threshold C2 was defined as the lowest concentration of capsaicin that evoked 2 or more coughs.

For statistical analysis C2 values were –log transformed and Pearson coefficients were calculated for correlation with reflux parameters.

Results: 13 consecutive patients with suspected LPR were evaluated. LPR episodes were detected by impedance monitoring in all patients. The number (median[interquartile range]) of LPR episodes was 15[19-29]. Cough sensitivity expressed as C2 concentration of capsaicin (geometric mean[95%CI]) was 13.4[6.6-27.1]μmol/l.There was a strong positive correlation between the cough sensitivity and the number of LPR episodes ($R = 0.77$, $P < 0.01$). In contrast there was no correlation between the total number of gastroesophageal reflux episodes in the esophagus ($R = 0.47$, $P > 0.1$). Total number of reflux episodes was detected by distal pH sensor placed 5 cm above manometrically determined lower esophageal sphincter. 5 of 13 patients had positive pH monitoring test based on DeMeester score > 14.72 indicating pathological distal esophageal acid exposure. The number of LPR episodes and cough sensitivity in these patients were virtually identical to those with negative pH monitoring test.

Conclusion: The number of laryngopharyngeal reflux episodes positively correlates with cough reflex sensitivity in patients with laryngopharyngeal reflux. These results may suggest a direct relationship between the intensity of laryngeal irritation and cough.

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Table 1: Correlation coefficients (Spearmen rank R) between nutritional patterns and esophageal function testing parameters.

	Number of refluxes/day, n	Number of acid refluxes/day, n	Number of weak acid refluxes, n	%time pH < 4 distal 1/3 of esophagus
Total energy, kKal/day	0.35*	0.35*	0.22*	0.19*
Protein, g/day	0.3*	0.25*	0.22*	0.13
Totalfat, g/day	0.33*	0.32*	0.21*	0.19*
Total carbohydrates, g/day	0.18*	0.24*	0.07	0.13
Dietary fiber, g/day	-0.22*	-0.14	-0.24*	-0.1

* - $p < 0.05$

P0496 ESOPHAGOGASTRIC JUNCTION MORPHOLOGY ASSESSMENT BY HIGH RESOLUTION MANOMETRY AND ITS RELATIONSHIP WITH GASTROESOPHAGEAL REFLUX DISEASE IN OBESE PATIENTS CANDIDATE TO BARIATRIC SURGERY

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Introduction: Obesity is a strong independent risk factor of gastroesophageal reflux disease (GERD), esophageal erosions and hiatal hernia (HH) development. Pure restrictive bariatric surgery should not be indicated in case of HH and GERD. In fact, if in most cases bariatric surgery can diminish reflux by losing a large amount of fat, on the other hand some restrictive procedure can worsen or cause the presence of GERD. Also, it is still unclear what is the real incidence of disruption of esophagogastric junction (EGJ) in patients candidate to bariatric surgery. Actually, high-resolution manometry (HRM) can provide accurate information about EGJ morphology, whereas impedance-pH monitoring (MII-pH) can highlight the presence of acid, weakly acid and weakly alkaline reflux and correlate it to symptoms.

Aims & Methods: Aim of this study was to describe the EGJ morphology determined by HRM in obese patients candidate to bariatric surgery and to verify if different EGJ morphologies are associated to GERD-related symptoms presence and to different GERD patterns determined by means of MII-pH. All patients underwent a standardized questionnaire for symptom presence and severity (GERDQ), upper endoscopy, HRM and MII-pH. EGJ was classified as: Type I, no separation between the lower esophageal sphincter (LES) and crural diaphragm; Type II, minimal separation (>1 and <2 cm); Type III, >2 cm separation. At MII-pH, total acid exposure time (AET, %) and total number of refluxes (TNR) were assessed. A healthy-volunteers group (HVs) was used as control.

Results: One hundred thirty-eight obese (BMI > 35) subjects and 15 HV (normal weight) were studied. Ninety-eight obese patients referred at least one GERD-related symptom, whereas 40 subjects were symptom-free. According to HRM features, EGJ Type I morphology was documented in 51 (36.9%) patients, Type II in 48 (34.8%) and Type III in 39 (28.3%). EGJ Type III subjects reported more frequently symptoms than EGJ Type I (38/39, 97.4%, vs. 21/59, 41.1% $p < 0.001$). Obese patients with EGJ Type I showed comparable mean LES pressure and peristaltic function than HV (30.5 ± 8.5 vs. 34 ± 5.2 mmHg, and 80 ± 10 vs. 90 ± 10 intact peristaltic waves with normal vigor, respectively). EGJ Type II and III patients showed a statistical significant reduction in LES pressure and peristaltic function (22.3 ± 12.2 vs. 34 ± 5.2 mmHg, $p < 0.05$ and 60 ± 10 vs. 90 ± 10 intact peristaltic waves with normal vigor, $p < 0.05$ respectively for Type II and 11.1 ± 5.3 mmHg, $p < 0.001$ and 40 ± 20 normal waves, $p < 0.001$ for Type III, respectively). At MII-pH, EGJ Type I patients showed similar reflux patterns to HVs (AET 3.4 vs. 2.3%, and TNR 27 ± 5 vs. 21 ± 6); EGJ Type II (AET 5.2, $p < 0.05$, and TNR 57 ± 21, $p < 0.05$) and III (AET 7.4, $p < 0.001$, and TNR 76 ± 33, $p < 0.001$) showed a significant increase in esophageal acid exposure and in TNR than HVs.

Conclusion: Obese subjects have a high risk of disruption of EGJ morphology. In particular, patients with HH often refer pre-operative presence of GERD symptoms. Thus, testing obese patients with HRM and MII-pH before undergoing bariatric surgery, especially for restrictive procedures, can be useful for assessing presence of HH and GERD.

Disclosure of Interest: None declared

P0497 EFFECTS OF OMEGA-LOOP GASTRIC BYPASS ON ESOPHAGOGASTRIC JUNCTION FUNCTION AND REFLUX

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Introduction: Several bariatric operations for morbid obesity have been developed in order to reduce excess body weight. In particular, omega-loop gastric bypass (OGB), consisting primarily of a long linear lesser-curvature gastric tube with a termino-lateral gastro-enterostomy 180–200 cm distal to the ligament of Treitz, was recently introduced with good results in terms of weight loss and improvement of obesity-related co-morbidities. However, concerns have been raised about the potential development of symptomatic biliary reflux gastritis/esophagitis and risk of gastric/esophageal cancer due to chronic biliary reflux. At present, no objective data are available on the effect of OGB on esophago-gastric junction (EGJ) function, reflux occurrence and symptoms.

Aims & Methods: We aimed to evaluate the possible effects of OGB on esophageal motor function and a possible increase in gastro-esophageal reflux. Consecutive obese patients underwent clinical assessment for reflux and dyspeptic symptoms by means of a validated questionnaire, and endoscopy plus high-resolution impedance manometry (HRiM) and 24-h impedance-pH monitoring off-therapy before and 1 year after OGB. During HRiM and impedance-pH tracings analysis we measured: intragastric pressure (IGP), gastroesophageal pressure gradient (GEPG), EGJ morphology, motility pattern according to Chicago classification, distal esophageal acid exposure, number of impedance-detected refluxes and symptom association probability. A group of obese patients who underwent sleeve gastrectomy (SG) was included as the control population.

Results: Fifteen OGB patients [5 males/10 females; mean age 38 ± 8.2 years; mean BMI 46.4 (38-60) kg/m^2] were included in the study. After surgery [mean BMI 31 kg/m^2 (28-42)], none of the patients reported "de novo" heartburn or regurgitation. At endoscopic follow-up 1 year after surgery, esophagitis was absent in all patients and no biliary gastritis nor presence of bile were recorded. Manometric features and patterns did not vary significantly after surgery, whereas IGPs and GEPGs statistically diminished (from a median of 15 to 9.5, $p < 0.01$ and from 10.3 to 6.4, $p < 0.01$, respectively) after OGB. In contrast, SG induced a significant elevation in both parameters (from a median of 14.8 to 18.8, $p < 0.01$ and from 10.1 to 13.1, $p < 0.01$, respectively). A dramatic decrease in the number of reflux events (from a median of 41 to 7; $p < 0.01$) was observed after OGB, whereas in patients who underwent SG a significant increase in esophageal acid exposure and number of reflux episodes (from a median of 33 to 53; $p < 0.01$) were noted.

Conclusion: In contrast to SG, OGB did not compromise the gastro-esophageal junction function and did not increase gastro-esophageal reflux, which explained by the lack of increased IGP and in GEPG as assessed by HRiM.

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P0498 REFLUX TYPE AND NUMBER ARE RELATED TO NUTRITIONAL PATTERNS IN GERD PATIENTS

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Introduction: Little is known about the influence of nutrition on number and reflux type in GERD, therefore dietary recommendations for patients are mostly empirical.

Aims & Methods: The aim of the study was to assess the relationship between GERD patients' nutrition pattern,presence of the disease and esophageal pH-impedance parameters.

Methods: One hundred twenty four GERD patients (54 men, 70 women, age (M ± m) 46 ± 17.7 yrs; BMI (M ± m) 28.5 ± 0.6 kg/m^2) and 41 controls (8 men, 33 women, age (M ± m) 42 ± 12.4yrs; BMI (M ± m) 28.3 ± 1.3 kg/m^2) were examined using validated food frequency questionnaire. Number and types of gastro-esophageal refluxes evaluated by 24-hours esophageal pH-impedance recordings (Ohmega, MMS, the Netherlands; 2pH-6 impedance channels catheters, UnisensorAG, USA). Correlation analysis was performed between the number of reflux episodes, their acidity, duration and frequency and quantity of protein, carbohydrates, total fat, fiber and energy intake using non-parametric statistics (Statistica 10, StatSoftInc, USA).

Results: Direct, medium strength correlation was found between presence of GERD and total energy ($R = 0.23$, $p < 0.05$) and daily fat ($R = 0.21$, $p < 0.05$) intake. Inverse medium strength correlation was found between dietary fiber intake and presence of GERD ($R = -0.26$, $p < 0.05$). Proportion of time with pH < 4 at 5 cm over EGJ significantly correlated with total daily energy and total daily fat intake.Correlation coefficients (Spearmen rank R) between nutritional patterns and esophageal function testing parameters are shown in the table 1.

Conclusion: The obtained data may reflect influence of nutritional patterns on pathogenesis of GERD and should be taken into the account when dietary advice is given to the patient.

Disclosure of Interest: None declared

P0499 THE PHENOMENON OF LEPTIN RESISTANCE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE AND DIFFERENT TYPES OF OBESITY

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Introduction: Gastroesophageal reflux disease (GERD) is one of the most prevalent diseases in the world. Overweight and obesity are recognized as independent risk factors for the emergence and progression of GERD. It is known that visceral fat produced by the biological-active substance (adipokines) to influence the feeding behavior. Leptin is one of the most important adipokines, which acts on the hunger and satiety centers in the hypothalamus, involves in the regulation of energy homeostasis and body weight control. It is known that leptin plays a role in the formation of erosive GERD forms, Barrett's esophagus, which may be associated with its pro-inflammatory activity, proliferative power to induction of epidermal growth factor, as well as antiapoptotic effect.
Aims & Methods: We had an aim to determine the characteristics of the course of GERD based on the study of clinical and endoscopic manifestations of the disease, results of pH monitoring and the phenomenon of leptinresistance in patients with different types of obesity. We performed open comparative cross-sectional studies. We examined 105 patients with GERD and obesity or overweight. We asked patients, assessed an anthropometric indices, did a biochemical analysis of blood, endoscope examination of the esophagus and stomach, pH monitoring, assessed levels leptin and its soluble receptor. We separated patients in two groups: the main group (n = 85) - patients with abdominal type of obesity, the comparison group (n = 20) - with normal volume of waist.
Results: Weight, height, body mass index, level of glucose was higher in main group ($p < 0.00003$, $p < 0.03$, $p < 0.(10)82$, $p < 0.02$, respectively). Leptin levels in patients with abdominal type of obesity was significantly higher and the level of its receptors was significantly lower (mediana of leptin levels 36,93 (14,69-47,60) in main group versus 9,59 (7,66-19,48), mediana of leptin's receptors 18,25 (14,69-24,26) versus 23,78 (18,83-32,67), respectively). Between these indicators in main group was revealed negative correlation of mild strength ($rs = (-0.424)$, $p < 0.002$). There were more patients with Nonalcoholic Fatty Liver Disease in main group ($p < 0.001$). According to the results of gastrointestinal endoscopy non-erosive GERD form was diagnosed in 92 (87.6%) patients and erosive form was revealed in 13 (12.4%). According to the results of endoscopy in patients with GERD comparison groups differences have not been identified. In group with abdominal type of obesity pH cardia and body of stomach was higher ($p < 0.04$, $p < 0.02$, respectively), but time of refluxate's contact with low pH (pH <4) in these departments was longer in the comparison group ($p < 0.05$). Positive relationship was found between leptin's receptors and contact's time in the range of pH from 3 till 6 in the stomach ($rs = (0.645)$, $p < 0.03$), in the range from 4 till 7 and less than 4 in the esophagus ($rs = (0.645)$, $p < 0.03$, $rs = (0.600)$, $p < 0.05$, respectively), the longest gastroesophageal ($rs = (0.624)$, $p < 0.03$) and alkaline refluxes ($rs = (0.640)$, $p < 0.03$).
Conclusion: The formation of leptinresistance in individuals with overweight and obesity based on the type of fat distribution is associated with course of the GERD.
Disclosure of Interest: None declared

P0500 ASSOCIATION BETWEEN THE FORM OF GASTROESOPHAGEAL REFLUX DISEASE, CARACTERISTICS OF ESOPHAGEAL PH-IMPEDANCE MONITORING AND CYTOKINES EXPRESSION

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Introduction: The gastroesophageal reflux disease (GERD) is one of the most common diseases, which affects about 15-25% of the world population. In GERD damage of the esophageal mucosa may occur as a result of different types of refluxate, i.e. gastric, biliary or duodenogastric/mixed. In patients with GERD, depending on the form of the disease, increased expression of pro-inflammatory or anti-inflammatory cytokines.
Aims & Methods: To determine correlations between the form of gastroesophageal reflux disease, parameters of esophageal pH-impedance monitoring and cytokines expression.
This prospective cohort study included 55 patients: 20 with non-erosive reflux disease (NERD) – 55% men; average age 37.7 ± 12.0, 20 with erosive esophagitis (EE) – 65% men; average age 38.3 ± 12.5, and 5 with Barrett's esophagus (BE) – 100% men; average age 34.2 ± 9.8, and 10 healthy volunteers. We performed on all patients an upper endoscopy, a 24-h esophageal pH-impedance monitoring and the determination of plasma cytokines (IL-4, IL-8, IL-10, IFN-γ, TNF-α) by flow cytometry. The statistical analyses were done using R Statistical Software.
Results: In patients with EE in comparison to patients with NERD and BE we registered a higher total number of acid reflux ($p < 0.0001$) and a higher esophageal acid exposure ($p < 0.0001$). Patients with BE, in comparison to patients with NERD and EE, had a higher total number of weakly acid reflux ($p = 0.01$) and higher esophageal weakly acid exposure ($p = 0.004$).
We found the correlations between the level of IL-8 and the total number of acid reflux (Kendall $\tau = 0.76$) and with esophageal acid exposure ($\tau = 0.42$). The level of TNF-α also correlated with total number of acid reflux ($\tau = 0.69$) and with esophageal acid exposure ($\tau = 0.48$). The level of IL-4 correlated with the total number of weakly acid reflux ($\tau = 0.48$) and with esophageal weakly acid exposure ($\tau = 0.50$) as well as the level of IL-10 ($\tau = 0.50$ and $\tau = 0.51$, respectively).
Conclusion: The levels of TNF-α and IL-8 correlated with total number of acid reflux and with esophageal acid exposure in patients with erosive esophagitis. The levels of IL-4 and IL-10 correlated with total number of weakly alkaline reflux and with esophageal weakly alkaline exposure in patients with Barrett's esophagus.
Disclosure of Interest: None declared

P0501 THE EFFICACY OF TRANSORAL INCISIONLESS FUNDOPLICATION (TIF) IN CONTROLLING CHRONIC GERD: RESULTS OF A DOUBLE BLIND, SHAM CONTROLLED STUDY

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Introduction: Until recently only two therapeutic options have been available to control symptoms and to heal the esophagitis in chronic gastroesophageal reflux disease (GERD) patients, i.e. life-long proton-pump inhibitor (PPI) therapy or antireflux surgery. Lately, Transoral Incisionless Fundoplication (TIF) has been developed and found to have a potential to offer a therapeutic alternative for these patients. As part of a comprehensive and stepwise evaluation strategy for the clinical use of TIF, we performed a double-blind, multi-center, sham-controlled study in GERD patients who were chronic PPI users.
Aims & Methods: Patients 18-80 years old, on daily PPIs for > 6 months, with persistent GERD symptoms without PPI therapy (during the titration phase of the study), were included in the trial if they had evidence of two or more of the following while off PPI therapy (>10 days): esophagitis (Los Angeles grade A, B or C), abnormal ambulatory pH study, or moderate to severe GERD symptoms. For enrolment we also required normal or near normal esophageal motility (by manometry or impedance), patients' willingness to cooperate with post-operative dietary recommendations and assessment tests and signed informed consent. After randomization, those allocated to TIF had the procedure completed during general anesthesia by the TIF2.0 EsophyX system with SerosaFuse fasteners (EndoGastric Solutions, Inc., Redmond, WA, USA). Sham procedure consisted of upper GI endoscopy under general anesthesia. Neither the patient nor the assessor was aware of the treatment group affiliation. The primary effectiveness endpoint was the proportion of patients in clinical remission after 6 months (without being classified as treatment failure). Secondary effectiveness parameters were: PPI consumption, esophageal acid exposure, reduction in GERD symptom scores as assessed by the Quality of Life in Reflux and Dyspepsia and Gastrointestinal Symptoms Rating Scale instruments and healing of reflux esophagitis.
Results: Out of 121 patients screened we finally randomized 44 patients with 22 patients confined to each group. The study groups were well balanced regarding demographic and disease-specific characteristics. The time in remission, during the first six months, is detailed in the table demonstrating a significant superiority offered by the TIF procedure. Likewise, the secondary outcome measures were all in favor of the TIF procedure. As an example, acid reflux time improved from 8.89 (Standard Error of Mean, SEM = 0.84) to 3.73 (SEM = 0.84) by the TIF intervention ($p = 0.0002$) whereas the sham procedure did not change the acid reflux profile at all.

Group	In Remission (n = 22)	Treatment Failure (n = 22)
Transoral Incisionless Fundoplication, n (%)	14 (64)	8 (36)
Sham, n (%)	2 (9)	20 (91)
P (Fisher's Exact test)		= 0.0004

Conclusion: Transoral Incisionless Fundoplication (TIF) was found to offer chronic GERD patients, being on long-term treatment with PPI, an effective therapeutic alternative.
Disclosure of Interest: None declared

P0502 PATIENTS WITH NON-ACID REFLUX DISEASE AND THOSE WITH EROSIVE AND NON-EROSIVE REFLUX DISEASE HAVE SIMILAR RESPONSE TO ANTI-REFLUX SURGICAL THERAPY

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Introduction: Combined impedance-pH monitoring is considered the gold standard for the detection of reflux episodes. Indeed, several studies demonstrated

the increased diagnostic yield of this technique in gastro-esophageal reflux disease (GERD) thanks to its ability to correlate symptoms with both acid and/or non-acid reflux episodes. However, limited data are available about the clinical usefulness of impedance-pH testing in GERD management.
Aims & Methods: We aimed to assess whether refractory GERD patients classified by means of endoscopy and impedance-pH as affected by non-acid reflux disease (NARD), erosive and non-erosive reflux disease (ERD and NERD) may benefit from anti-reflux surgery. Consecutive patients with persisting heartburn and/or regurgitation despite 8 weeks of proton pump inhibitors therapy, were prospectively enrolled in this open label trial. All patients underwent upper endoscopy and 24-hour impedance-pH testing off-therapy. We measured distal esophageal acid exposure time (AET), characteristics of reflux episodes (acid/non-acid) and symptom-reflux association. Then, patients with ERD (endoscopy+), NERD (endoscopy-, AET > 4.2% and/or SAP/SI+ for acid reflux) and NARD (endoscopy-, AET < 4.2% and SAP/SI+ for non-acid reflux or both kind of reflux) underwent laparoscopic Nissen fundoplication (LNF). Before LNF and at 1, 6 and 12 months after surgery, reflux symptoms and quality of life were assessed by using validated questionnaires. Upper endoscopy and impedance–pH monitoring was repeated 1 year after surgery. Surgical treatment failure was considered in case of: persisting typical reflux symptoms and/or objective evidence of GERD (esophagitis at upper endoscopy, abnormal AET and/or number of refluxes, positive symptom association) and/or poor quality of life.
Results: Out of sixty-five refractory patients, forty-eight (24F/24M; mean age 49; 14 ERD, 22 NERD and 12 NARD) were included. At 1 year follow-up after surgery, LNF had similar pathophysiological effects in all groups. Indeed, percentage of patients with abnormal AET (ERD 93% vs 7%, NERD 71% vs 0%) and/or increased number of reflux episodes (ERD 93% vs 0%, NERD 86% vs 0%, NARD 83% vs. 0%), mean AET (ERD 12.9% vs 1.8%, NERD 6.1% vs 0.7, NARD 0.7% vs 0.4%) and median number of total (ERD 100 vs 6, NERD 73 vs 9, NARD 72 vs 10), acid and non-acid refluxes significantly decreased (in all cases, $p < 0.01$). As to the surgical outcome, the percentage of patients with resolved or markedly improved typical symptoms at 12 months after surgery was similar among the study groups (ERD 93% vs. NERD 82% vs NARD 83%, p = ns). Quality of life similarly improved in all groups (p = ns). Finally, the percentage of failure and/or adverse events did not differ among the groups (ERD 21% vs. NERD 23% vs NARD 17%, p = ns).
Conclusion: Our data show that LNF was a safe and effective procedure in relieving typical reflux symptoms in PPI-refractory patients identified as affected by ERD, NERD and NARD, by means of endoscopy and impedance-pH monitoring. Therefore, impedance-pH testing allowed a more clear identification of refractory patients whose symptoms are related to reflux, thus improving their management and outcome.
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P0503 INFLUENCE OF THORACIC AND ABDOMINAL BREATHING ON THE BASAL PRESSURE OF THE LOWER ESOPHAGEAL SPHINCTER

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Introduction: The lower esophageal sphincter and the adjacent crura of the diaphragm form a functional unit preventing gastroesophageal reflux. Esophageal manometry describes the function of this esophagogastric junction. Active abdominal breathing activates the diaphragmatic crura thus contributing to esophagogastric junction pressure (pEGJ). We performed a controlled prospective study to determine the influence of abdominal versus thoracic breathing on pEGJ using esophageal manometry.
Aims & Methods: After routine High-Resolution esophageal manometry confirming normal esophageal function, 10 patients changed into a standing position. Subjects were then instructed to take 10 breaths targeted towards the thorax, followed by 10 breaths with active abdominal breathing, followed by 10 breaths of abdominal breathing with increased airway resistance (compression of one nostril). In addition to standard manometric measurements, we analyzed the fraction of time in percent of pEGJ over 10, 15, 20, 25 and 30 mmHg. Manometric recordings of esophageal motor function were evaluated with the Manoview™ software. ANOVA and Post-Hoc tests were used for statistical analysis.
Results: During thoracic breathing p_{max}EGJ (maximal pressure; median ± upper/lower quantile) showed normal values (39 mmHg ± 24/44) and significantly increased during abdominal breathing (62 mmHg; ± 52/85). Abdominal breathing with increased airway resistance did not show an additional effect (70 mmHg ± 63/92). During abdominal breathing with increased resistance the time of pEGJ over 20 mmHg, 25 mmHg and 30 mmHg was significantly longer compared to thoracic breathing (> 20 mmHg: 44% (39/50) versus 76% (42/93); > 25 mmHg: 38% (30/41) versus 57 % (36/69); > 30 mmHg: 28% (19/33) versus 48% (33/63)).
Conclusion: Our study clearly shows that the type of breathing significantly influences pEGJ. In addition, we found that pEGJ reaches longer time intervals with competent pEGJ in abdominal compared to thoracic breathing. Current recommendations for routine esophageal analysis do not include breathing type. We suggest that breathing type should be taken into consideration when interpreting esophageal manometric data. We have already shown that controlled breathing training can improve symptoms in patients suffering from gastroesophageal reflux. Our current data suggests that a direct training effect on diaphragmal muscles might be an explanation for the findings of our previous studies.
Disclosure of Interest: None declared

P0504 OUTCOMES OF REDO SURGERY FOR FAILED LAPAROSCOPIC FUNDOPLICATION IN JAPANESE PATIENTS

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Introduction: Laparoscopic fundoplication (LF) is an established surgical treatment for GERD. In our institution, about 95% of patients reported a high degree of satisfaction with surgery. On the other hand, some patients were expected to undergo redo surgery for reasons such as recurrence of hiatal hernia and/or reflux esophagitis.
Aims & Methods: The aim of this study was to investigate the outcomes of redo surgery for failed laparoscopic fundoplication in Japanese patients. Four-hundred and seventy-four patients underwent laparoscopic anti-reflux surgery between December 1994 and January 2015 in our institution. Among them, 11 patients who had redo surgery were studied. Their mean age was 57.7 ± 15.1 (range, 29-78) years, and 6 of them (45%) were female. Their clinical data were collected in a prospectively fashion and retrospectively reviewed. The outcomes were assessed in terms of indications for redo surgery, operative procedure, operation time, blood loss, perioperative complications, and postoperative course.
Results: No operative mortality occurred. The indications for surgery (some were overlapped) were dislocations of fundic wrap in 5 (45%), recurrence of paraesophageal hiatal hernia or erosive reflux esophagitis in 3 (27%) each, tight Nissen or esophageal motility disorder in 1 (9%) each. Ten (91%) were approached laparoscopically and another (9%) required conversion to open surgery. Eight (73%) underwent redo fundoplication, and the others underwent hiatal hernia repair alone. The mean operation time was 202 ± 46 (range 125-256) minutes and the mean blood loss was 56 ± 100 (range 0-292) ml. No patient required blood transfusion. Perioperative gastric wall injury was observed in 3 patients (27%). Almost all patients' postoperative courses were uneventful and the median time to start postoperative oral intake and the median post-operative hospital stay were post-operative day 1 and 8, respectively. Three patients (27%) required prescription of proton pump inhibitors (PPIs) despite surgery and 2 patients (18%) had recurrence of hiatal hernia. Postoperative questionnaire was answered by 7 of 11 patients (74%). All patients reported full points 5 (range 1-5) as a satisfaction to surgery.
Conclusion: Redo surgeries for failed laparoscopic fundoplication were safely performed under laparoscopy. Recurrence rate after redo surgery was about 20% and more than 70% of patients could be withdrawn from PPIs.

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Disclosure of Interest: None declared

P0505 PRELIMINARY RESULTS OF A PROSPECTIVE MULTI-CENTER OBSERVATIONAL REGISTRY OF LOWER ESOPHAGEAL SPHINCTER STIMULATION FOR GERD: THE LESS-GERD REGISTRY

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Introduction: The electrical stimulation of the lower esophageal sphincter (LES-ES) using the EndoStim® LES Stimulation System (The Hague, The Netherland) was shown to be effective and safe in clinical trials. So far there no data was reported in routine clinical practice.
Aims & Methods: An ongoing, prospective multicenter web-based registry for the evaluation of LES-ES is prospectively collecting data at baseline and at routine follow-ups for 5-year on patient undergoing LES-ES in routine clinical practice for disruptive GERD symptoms despite daily PPI use. Demographics, adverse events, GERD symptoms using daily diaries and GERD health related quality of life score (GERD-HRQL) for reflux symptoms, structured GI symptom questionnaire for extra-esophageal symptoms, recorded use of proton pump inhibitors (PPIs) and objective endoscopic and physiological data (esophageal pH / manometry) when available.
Results: Currently, data from 46 enrolled patients is available in the registry, of whom 24 had data at 6 months post-op. All but one (23/24; 96%) patient showed an improvement in their GERD-HRQL score. Overall, the median (IQR) composite GERD-HRQL score of 21.5 (17.5-25.5) preoperatively improved to 6.5 (3.0-10.5) after 6 months ($p < 0.0001$). The median distal esophageal acid exposure improved from 8.8 (3.4-18.5) % at baseline to 2.65 (1.6-5.1) % at 6 months (p = NS). The proportion of patients with moderate to severe regurgitation decreased from 72% on-therapy preoperatively to 29% after 6 months of LES-ES ($p < 0.04$). Bothersome reflux symptoms during sleep improved from 43%

pre-op to 4% ($p < 0.004$) at 6 months. Recurrent cough decreased from 21% patients preoperatively to none after 6 months. One patient reported severe dysphagia pre-op that was resolved post-op. There was no change in the rate of occasional dysphagia reported. All patients were on long-term PPI at baseline. At 6 months, 17 (70%) patients were completely free of PPI use, 4 patients (17%) were still taking daily PPI and another 3 patients (13%) used PPI occasionally or had reduced their dose by > 50%. There were two serious adverse events (both resolved) classified as unrelated to device or procedure: acute pain from pre-existing gall-stones and intestinal atony occurring two weeks post-op. There were no GI side-effects related to the procedure or stimulation therapy reported.

Conclusion: LES-ES is safe and effective in routine clinical practice with improved quality of life and elimination of a PPI maintenance therapy in most patients. LES-ES may be considered a viable treatment option for well selected GERD patients with bothersome symptoms on PPI.

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P0506 INADEQUATE SYMPTOM CONTROL ON LONG-TERM PPI THERAPY IN GERD – FACT OR FICTION?

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Introduction: Randomized controlled trials report about 30% of GERD patients complain of bothersome remaining symptoms (heartburn, regurgitation) despite PPI. General practice physicians estimate this to be an over-representation.

Aims & Methods: In a prospective, multicenter, observational study, which was conducted in 16 general practice clinics over 3 months, patients with GERD and taking PPI for over 1 year were asked to complete a questionnaire. Patients were asked the duration of their GERD, duration of PPI therapy, satisfaction with their condition on PPI, whether they have received diagnostic evaluation related to GERD (endoscopy, pH monitoring, manometry), whether they have received surgical consultation for GERD, and the frequency of any remaining complaints in the past week (i.e. heartburn, regurgitation, sleep disruption) as part of a validated questionnaire for the diagnosis of GERD (GerdQ). ''Lost Patients'' were defined as those likely to be suffering from true GERD as predicted by the GerdQ questionnaire, dissatisfied on their current PPI therapy, and had not previously received any specific GERD diagnostics (pH-metry or manometry).

Results: 323 consecutive patient responses were collected. Patients suffered from GERD for an average of 8.42 years and prescribed PPI therapy for an average duration of 6.26 years. 39% of patients reported heartburn at least 2 days per week (20% 4-7 days per week), 29% complained of regurgitation at least 2 days per week (13% 4-7 days per week), and 22% reported symptoms disrupting sleep at least twice per week (7% 4-7 days per week). 20% of patients were dissatisfied on their current PPI therapy (score of 1 or 2 on a scale of 1-5, 1 = very dissatisfied, 5 = very satisfied), and 13% were both dissatisfied and had a high likelihood of complaints correlating to pathological pH based on the GerdQ questions. A total of 85% of patients received an upper endoscopy in the past, but only 7% had a prior pH-metry and 2% manometry. Only 7% received prior surgical consult for GERD. The rate of ''Lost Patients'' was 10%.

Conclusion: Inadequate control of symptoms is common in GERD patients prescribed PPI therapy, and is often overlooked in daily practice. These patients with insufficient symptom control should be methodically identified and considered for further diagnostics and/or treatment modification, for example with a screening questionnaire.

Disclosure of Interest: None declared

P0507 GLOBAL CLINICAL EXPERIENCE WITH ENDOSTIM® LOWER ESOPHAGEAL SPHINCTER STIMULATION THERAPY: AN INDIVIDUAL PATIENT DATA META-ANALYSIS OF THE OPEN LABEL CLINICAL TRIALS

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Introduction: Electrical Stimulation of the LES is emerging as a new theraputic modality for refractory GERD

Aims & Methods: To assess efficacy and safety of LES stimulation in GERD patients by performing an individual patient data meta-analysis.

A systematic literature search and contact with EndoStim confirmed that no additional clinical trials on LES stimulation in GERD patients other than the two open-label clinical trials were available [1,2]. The individual patient data from the 2 trials were used for this meta-analysis after it was shown that the two trials had identical design, with no significant differences in the baseline inclusion and exclusion criterial of the trials, and no heterogeneity in baseline and follow-up summary data. Each patient's baseline data was used as control data and 6-month data was used as on-treatment data.

Results: Sixty-six patients, with 43% women at 11 centers in Europe, South America and Asia, were included. Median age was 52 (IQR = 43-62) years. Ninety-five percent (63/66) of patients were using daily PPIs with one-third of them using PPIs twice daily. At their 6 months follow-up, 89% (58/65) were no longer using PPIs and 5% (3/65) were using PPIs on < 50% of days. Median distal esophageal acid exposure at baseline was 10.0% (IQR = 7.7-12.9), which had improved to 4.9% (IQR = 2.4-7.3) % at 6 months follow-up ($p < 0.001$). Median GERD-HRQL scores at baseline on-PPI were 10 (IQR 8-21) and off-PPI 28 (IQR 22-34) which improved to 4.0 (IQR 1-9) at 6 months on LES stimulation therapy ($p < 0.001$ vs. both on and off-PPI). Significant improvement in median days with heartburn and regurgitation at day and night vs. baseline both on- and off-PPI ($p < 0.001$), and near-complete elimination of regurgitation and nocturnal symptoms were observed. There were no statistically significant differences in efficacy outcomes between geographical locations (Europe vs. South America vs. Asia). In total, 2 SAEs related to the device or procedure (trocar perforation and asymptomatic lead erosion) were managed with device explant. There were 65 device and/or procedure-related non-serious adverse events, all typical of a laparoscopic implant procedure and resolving without any invasive intervention.

Conclusion: This meta-analysis confirms the results of previous trials on safety and efficacy of LES electrical stimulation in GERD patients and provides a robust estimate of the effect size among a larger number of patients and across multiple geographical locations.

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P0508 ASSOCIATION OF SLEEP DISTURBANCES WITH SPECTRUM OF GASTRO-OESOPHAGEAL REFLUX DISEASE IN A CHINESE GENERAL POPULATION

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Introduction: Previous studies have shown a complex relationship between sleep disturbances and gastro-oesophageal reflux disease (GORD). Since GORD could be further categorized into subgroups based on the endoscopic findings and the presence of typical reflux symptoms, whether the GORD spectrum are associated with different impact on the sleep quality remains unclear.

Aims & Methods: We aim to investigate the association of subjective and objective sleep disturbance with the heterogeneous manifestations of GORD in a Chinese general population. We prospectively recruited 561 subjects who voluntarily underwent an electrocardiogram-based cardiopulmonary coupling analysis as part of a comprehensive health check-up at the National Taiwan University Hospital during 2012-2013. All subjects received the Reflux Disease Questionnaire (RDQ) and an upper endoscopy to determine the presence of erosive oesophagitis (EO) and non-erosive reflux disease (NERD), defined as subjects with troublesome symptoms (a heartburn/regurgitation score > 3 by RDQ) but without definite endoscopic mucosa breaks. Subjective sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI) and sleep dysfunction was defined as a PSQI > 5. Sleep-disordered breathing was defined as the apnoea–hypopnoea index derived from the cardiopulmonary coupling analysis > 15 event/hour. Detailed demographics, anthropometrics, metabolic profile and psychological status were also obtained. Comparisons were made between subjects with and without GORD and subjects within the different categories of GORD spectrum for a range of subjective and objective sleep parameters.

Results: Of the 277 subjects (49.4%) who were diagnosed as having GORD, EO was found in 198 subjects (35.3%), in whom 123 (21.9%) were symptomatic and 75 (13.3%) were asymptomatic (RDQ = 0). NERD was diagnosed in 79 subjects (14.1%). Subjects with GORD had higher global PSQI scores (6.99 ± 3.97 vs. 6.07 ± 3.73, $P = 0.005$) and a higher prevalence of sleep dysfunction (60.6% vs. 49.6%, $P = 0.009$) than those without GORD. Subjects with EO had a significantly higher prevalence of sleep-disordered breathing than those without (42.9% vs. 33.9%, $P = 0.034$). Presence of troublesome reflux symptoms was independently associated with sleep dysfunction in the multivariate analysis (adjusted odds ratio = 2.05; 95% confidence interval = 1.39-3.00). Across the GORD spectrum, subjects with symptomatic EO had the highest PSQI scores (7.68 ± 3.93) as well as the prevalence of sleep dysfunction (70.7%), while the prevalences of sleep-disordered breathing among the subgroups were not significantly different.

Conclusion: We demonstrated a high prevalence of subjective and objective sleep disturbances among the GORD patients in this Chinese population. Different manifestations across the GORD spectrum were associated a variety of impairment on the sleep quality. Further interventional studies to explore the

effect of aggressive GORD treatment on the various aspects of sleep quality of GORD patients are warranted.
Disclosure of Interest: None declared

P0509 OUTCOME OF ESOPHAGO-GASTRIC JUNCTIONAL ADENOCARCINOMA TREATED BY ESD

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Introduction: Esophago-gastric junctional adenocarcinoma (EGJAC) was rare in Japan. However, recently the incident of EGJAC has been increasing. And the outcome of endoscopic submucosal dissection (ESD) for EGJAC is unknown.
Aims & Methods: The aim of study is to investigate the outcome of EGJAC treated by ESD.
EGJAC was defined as adenocarcinoma located between 1cm oral and 2cm anal from EGJ. 92 patients (80 males and 12 females) with EGJAC were treated by ESD from January, 2000 to December, 2011. Follow up examination including annual CT and EGD was performed. R0 resection rate, complications and prognosis were investigated. Additional therapy was recommended for the T1bSM2 (501 micrometer or deeper) patients. The median age and follow up period was 74 (32-89) and 65 (6-173) months, respectively. The median diameter of the resected lesions and specimens was 18 (3-61) and 40 (20-82) mm, respectively. Protuberant, flat and depressed type was 44, 4 and 44 lesions, respectively. Differentiated and poorly differentiated adenocarcinoma was 88 and 4 lesions, respectively.
Results: 1. Complete resection rate was 100%. R0 rate resection was 99% (91/92).
2. Complications: The bleeding during ESD and delayed bleeding required blood transfusion was 0% and 1% (1/92). The perforation during ESD and delayed perforation was 1% (1/92) and 0%. Stenosis was 11% (10/92), and all of 10 cases were treated by endoscopic balloon dilatation.
3. T1a-M, T1b-SM1(less than 500 micrometer) and T1bSM2 was 62, 15 and 15 lesions, respectively.
4. Local recurrence rate was 0% in any groups.
5. Prognosis.
5-1 T1a-M and T1b-SM1: No patient died of EGJAC.
5-2 T1bSM2: Additional gastrectomy was performed for 7 of 15 T1b-SM2. And, only one case had lymph node metastasis. 7 patients were followed up without gastrectomy. One patient was treated by additional radiation, and lymph node metastasis was found after radiation. Only this patient died of EGJAC.
Conclusion: T1a-M and T1bSM1 EGJAC are good candidate for ESD. However, additional therapy should be recommended for T1bSM2 EGJAC patients.

Disclosure of Interest: None declared

P0510 FEASIBILITY AND USEFULNESS OF EUS-FNA IN THE DIFFERENTIAL DIAGNOSIS BETWEEN MALIGNANT AND BENIGN LESIONS FOR RELATIVELY SMALL DUODENUM SUBMUCOSAL TUMORS

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Introduction: Duodenal submucosal tumors (SMTs) with malignant potentials including gastrointestinal stromal tumors (GIST) are relatively rare, but we sometimes need to make a differential diagnosis of duodenal SMTs. Although it is generally accepted that EUS-FNA is a gold standard for making a histological diagnosis of gastric SMTs, the feasibility and usefulness of EUS-FNA for duodenal SMTs have yet to be determined. In general, tissue sampling of duodenal SMTs by EUS-FNA is more difficult than that of gastric SMTs.
Aims & Methods: The aims of the present study were to assess feasibility, safety, and usefulness of EUS-FNA for duodenal SMTs. Between June 2009 and March 2015, a total of 17 patients with duodenal SMTs who had undergone EUS-FNA were enrolled in the present study and were retrospectively reviewed. A linear EUS scope (UCT260-AL5; Olympus, Tokyo, Japan) together with needle devices (22G, 25G) were used for EUS-FNA with rapid on-site evaluation (ROSE). We evaluated success rate of sampling, diagnostic yield and procedure-related complications.
Results: The mean diameter of duodenal SMTs was 22.4 mm in size ranging from 8 to 59 mm. The puncture could be completed in all 17 patients. The mean number of FNA passes was 3.8 ranging from 1 to 7. All samples were satisfactory for making a histological diagnosis. As a result, ten patients were diagnosed with GIST, one with gangliocystic paraganglioma, one with neuroendcrine tumor and five with benign tumors. There were no procedure-related complications. Although most samples obtained by EUS-FNA in the present study were smaller than those usually obtained with gastric SMTs, we could make a differential diagnosis between malignant tumors and benign lesions in all cases.
Conclusion: This is the first case series showing feasibility of EUS-FNA for relatively small duodenal SMTs. EUS-FNA could be a useful diagnostic tool for surgical decision making not only in gastric SMTs but also in duodenal SMTs.
Disclosure of Interest: None declared

P0511 LONG-TERM GASTRIC CANCER RISK IN SMOKING MEN WITH ATROPHIC GASTRITIS

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Introduction: The incidence of gastric cancer has declined dramatically during last decades in western countries. In Finland, the age-standardized incidence being 6.3 / 100 000 for men and 3.6 / 100 000 for women [1]. Because of the low incidence, screening programs are not considered effective in the West. Early gastric cancer rarely causes symptoms, and, thus majority of gastric cancers are diagnosed in advanced, symptomatic stage.
Atrophic gastritis in the best known premalignant condition of gastric cancer, and it has been suggested that persons who have extensive atrophic changes in stomach should undergo surveillance.
Aims & Methods: Our aim was to evaluate the long-term gastric cancer risk in smoking men with atrophic gastritis.
Serum pepsinogens (SPGs) were measured from 22,436 smoking men (age 50-69 years) who participated The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study in Finland [2-3]. Low serum pepsinogen I (SPGI) was measured in 2132 men, and they were invited to gastroscopy [4]. Endoscopy was performed to 1344 men, and after excluding the men with gastric cancer in a beginning of study, 1326 men were enrolled in this study.
The first gastroscopies were performed between years 1989-1993, and the surveillance continued until the end of year 2012, the gastric cancer diagnosis, or the death. The median follow-up time was 13.6 years (range 16 days – 23.3 years). Thirty three gastric cancers were diagnosed during the follow-up period.
Results: Most of the men (80.2%) had atrophic gastritis of some degree in the histological samples of the corpus (mild 11.4%, moderate 41.7%, marked 27.1%). Atrophic gastritis of the antrum was found only in 34.0% of the subjects. Mild to marked intestinal metaplasia appeared in 66.5% patients in corpus and 40.1% in antrum.
The gastric cancer incidence was 1.89 / 1000 patient-years. The incidence of gastric cancer increased as the grade of the atrophy of the corpus mucosa increased: 1.54/1000, 1.77/1000, and 2.05/1000 in mild, moderate, and severe mucosal corpus atrophy, respectively. In the antrum mucosa, the effect of the degree of the atrophy had similar effect on the gastric cancer incidence: 2.16/1000, 2.21/1000, and 3.44/1000 in mild, moderate, and severe atrophy.
The gastric cancer incidence was 1.35/1000, 2.27/1000, and 2.84/1000 in mild, moderate, and severe corpus intestinal metaplasia (IM), respectively. In the antrum, the incidence of gastric cancer was 1.87/1000, 2.23/1000, and 3.99/1000, in mild, moderate, and severe IM, respectively.
Conclusion: The risk of gastric cancer increased as the grade of the mucosal atrophy and intestinal metaplasia increased. The risk of gastric cancer seems to be within limits of previous publications (0.1-0.2% person years).

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Disclosure of Interest: None declared

P0512 OLGA AND OLGIM STAGING SYSTEMS IN MEN WITH ATROPHIC GASTRITIS

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Introduction: Intestinal type of gastric cancer develops through precancerous changes, but minority of these changes progress to cancer. Endoscopical surveillance is allocated for patients with extensive gastric atrophy or intestinal metaplasia. To target endoscopy for high-risk patients, two staging systems (Operative Link for Gastritis Assessment [OLGA][1] and Operative Link on Gastric Intestinal Metaplasia Assessment [OLGIM][2]) have been created. The focus is on severity and topography of atrophy and intestinal metaplasia.
Aims & Methods: In our scope was to investigate the predictive value of OLGA and OLGIM staging systems in smoking males with atrophic gastritis.
Serum pepsinogens (SPGs) were measured from 22,436 smoking men, aged 50-69 years, who participated The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study [3] in Finland. Low serum pepsinogen I (SPGI) was measured in 2132 men, and they were invited to gastroscopy [4]. Endoscopy was performed to 1344 men, and after excluding the men with gastric cancer in a beginning of study and 180 men with history of gastric surgery by benign cause, 1146 men were enrolled in this study.
The first gastroscopies were performed between years 1989-1993, and the surveillance continued until the end of year 2012, the gastric cancer diagnosis, or the death. The median follow-up time was 13.7 years (range 16 days – 23.3 years). Twenty seven gastric cancers were diagnosed during the follow-up period.
Results: Gastric cancers (n = 27) distributed by OLGA stages following: 1, 3, 17, 1, and 5 (stages 0-IV, respectively), and OLGIM stages: 2, 7, 10, 4, and 4 (stages

0-IV, respectively). By OLGIM staging system, gastric cancer risk elevated with stages ($p = 0.02$). The trend was not as distinct with OLGA staging ($p = 0.10$). Three gastric cancers developed to patients with OLGA / OLGIM stage 0, and histological type was known in only one of these patients, who had diffuse type of cancer.

Conclusion: Interobserver agreement is excellent with intestinal metaplasia, but weaker with atrophy and dysplasia [2;5]. Also in our study, OLGIM was more sensitive to predict gastric cancer risk over OLGA. Histological type can confound the interpretation, as cancerous cascade with atrophy and intestinal metaplasia are illustrated with intestinal, not diffuse, type of gastric cancer.

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P0513 PREDICTIVE FACTORS FOR RESPONSE TO NEO-ADJUVANT CHEMOTHERAPY IN PATIENTS WITH RESECTABLE GASTRIC CANCER

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Introduction: Neo-adjuvant chemotherapy (CT) has been shown to improve survival in locally advanced gastric cancer. It has been suggested that the clinical outcome is associated with preoperative down staging. CT is also associated with toxicity and poor patient tolerance.

Aims & Methods: Our aim was to identify predictive factors of response to perioperative CT. We conducted a prognostic study using an academic centre retrospective cohort of patients with gastric adenocarcinoma diagnosed between January 2012-December 2014 and submitted to perioperative CT. Response to pre-operative CT was evaluated by radiologic criteria and on the surgical specimen. We built a prognostic model using logistic regression analysis including demographic, clinical and morphological characteristics. Explanatory variables were kept when $p < 0.20$.

Results: A total of 160 patients were diagnosed of which 42 were submitted to perioperative CT. Mean age was 68 ± 10 years-old, 28 (67%) were male. Esophagogastric junction was involved in 5 (12%), gastric body in 19 (45%) and antrum in 18 (43%). The histology was intestinal type in 31 (74%) and diffuse in 11 (26%). ECF/EOX was used in 34 (81%) and FOLFOX/XELOX in 8 (19%). Response was observed in 30 (71%) with complete pathological response in 3 (7%). Toxicity was reported in 27 (64%) cases with interruption in 16 (38%). Median follow-up was 15.5 months (IQR 8.75-19.25). Mortality was 15 (35.7%). The final model included the following predictors: age (OR 0.898, CI 0.787-1.024; $p = 0.109$), female gender (OR 27.676, CI 0.679-1127.883; $p = 0.079$), poor CT tolerability (OR 0.115, CI 0.028-0.468; $p = 0.002$) and gastric body tumor (OR 0.071, CI 0.005-0.989; $p = 0.049$) were included in the model. The AUROC for the model was 0.943. Histological type, microsatellite instability and E-cadherin immunoexpression didn't show association with response to CT.

Conclusion: Increasing age, male gender, poor CT tolerability and gastric body location were independent predictors of non-response. Our model was able to accurately predict pre-operative CT response. Prospective evaluation is warranted before clinical application.

Disclosure of Interest: None declared

P0514 RELATIONSHIP BETWEEN GASTROPANEL AND O.L.G.A IN THE DETECTION OF CHRONIC ATROPHIC GASTRITIS IN A PRIMARY CARE SETTING

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Introduction: Chronic Atrophic Gastritis (CAG) is the most important independent risk condition for gastric cancer, histology being considered the gold standard for both diagnosis and follow up. The Operative Link for Gastritis Assessment (O.L.G.A) is an innovative histological system proposed for staging atrophic gastritis in a prognostic view.

GastroPanel® (Biohit, Helsinki, Finland) is a serological kit for a non-invasive diagnosis of chronic atrophic gastritis (CAG), including serum pepsinogen I (PGI), pepsinogen II (PGII), gastrin-17 (G-17) and IgG anti-*Helicobacter pylori* antibodies (IgG-*H.p.*).

Clinical practice is lacking of a non invasive instrument useful to predict and to follow the stage of atrophic gastritis.

Aims & Methods

Aim: To evaluate correlation between GastroPanel® and O.L.G.A stage, in a cohort of dyspeptic patients referred from a primary care setting.

Subjects and Methods: Histological evaluation of gastric biopsies was performed in 249 patients (M = 129, mean age 49 years, range 21-79 years). Atrophy was assessed according to the O.L.G.A staging system.

O.L.G.A stages III and IV are considered at high risk for gastric cancer development. From each subject, a blood sample was taken for GastroPanel® analysis.

Results: GastroPanel® analysis showed that 82 patients were normal (mean age 46 years, range 21-64 years, M = 49), 116 patients had a *H.p.*-related chronic gastritis (mean age 54 years, range 35-79 years, M = 68) and 51 had atrophic gastritis picture (mean age 61 years, range 21-79 years, M = 22).

Comparing GastroPanel® results to the histological findings, 77 patients had an O.L.G.A stage 0-II, 4 pts have an OLGA stage III, 1 stage IV.

Among the patients with Hp-related gastritis, 112 patients had an O.L.G.A stage 0-II, 3 patients had an O.L.G.A stage III and 1 patient had O.L.G.A stage IV.

Twenty-two out of the 51 patients with evidence of CAG at GastroPanel® had an O.L.G.A stage 0-II, 29 patients had an O.L.G.A stage III-IV. The negative predictive value (NPV) of GastroPanel® for CAG is 95,0%, being the positive predictive value (PPV) 75,0%.

O.L.G.A					
Gastropanel®	**0**	**I**	**II**	**III**	**IV**
Normal values	46	17	14	4	1
H.p.-related gastritis	51	23	38	3	1
Chronic atrophic gastritis	1	5	16	19	10

Conclusion: GastroPanel® showed an high NPV to predict absence of atrophic gastritis.

The relationship beetween GastroPanel and O.L.G.A system seems to confirm the clinical performances of the test.

Disclosure of Interest: None declared

P0515 ENDOSCOPIC BAND LIGATION WITHOUT RESECTION IN SELECTED PATIENTS FOR SMALL AND SUPERFICIAL UPPER GASTROINTESTINAL TRACT LESIONS

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Introduction: Band ligation with electrosurgery of early small lesions of upper gastrointestinal (UGI) tract (dysplasia or T1a-b) or subepithelial tumors (neuroendocrine tumors (NETs) are associated with complications especially in duodenal lesions.

Aims & Methods: The aim of this study is to investigate the efficacy and safety of endoscopic band ligation (EBL) without electrosurgery in selected patients where surgery is contraindicated. Twelve patients from 2010 through 2015 with early UGI (upper gastrointestinal) lesions treated with EBL for autoamputation (1.83 rubber bands/session) were included prospectively and analyzed retrospectively. All were discussed in a UGI multidisciplinary cancer committee where it was concluded that owing to patient's conditions surgery was not possible and that not getting histology would not change the clinical management. Before the procedure, a CT and/or radial echoendoscope was performed. In flat lesions (Paris Classification: Is-IIa) chromoendoscopy with spray catheter and argon plasma coagulation were used to delimit the margins before the banding. With a Duette® Multi-Band Mucosectomy device the rubber bands were deployed. Second endoscopy with biopsies was planned in 4-8weeks. If there was no persistence of the lesion, a new control was programmed at 6 and then at 12 months. On the contrary, if there was histologic persistence a new treatment was applied.

Results: The group included 5 esophagus lesions (adenosquamous carcinoma (n = 1); carcinoma squamous (n = 2); adenocarcinoma (n = 2)); 4 gastric lesions (high grade dysplasia (n = 1); adenocarcinoma (n = 2); NET (n = 1)) and 3 duodenal lesions (NET (n = 3)). The mean tumor diameter was 9.3+/-3.7mm (range 4-17.5). Only 1 adverse event in one patient was described, which was mild chest pain. Observation for 8 hours was possible in all patients except in 2 cases. After a median of 7 weeks the treatment, there was endoscopic remission in 92% (n = 11/12) and histologic remission in 75% (n = 9/12). In the 6-month biopsies, there were 70% (n = 7/10) of negative biopsies and in the 12 months 80% (n = 4/5). The persisting lesions were T1 cancers (T1 esophagus (n = 3), T1 stomach (n = 1)) but with a new EBL two of the T1 cancers got negative

Abstract number: P0515

	Age, years	Sex	Comorbidity
1	83	M	Asthma, ischemic heart disease, peripheral vascular disease, low social support
2	59	M	Lung cancer in treatment, previous ORL cancer, esophageal stricture, trismus
3	68	M	Decompensated cirrhosis, COPD, peripheral vascular disease
4	77	F	Atrial fibrillation, cerebrovascular accident
5	82	F	Cognitive disorder, previous gastric ADK (Billroth I)
6	75	M	Previous oral carcinoma, intestinal ischemia twice
7	83	F	Asthma, ischemic optic neuropathy
8	80	M	Atrial fibrillation, pituitary adenoma, monoclonal gammopathy
9	69	F	Previous intestinal resection
10	77	F	Decompensated cirrhosis, hepatocellular carcinoma, systemic lupus erythematosus, vaginal cancer, peripheral vascular disease
11	76	F	Cognitive disorder, atrial fibrillation, previous, breast cancer
12	62	M	Decompensated cirrhosis, COPD

biopsies in the next endoscopy. The median follow-up is of 20.9 months (range 5.9-60 months).
Conclusion: EBL without electrosurgery is an easy and safe technique that should be considered in patients with multiple morbidities.
Disclosure of Interest: None declared

P0516 ENDOSCOPIC RESECTION OF DUODENAL NEUROENDOCRINE TUMORS: A CASE SERIES OF A SINGLE INSTITUTION

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Introduction: Duodenal neuroendocrine tumors (dNETs) are rare, being 1-3% of all primary duodenal tumors. With the widespread use of upper GI endoscopy, these tumors have been increasingly recognized.
Duodenal NETs not located in the periampullary region are suitable for endoscopic treatment if limited to the submucosal layer, without metastases and with a diameter less than 10 mm. Nevertheless, few data are available concerning the efficacy of this approach.
Aims & Methods: We reviewed our data about dNETs treated with endoscopic resection (ER).
Results: From January 2012 to December 2014, 11 dNETs were diagnosed during upper GI endoscopy. Five tumors underwent ER whereas 6 did not because of the presence of metastases (n = 2), patient's comorbidities (n = 1), papillary location (n = 1) and surgical treatment (n = 1).
ER was performed with a high definition single-channel endoscope (EG29i series, Pentax). The resection technique was chosen according to the endoscopist's preference, morphological characteristics, site and endosonographic features of each lesion. En-bloc resection was obtained in all cases. Endoscopic mucosal resection (EMR) was used for 3 bulb tumors and endoscopic submucosal dissection (ESD) for one bulb tumor. One tumor of the duodenal third part was treated with Hybrid-ESD (HESD). In 4 cases the resection site was closed with metal clips. The mean size of resected specimens was 14 mm (range 7-22 mm); histologically the tumor mean size was 9 mm (range 5-12 mm). The invasion depth was limited to the submucosal layer. Lateral or deep edge involvement occurred in 2 cases (one tumor treated with EMR and one with HESD). All lesions were well-moderately differentiated tumors with less than 1-2 mitosis per high power field. Ki67 proliferation index was 2-4% in 4 tumors and 16% in one.
One immediate perforation occurred and was treated conservatively. No patient underwent a second ER or surgical treatment. The mean follow up period was 17 months (range 6-31 months). No local recurrence was observed during endoscopic follow-up. A liver metastasis was detected at CT-scan one year after resection in one patient.
Conclusion: ER in the duodenum has a higher incidence of complications than in other sites of gastrointestinal tract because of the thickness duodenal wall. In order to avoid delayed perforation and bleeding, all resections except one, were treated with clips. Despite en-bloc resection was obtained in all cases, a complete pathological resection was confirmed in only 60% of cases. We suppose that such incomplete pathological resection is due to the paucity and laxity of submucosal duodenal tissue, which is destroyed during resection. In fact, because of the narrow duodenal lumen, can be technically difficult to avoid excessive burning of the peritumoral submucosal duodenal tissue. To support this hypothesis we did not observe any local recurrence at follow-up endoscopy. Our experience, although limited and retrospective, confirms the safety and efficacy of ER for the treatment of dNETs limited to the submucosal layers. However, additional studies with longer follow up are needed.
Disclosure of Interest: None declared

P0517 THE COMBINATION OF SERUM TREFOIL FACTOR 3 AND PEPSINOGEN TEST IS AN EFFECTIVE BIOMARKER FOR EARLY DETECTION OF GASTRIC CANCER

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Introduction: The serum pepsinogen test has been used as a non-invasive biomarker for gastric cancer screening in Japan. However, there are limitations of its predictive power.
Aims & Methods: We aimed to investigate whether the combination of serum trefoil factor 3 (TFF3) and pepsinogen test could be an effective biomarker of gastric cancer screening. Two hundred and eighty-one gastric cancer patients who underwent endoscopic submucosal dissection in Korea were enrolled. And serum was collected from 708 healthy individuals without cancer in Japan. Serum levels of TFF3 were examined by enzyme-linked immunosorbent assays. Serum levels of pepsinogen I and pepsinogen IIwere measured using a latex-enhanced turbidimetric immunoassay.
Results: The mean serum TFF3 concentration in patients with gastric cancer was 9.36 ± 4.67 (95%CI [8.86,9.96]). For the prediction of gastric cancer presence, the area under the receiver-operating characteristic curve of TFF3 was 0.7489. Using cutoff of 6.728 ng/ml, patients with gastric cancer were detected with 80.4% sensitivity, and 57.3% specificity by the TFF3 test. One hundred and seventy-one of 281 patients were not identified as bearing gastric cancer with pepsinogen test. However, adding TFF3 test to the pepsinogen test, 136 of these 171 patients who were not identified by pepsinogen test could be detected by the TFF3 test. If the TFF3 was added to the pepsinogen test, the sensitivity (87.5%) for gastric cancer prediction was superior to the sensitivity (39.1%) of the pepsinogen test.
Conclusion: The combination of the serum TFF3 and pepsinogen test could be an effective non-invasive biomarker for gastric cancer screening.
Disclosure of Interest: None declared

P0518 CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUBMUCOSAL INVASIVE EARLY GASTRIC CANCER

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Introduction: The Japanese Gastric Cancer Association has proposed expanded criteria for the curative endoscopic resection of early gastric cancer as follows: a) differentiated intramucosal tumour without ulceration or scarring; b) differentiated intramucosal adenocarcinoma with ulceration or scarring, tumour $\leq$3 cm; c) differentiated adenocarcinoma with minimal submucosal invasion (SM1: $\leq$500 μm from the muscularis mucosae), $\leq$3 cm; and d) undifferentiated intramucosal adenocarcinoma without ulceration or scarring, $\leq$2 cm. However, it remains controversial whether endoscopic submucosal dissection (ESD) for submucosal invasive early gastric cancer (SM-EGC) is feasible or not.
Aims & Methods: The aim of our study was to assess the feasibility of ESD for SM-EGC. We retrospectively collected clinical data of 1030 consecutive patients with 1304 gastric lesions who had undergone ESD at our hospital between January 2005 and March 2015. Of these, 179 lesions (13.7%) were classified as SM-EGC by pathological evaluation using the ESD specimen; 87 lesions (48.6%) had submucosal invasion of less than 500 μm (SM1-EGC), and the remaining 92 lesions (51.4%) had invasion of 500 μm or more (SM2-EGC).
Results: There were no significant differences in patient age, gender, location, and histology or morphological type between patients with SM1-EGC and SM2-EGC. Tumour size in SM1-EGC and SM2-EGC was 19.8 ± 11 cm and 26.7 ± 16 cm, respectively ($p < 0.005$). Lymphovascular involvement was found in 13 patients with SM1-EGC (14.9%) and 49 patients with SM2-EGC (53.3%) ($p < 0.005$). The complete resection rates for SM1-EGC and SM2-EGC were 87.4% and 60.8%, respectively ($p < 0.005$). The procedure time for SM1-EGC and SM2-EGC was 74.6 ± 47 min and 101.9 ± 63 min, respectively ($p < 0.005$). There were no significant differences in post-procedure bleeding rate (6.9% vs. 6.5%) and perforation rate (4.6% vs. 6.5%). Twenty-three SM1-EGC patients

(26.4%) underwent surgical resection after ESD as an additional treatment, and lymph node metastasis was found in only 1 case with lymphatic invasion. Additional surgical resection was performed for 63 patients (68.5%) of SM2-EGC patients, and lymph node metastasis was observed in 8 of these patients. Of 29 patients who did not undergo additional curative surgical resection, 2 patients with SM2-EGC had recurrence of lymph node metastases and underwent surgery, but no patient with SM1-EGC had lymph node metastases or local recurrence.
Conclusion: ESD for SM-EGC based on expanded criteria may be feasible, but additional long-term follow-up data are needed.
Disclosure of Interest: None declared

P0519 CLINICOPATHOLOGIC FEATURES OF GASTRIC CANCER WITH SYNCHRONOUS AND METACHRONOUS COLORECTAL CANCER IN KOREA: ARE MICROSATELLITE INSTABILITY AND P53 OVEREXPRESSION USEFUL MARKERS FOR PREDICTING COLORECTAL CANCER IN GASTRIC CANCER PATIENTS?

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Introduction: A large-scale study was performed to identify the risk factors for developing synchronous and metachronous colorectal cancer (CRC) in gastric cancer (GC) patients including microsatellite instability (MSI) and p53 overexpression.
Aims & Methods: A total 1041 GC patients who underwent endoscopic resection or surgery and who underwent colonoscopy simultaneously or during the surveillance of GC were consecutively included.
Results: Of the 1041 patients, CRCs were detected in 67 (6.4%) patients with GC. Forty six (4.4%) had synchronous CRC and 21 (2.0%) had metachronous CRC. Univariate analysis indicated that age $\geq$55 ($P < 0.001$), male ($P < 0.001$) and p53 overexpression ($P = 0.040$) had a higher incidence of CRC. However, body mass index, smoking, tumor location, tumor multiplicity, tumor histology, TNM stage and MSI were not significantly associated with the incidence of CRC. Age $\geq$55 (OR: 4.143; 95% CI: 1.863-9.213; $P < 0.001$) and male (OR: 2.951; 95% CI: 1.323-6.583; $P = 0.008$) were the risk factors of CRC in GC patients by multivariate analysis.
Conclusion: GC patients who are 55 years and older or male are recommended to receive colonoscopy to detect CRC. MSI and p53 overexpression were not useful molecular markers for prediction of CRC in GC.
Disclosure of Interest: None declared

P0520 CLINICAL OUTCOME OF DOUBLET AND TRIPLET NEOADJUVANT CHEMOTHERAPY FOR MARGINALLY AND POTENTIALLY RESECTABLE GASTRIC CANCER. RETROSPECTIVE SINGLE CENTER CASE CONTROL STUDY

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Introduction: Gastric cancer is the fourth most common malignancy in the world, and the second leading cause of cancer-related deaths and the highest mortality rates are reported in East Asia. Early detection and surgery are currently considered the mainstay of treatment, and approximately half of gastric cancer patients can be treated by curative surgical or endoscopic resection. However, the rate of recurrence and metastasis following radical resection remains disappointingly high. Thus, improving the rates of survival and cure is a critical goal. Theoretically the administration of the neoadjuvant chemotherapy (NAC) appears to have potential benefits for locally advanced gastric cancer, while its survival gain and surgical benefit remains controversial.
Aims & Methods: The aim of this study was to evaluate the effectiveness of NAC in treatment of marginally and potentially resectable gastric cancer and find out the associated factor of resistance to NAC. We retrospective reviewed the patient medical record. This study enrolled 179 patients who underwent NAC followed by surgery (n = 41) or surgery only (n = 138) for treatment of stage IIIa or IIIb locally advanced gastric cancer. For sampling, we applied a random sample extraction method. We categorized the NAC group and the Surgery only group according to gender and age, then we applied a serial number to each category. We used two chemo-regemen FOLFOX (n = 28) and DCF (n = 13). The basal characteristics and clinical outcome were compared between two groups. NAC related objective response, safety and toxicity were also analyzed.
Results: The basal characteristics including mean age and sex was not significant difference between two groups. Initial stage was significantly high ($P = 0.001$) in NAC followed by surgery (3.12 0.56) than surgery only group (2.57 0.54). After NAC, the tumor down-stage rate was 58.5% (24/41). Both tumor size and differentiation were predictive factor of resistance to NAC. But overall survival ($P = 0.518$), disease free survival ($P = 0.621$) and recurrence rate ($P = 0.142$) were not statistically difference between two groups. In subgroup analysis we compared clinical outcome between doublet (n = 28) and triplet (n = 13) NAC group. As a result, age, sex, tumor down stage rate and recurrence were similar between two groups. But drug toxicity ($P = 0.019$) and initial stage ($P = 0.010$) were significant higher in triplet NAC than doublet NAC group.
Conclusion: Compared with surgery only versus NAC followed by surgery was not associated with a survival gain or lower recurrence rate. However, Down of N stage is significantly improved statistically. In our data, tumor size and differentiation was the important clinical predictor. Therefore NAC may be benefit for selective treatment option and assessing individual prognosis.
Disclosure of Interest: None declared

P0521 FOLLOW-UP RESULT OF ENDOSCOPIC TREATMENT FOR GASTRIC ADENOMA

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Introduction: Gastric adenoma(GA) is well known for premalignant lesion. Endoscopic treatment has been widely conducted for the treatment of gastric adenoma. However, the risk factors related to recurrence of adenoma and occurrence of adenocarcinoma after endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) for gastric adenoma have not been reported so much.
Aims & Methods: The aim of this study was to evaluate these factors. We reviewed medical records of total 667 lesions from 641 patients who underwent EMR/ESD for gastric adenoma from January, 2007 to December, 2013 at Chungnam National University Hospital. For all subjects, the data collected included sex, age, site of lesion, morphology, treatment method, severity of atrophy, intestinal metaplasia, resection margin and degree of dysplasia.
Results: The median follow up period was 29th month (range, 12-81 months). There were 98 recurrence of adenoma (14.7%) and 31 occurrence of adenocarcinoma (4.6%). The risk factors related to the recurrence of gastric adenoma were male ($p = 0.024$), intestinal metaplasia ($p = 0.004$) and incomplete resection margin ($p = 0.004$). The risk factors related to the occurrence of gastric adenocarcinoma were male ($p = 0.015$) and High grade dysplasia ($p = 0.019$).
Conclusion: After EMR/ESD for gastric adenoma, the recurrence of gastric adenoma was associated with sex, intestinal metaplasia and resection margin, and the occurrence of adenocarcinoma was associated with sex and grade of dysplasia.
Disclosure of Interest: None declared

P0522 HOW TO MANAGE SUPERFICIAL NON-AMPULLARY DUODENAL TUMORS

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Introduction: As a minimally invasive therapy, endoscopic resection (ER) and laparoscopy endoscopy cooperative surgery (LECS) of superficial non-ampullary duodenal tumors (SNADT) have been performed recently. However, the indication criteria have not been clearly determined yet. It is difficult to carry out ER safely because of the thin wall of the duodenum, so ER of SNADT includes serious complications such as perforation. Uedo *et al.* reported that the location of the lesions in distal side from Vater's ampulla was associated with the occurrence of delayed perforation. At the cancer institute hospital, ER is done only for SNADT measuring ≧20mm, whose ulcer floor can be closed completely using endoclips. LECS is the treatment choice for SNADT not amenable to ER in terms of technical and/or oncological reasons.
Aims & Methods: The aim of this study was to examine the validity of the treatment based on analyzing the therapeutic outcome. At the cancer institute hospital, 74 patients with SNADT treated by ER and 14 patients by LECS between September 2006 and December 2014. The ER methods used to carry out en bloc resection were endoscopic mucosal resection (EMR: n = 35) or endoscopic submucosal dissection (ESD: n = 39). The procedure of LECS was to close the mucosal defect after ESD with seromuscular suturing by laparoscope. We analyzed the therapeutic outcome of ER and LECS for SNADTs according to the location of the lesions that is proximal or distal side of Vater's ampulla.
Results: First, we analyzed the clinical outcomes of ER by comparing the EMR group and the ESD group. We treated 36 SNADTs located in the proximal side from Vater's ampulla (PVA) (21 with EMR and 15 with ESD) and 38 SNADTs located in the distal side from Vater's ampulla (DVA) (14 with ER and 24 with ESD). In the gross type, most frequent types were 0-IIa in EMR, 0-IIc in ESD. ($p < 0.001$) The median tumor sizes were 9.5mm in EMR and 13mm in ESD, so the lesion treated with ESD was significantly larger than that of EMR. ($p < 0.024$) In R0 resection (negative margins), EMR was 15 lesions located in PVA (71%) and 12 lesions located in DVA (86%), ESD was 14 lesions located in PVA (93%) and 22 lesions located in DVA (92%). ESD was significantly higher than EMR in each lesion. No complication was found in EMR. Intraoperative perforation occurred in 2 patients (5.3%) and delayed perforation occurred in 2patients (5.3%) in ESD. All of the lesions were located in DVA. The lesion recurrence was found in 1 patient only in EMR. The lesion was also located in DVA. Then, in LECS group, the lesions located PVA and DVA were 4 and 10 patients, respectively. The median tumor size was 23.5mm. All of the lesions were achieved R0 resection. In the treatment of SNADTs located in DVA, postsurgical infection occurred in 2 patients (20%). Although they were cured with conservative management, a long hospital stay was required.
Conclusion: ER and LECS of SNADT are ideal and less invasive treatments compared with open surgical resection. However, these treatments include serious complications such as perforation, residual tumor and infection, especially in patients with lesions located in DVA. In the case of the lesions located in

DVA, we should consider that open surgical resection is one of the safe and reliable treatments. In contrast, ER and LECS should be considered for the treatment of the lesions located in PVA to avoid unnecessary surgery and preserve patient's quality of life.
Disclosure of Interest: None declared

P0523 GASTRIC ADENOCARCINOMA OF THE FUNDIC GLAND TYPE (CHIEF CELL PREDOMINANT TYPE): A MULTICENTRE STUDY OF 70 CASES

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Introduction: Gastric adenocarcinoma of the fundic gland type (chief cell predominant type, GA-FG-CCP) has recently been proposed as a new variant of gastric adenocarcinoma. In 2010 and 2014, we described the clinicopathological and endoscopic features of GA-FG-CCP (Ueyama H. *Am. J. Surg. Pathol* 2010, Ueyama H. *Endoscopy* 2014). We found that GA-FG-CCP is rare but has distinct clinicopathological features, especially in terms of tumour location, histological findings, phenotypic expression, and low-grade malignancy. However, the treatment strategies and long-term outcomes of GA-FG-CCP have not been thoroughly investigated by studies with large sample sizes.
Aims & Methods: The aim of this study was to collect a large number of GA-FG-CCP cases and perform a detailed analysis of the clinicopathological features of GA-FG-CCP. A total of 70 GA-FG-CCP cases were retrospectively collected from 25 institutions between January 2008 and December 2014.
Results: A total of 70 patients [65.4 y (range 41-81 y), 50 male, 20 female] with 70 lesions were treated as follows: ESD/EMR/surgery = 48/11/11. A total of 88% of patients were negative for *H. pylori* infection. In regards to lesion location, 55 were detected in the upper stomach, 14 in the middle stomach, and 1 in the lower stomach. Macroscopically, 44 lesions had a protruded shape (SMT shape: 22, 0-IIa:18, 0-I:4), whereas 26 had a flat/depressed shape (IIb:7, IIc:19). The mean tumour size was 12.0 (2-85) mm. Histologically, there were 20 intramucosal cancers and 50 submucosal invasive cancers. The mean depth of the submucosal invasion was 476.7 (50-4000) μm. Lymphovascular invasion was observed in 4 cases (5.7%). Lymph node metastasis was only observed in one out of 11 patients who underwent surgery (9.1%, 1/11). Follow-up data were available for 38 cases, and during the follow-up period (median 28.7 (1-104) months), no local recurrence or metastasis was detected in any case. For 7 of the 38 patients with follow-up data, endoscopic resection was determined to be non-curative, and of those 7 patients, four did not undergo additional surgery. However, there was no local recurrence and metastasis at a median of 32 months (4-82) follow-up after endoscopic treatment.
Conclusion: The findings of high-grade atypism, lymphovascular invasion, and LN metastasis in some GA-FG-CCP cases indicate that GA-FG-CCP may alter the atypism and cell differentiation of the tumour during the course of tumour progression, resulting in the development of high-grade malignancy. However, endoscopic treatment appeared to be effective, because neither recurrence nor metastasis was detected in any case regardless of whether additional surgery was performed. Therefore, the prognosis of GA-FG-CCP may be better than those of more common gastric cancers. Moreover, GA-FG-CCP should be categorized as a gastric adenocarcinoma that occurs without *H. pylori* infection, because *H. pylori* infection was considered an accidental phenomenon in this case series. Further studies will be needed to elucidate the natural history and carcinogenesis of GA-FG-CCP.
Disclosure of Interest: None declared

P0524 OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER WITH SCARRING

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Introduction: Recently, with the advent and widespread use of endoscopic submucosal dissection (ESD), *en bloc* resection of early gastrointestinal cancer has become possible irrespective of the location and diameter. However, the technical difficulty is greatly dependent on the condition of the lesion and the skill of the endoscopist; a lesion with scarring, in particular, is technically challenging. The Japanese Treatment Guidelines for Gastric Carcinoma suggests that presence or absence of scarring may become a decisive factor in curative resection and an important finding for judging whether expanded surgery might be required. In addition, some reports have indicated that it is difficult to determine if scarring is present before performing ESD. The clinical management, including diagnosis, of cases with scarring before ESD has not been well investigated.
Aims & Methods: This study aimed to investigate clinicopathological characteristics and clinical management of early gastric cancer with scarring. We analysed 315 lesions and 318 cases of early gastric cancer treated by ESD at our hospital between April 2009 and February 2015 (225 males and 93 females; mean age 69.7 y). According to the presence or absence of pathologically diagnosed scarring, the cases were divided into two groups for comparison: Group UL+, 28 lesions in 27 cases (18 males and 9 females; mean age 72 y); and Group UL-, 323 lesions in 291 cases (210 males and 81 females; mean age 71.7 y).
Results: Scarring was accurately diagnosed endoscopically before ESD in 13 of 28 cases (46%) in Group UL+. There was no significant difference between the two groups in the following parameters (Group UL+ vs. Group UL-): the location of the lesion (U/M/L), 11/13/4 vs. 141/147/35; the operation time, 89.3 min vs. 63.7 min; the tumor diameter, 17.9 mm vs. 15.7 mm; and the diameter of the resected specimen, 39.0 mm vs. 36.9 mm. Macroscopically, the depressed type was significantly more often observed in Group UL+ (flat and elevated type/depressed type = 11%/89% in Group UL+ and 45%/55% in Group UL-, $P < 0.01$). Histologically, the mixed type (differentiated and undifferentiated cancer) was observed significantly more often in Group UL+ (differentiated type/mixed type = 75%/25% in Group UL+ and 88%/12% in Group UL-, $P < 0.05$). Despite no significant difference in invasion depth, SM cancer tended to be observed more frequently in Group UL+ (M/SM = 71%/29% in Group UL+ and 86%/14% in Group UL-, $P = 0.06$). The curative resection rate was significantly lower in Group UL+ (57% in Group UL+ and 86% in Group UL-, $P < 0.01$).
Conclusion: This study elucidated that early gastric cancer with scarring has high malignant potential and aggressiveness. It is often difficult to diagnose depth of invasion before ESD in cases of early gastric cancer with scarring.
Disclosure of Interest: None declared

P0525 GIST OR NON-GIST, THAT IS THE QUESTION: BASKET-LIKE HYPERVASCULARIZATION IN DOPPLER ENDOSCOPIC ULTRASONOGRAPHY- A HIGHLY SPECIFIC CRITERION FOR THE DETECTION OF A GASTROINTESTINAL STROMAL TUMOR

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Introduction: Endoscopic ultrasonography (EUS) is the most important imaging method for diagnosis of subepithelial lesions of the gastrointestinal tract. However, it still has limits in the differentiation between Gastrointestinal Stromal Tumors (GISTs) from other malignant and benign tumors (Non-GISTs). As a result of the development of effective oncological therapy there is a high need for an imaging method to the diagnosis and follow-up of GISTs. In recent years Doppler EUS has been proposed as a method to distinguish GISTs from Non-GISTs. Therefore we initiated a prospective study to evaluate Doppler EUS criteria for the detection of a GIST.
Aims & Methods: Thirty-one patients (19 women, 12 men) with subepithelial lesions (n = 32) were prospectively investigated using the EUS platform Olympus GF-UCT140 (Olympus Europe, Hamburg, Germany) and HDI 5000 (Philips Ultrasound, Bothell, USA). All Doppler EUS examinations were performed by one operator unaware of the histological results. Defined ultrasound parameters were used to determine the Doppler EUS observations. All tumors were proven histologically. The exact Chi-square Test (Fisher's Test) was used to find significant differences between GISTs and Non-GISTs. P-values of less than 0.05 were considered to be significant. The study was conducted following the Good Clinical Practice Guidelines and according to the guidelines of the Helsinki Declaration.
Results: See table 1. Basket-like hypervascularization in Doppler endoscopic ultrasonography is a highly specific criterion in the differentiation between Gastrointestinal Stromal Tumors from other malignant and benign tumors (Non-GISTs). **Table 1:** Results of Doppler EUS examinations.

Criteria	GIST present	GIST absent	Non-GIST present	Non-GIST absent	p-value
Vessels detected	10	0	14	8	0.035
Afferent vessel	9	1	7	15	0.006
Basket-like hypervascularization	9	1	4	18	0.0002

Significance level: p-value less than 0.05

Conclusion: The differentiation of GISTs from other malignant and benign subepithelial lesions is a major issue in the management of these tumors. With this prospective study, we have addressed the need to evaluate diagnostic criteria for Doppler EUS criteria. The results demonstrated a basket-like hypervascularization is a highly specific criterion in the detection of a GIST. In the future, the direct detection of vessels could be the most important advantage of Doppler EUS contrary to other imaging methods.
Disclosure of Interest: None declared

P0526 ENDOSCOPIC GASTRIC ATROPHY IS A PREDICTING FACTOR IN HISTOLOGIC DISCREPANCY BETWEEN FORCEPS BIOPSY AND ENDOSCOPIC RESECTION IN LOW GRADE DYSPLASIA

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Introduction: Histologic discrepancy between specimens obtained by forceps biopsy and endoscopic resection (ER) often occurs in gastric adenomatous lesions. The purpose of this study was to investigate that gastric atrophy could be one of clinical diagnostic factor for predicting histologic discrepancy between forceps biopsy and ER.
Aims & Methods: This study involved 203 gastric low grade dysplasia (LGD) that were proven on the basis of forceps biopsy and checked serum pepsinogen I/II level. ER is composed of 17 endoscopic mucosal resection and 186 endoscopic submucosal dissection. The lesions were grouped according to the histologic

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Table 1: Histologic discrepancy between specimens obtained by forceps biopsy and endoscopic resection.

Variables	Condordant(n = 179), n(%)	Discordant(n = 24), n(%)	Univariate analysis P value	Multivariate analysis P value	odds ratio (95% CI)
Atrophy around the lesion			0.012	0.036	3.106 (1.075-8.980)
Yes	83 (46.4)	18 (75.0)			
No	96 (53.6)	6 (25.0)			
PGI ≤ 70 and Ratio ≤ 3.0	74 (41.3)	16 (66.7)	0.023	0.129	2.082 (0.807-5.370)
Lesion type, n(%)			0.837	0.511	2.142 (0.221-20.792)
Depressed	6 (3.4)	1 (4.2)			
Elevated/flat	173 (96.6)	239 (95.8)			
Location			0.003	0.018	5.641 (1.350-23.567)
Non-upper	172 (96.1)	19 (79.2)			
Upper	7 (3.9)	5 (20.8)			
Size (mm)			0.259	0.540	
≤10	80 (51.0)	9 (37.5)	Reference		
>10 and 20≤	56 (35.7)	8 (33.3)	0.644	0.579	0.720 (0.226-2.296)
>20 and 30≤	17 (10.8)	6 (25.0)	0.053	0.569	1.904 (0.502-7.220)
>30	4 (2.5)	1 (4.2)	0.496	0.916	1.267 (0.102-15.806)
		zx			
Ulcer	12 (6.7)	2 (8.3)	0.674	0.790	1.287 (0.201-8.249)

discrepancies between forceps biopsy and ER; concordant or discordant. The definition of discordance is histologic upgrade from LGD of forceps biopsy to high-grade dysplasia (HGD) or differentiated adenocarcinoma of ER. Gastric atrophy was diagnosed when either a endoscopic atrophy was confined around the adenomatous lesion or both serum pepsinogen level I ≤ 70 and pepsinogen I/II ratio ≤ 3.0 was satisfied.

Results: Histologic discrepancy between forceps biopsy and ER in gastric adenoma was 11.8% (24/203). The histologic upgrade to HGD or differentiated adenocarcinoma accounted for 5.4% (11/203) and 6.4% (13/203), respectively. Atrophy around the lesion in endoscopy accounted for 49.7%(101/203) and satisfaction of both serum pepsinogen I ≤ 70 and pepsinogen I/II ratio ≤ 3.0 accounted for 44.3%(90/203). In univariate analysis, atrophy around the lesion, upper third located lesion, erythema of the lesion, and satisfaction of both pepsinogen I ≤ 70 and pepsinogen I/II ratio ≤ 3.0 was found to be statistically significant factors affecting histologic discrepancy. In multivariate analysis, atrophy around the lesion (odd ratio [OR], 3.106; 95% confidence interval [CI], 1.075-8.980; P = 0.036), upper third located lesion(OR, 5.641; 95% CI, 1.35-23.567; p = 0.018) were significant factors associated with histologic discrepancy.

Conclusion: We should consider histologic discrepancy and tentative endoscopic resection for gastric LGD that is located upper third or accompanying atrophy around the lesion.

Disclosure of Interest: None declared

P0527 THE ROLE OF FOLLOW-UP ENDOSCOPY AND COMPUTED TOMOGRAPHY SCAN AFTER ENDOSCOPIC OR SURGICAL TREATMENT OF EARLY GASTRIC CANCER: A PRELIMINARY REPORT

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Introduction: Clinical outcome of early gastric cancer (EGC) is excellent, attributable to the progress in diagnostic and therapeutic methods. However, there is no relevant guideline for surveillance endoscopy and/or computed tomography (CT) scan, especailly for EGC.

Aims & Methods: The aim of this study was to investigate the role of regular endoscopy and CT scan surveillance after treatment of EGC. A total of 603 patients with EGC treated either by endoscopic [endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD)] or surgical treatment (gastrectomy with lymph node dissection) between January 2007 and December 2009 were retrospectively reviewed. All of the gastric lesions were completely resected and all of them had one or more endoscopy and CT scan examination during the follow-up.

Results: In the gastrectomy group (n = 492; mean follow-up, 46.1 months), 10 patients revealed tumor recurrence during the follow-up, including 3 cases with metachronous gastric adenoma, 1 with anastomosis site cancer recurrence, 1 with regional lymph node metastasis, and 5 with distant metastasis. All metachronous gastric adenomas were detected by endoscopy with biopsy. Six cases (5 distant metastases and 1 regional lymph node metastasis) were diagnosed by abdominal CT; the anastomosis site recurrence case was detected by both CT and endoscopy; all of these 7 cases were sm cancers and 2 of them had regional lymph node metastasis in the initial surgical pathology. In EMR/ESD group (n = 111; mean follow-up 51.3 months), 3 revealed metachronous gastric adenocarcinoma during the follow-up, all of which were deteced by endoscopy with biopsy; 2 of them also showed tumor recurrence in abdominal CT scan. All of these 3 cases meet the absolute criteria of ESD (< 2cm in size, m cancer, differentiated pathology) according to the initial resection specimen.

Conclusion: According to our preliminary report, regular follow-up of both endoscopy and CT scan is recommended after the surgery in the EGC patients. Especially, CT scan seems to be more valuable in case of sm cancers and/or lymph node metastasis. After endoscopic resection of EGC, all the recurrence could be detected by endoscopy with biospy, so CT scan might have a limited role for the surveillance of EGC after endoscopic resection of EGCs which meet the absolute criteria. However, further study is warranted in this issue.

Disclosure of Interest: None declared

P0528 ASSOCIATED FACTORS THAT LEAD TO RESIDUAL TUMOR IN PATIENTS WHO UNDERWENT ADDITIONAL GASTRECTOMY AFTER INCOMPLETE ENDOSCOPIC RESECTION FOR EARLY GASTRIC CANCER IN KOREA

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Introduction: The aim of this study was to evaluate the clinicopathological characteristics and factors that lead to residual tumors in patients who underwent additional gastrectomy for incomplete endoscopic resection in Korea.

Aims & Methods: Between 2003 and 2013, the medical records of patients underwent additional gastrectomy after incomplete ER were retrospectively reviewed. Those diagnosed with the presence of histologic residual tumor in specimens obtained by gastrectomy were assigned to the residual tumor (RT) group (n = 47); those diagnosed with the absence of histologic residual tumor in specimens obtained by gastrectomy were assigned to the non-residual tumor (NRT) group (n = 33). We analyzed comparison of the clinicopathologic characteristics of RT and NRT group, clinical factors influencing the presence of residual tumor, pathologic discrepancies between ER and additional gastrectomy, relationship between positive margins, depth of invasion with residual tumors and lymph node metastasis, cases of lymph node metastasis.

Results: The frequency of additional gastrectomy due to incomplete resection after ER for EGC was 8.7% (80/911), and 58.7% (47/80) of those patients had residual tumors. The rates of *H. pylori* infection, mixed macroscopic finding, tumor size over 2cm, endoscopic piecemeal resection, submucosal invasion, both (lateral and vertical) margin involvement were significantly higher in the RT group than in the NRT group ($p < 0.05$). In the multivariate analysis, endoscopic piecemeal resection (Odds ratio [OR]: 5.02, 95% confidence interval [CI]: 3.78-6.24), H. pylori infection (OR: 1.45, 95% CI: 0.98-1.92), large tumor size (> 2cm, OR: 2.96, 95% CI: 2.37-3.55), and both (lateral and vertical) marginal involvement (OR: 4.96, 95% CI: 4.13-5.79) were independent factors, predictive of the presence of residual tumor in additional gastrectomy after incomplete resection ER for early gastric cancer ($p < 0.05$)

Conclusion: Before ER, endoscopic examination along with EUS and MDCT should be used to accurately determine the GC invasion depth and the presence of LN metastasis. During ER, surgeons should attempt to perform en bloc resection when performing ER and attempt to resect the mucous membrane with adequate safety margins to prevent tumor invasion into the lateral and vertical margins. After ER, effort should be made to ensure timely and accurate decisions about whether additional gastrectomy is needed using the pathological findings of the resected tissues, to ensure that there is no delay in surgery.

Disclosure of Interest: None declared

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Factors OR (95%CI)	Well-estimation P value	OR (95%CI)	Overestimation P value	OR (95%CI)	Underestimation P value	
Size		0.177		<0.001		<0.001
≤ 1cm			10.00(4.52-2.19)		reference	
>3cm			Reference		15.66(6.29-38.46)	
Marcoscopic type		0.006				0.201
Elevated	2.37(1.28-4.38)		Reference	0.026		
Flat/depressed	reference		2.75(1.733-5.85)			
Presence of adenomatous component		0.014		0.014		0.099
Absence	reference		Reference			
Presence	2.67(1.22-5.87)		2.67(1.22-5.86)			

P0529 THE RISK FACTORS OF LYMPH NODE METASTASIS FOR MIXED ADENOCARCINOMA IN EARLY GASTRIC CANCER

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Introduction: Endoscopic submucosal dissection (ESD) is widely accepted as treatment for early gastric cancer (EGC) due to its minimal invasiveness, and better quality of life associated with preserving gastrointestinal function. However, there is no consensus on ESD for mixed adenocarcinoma. This study aimed to evaluated the risk factor of lymph node (LN) metastasis and validate the ESD criteria as a curative resection for mixed adenocarcinoma in EGC.

Aims & Methods: Of 692 EGC patients who had undergone gastrectomy with LN dissection between 2001 and 2013, 60 were diagnosed as mixed adenocarcinoma after histological evaluation in surgical specimens and were analyzed retrospectively.

Results: LN metastasis was detected in 13 (21.7%) of 60 mixed adenocarcinoma. There were no significant differences in the gender ratio of male to female (74.5%: 25.5% in LNN group vs. 53.8%: 46.2% in LNP group, $p = 0.181$) and age (58.9 ± 11.7 in LNN group vs. 57.8 ± 12.3 in LNP group, years, $p = 0.770$) between LN negative group (LNN group) and LN positive group (LNP group). The histological evaluation showed that the size of EGC was significant larger in LNP group than in LNN group (26.1 ± 10.0 in LNN group vs. 36.1 ± 8.7 in LNP group, mm, $p = 0.002$). The rates of LN metastasis were different according to the tumor size (35.1% in tumor > 20 mm vs. 0% in tumor ≤ 20 mm, $p = 0.003$) and the presence of submucosal invasion (32.5% in submucosal cancer vs. 0% in mucosal cancer, $p = 0.006$). None of mucosal cancer ≤ 20 mm and 48.1% of submucosal cancers > 20 mm in size had LN metastasis.

Conclusion: The risk of LN metastasis is high in mixed adenocarcinoma with more than 20 mm in size and submucosal invasion. Therefore, additional surgical treatment should be recommended in mixed adenocarcinoma with high risk factors even after complete resection by endoscopic procedures.

Disclosure of Interest: None declared

P0530 ENDOSCOPIC ESTIMATION OF TUMOR EXTENT USING LONG AND SHORT DIAMETER IN EARLY GASTRIC CANCER

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Introduction: Exact measurement of lesion extent in gastric epithelial neoplasm is critical for deciding treatment strategy. Although maximal diameter of the lesion is usually indicated as an actual tumor burden in early gastric cancer (EGC), certification of its validity has not been determined.

Aims & Methods: The purpose of the study was to evaluate the validity of lesion diameter and calculated lesion area for predicting actual tumor burden. We also aimed to assess the clinicopathologic factors related to discrepancy between PTE and ATE. We prospectively enrolled 302 EGCs from 290 consecutive patients who underwent endoscopic submucosal dissection as a primary treatment modality and in whom histologic results showed complete resection. Biopsy forcep method was used to measure the pre-sectional long and short diameter of the lesion. Predictive tumor extent (PTE) was calculated using pre-resectional long and short diameter (long diameter x short diameter x 0.5, mm^2). Actual tumor extent (ATE) was measured as mm^2 unit using histologically constructed report and ImageJ Program (NIH Image version 1.55). Correlation between pre-resectional long/short diameter, PTE and ATE were analyzed. The well-estimated group was defined as lesion with ratio of PTE/ATE from 0.7-1.3. The underestimated and overestimated groups were defined as lesions with ratios of PTE/ATE less than 0.7 and more than 1.3, respectively.

Results: Correlation coefficient between pre-resectional long diameter and ATE, and PTE and ATE were 0.67 ($P < 0.01$) and 0.69 ($P < 0.01$), respectively. There was no significant different between PTE and ATE (167.00 ± 13.08 mm^2 vs 166.12 ± 10.89 mm^2). Number of well-estimated, underestimated and overestimated groups were 89 (29.5%), 94 (31.1%) and 119 (39.4%), respectively. Elevated macroscopic morphology and absence of adenomatous component were significant independent factors for well-estimation. Depressed or flat macroscopic morphology, presence of adenomatous component and histologic lesion size less than 1 cm were significant independent factors for overestimation. Histologic lesion size was the only independent factor related to underestimation

Conclusion: Endoscopically measured tumor extent using long and short diameter can be a useful indicator for actual tumor extent in EGC. Marcoscopic morphology, presence of adenomatous component and histologic lesion size were the significant clinicopathlogic factors related to accurate endoscopic estimation of actual tumor extent.

Disclosure of Interest: None declared

P0531 THE USEFULNESS OF MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING FOR PREDICTION ON PRE- AND POST-RESECTIONAL HISTOLOGIC DISCREPANCIES IN GASTRIC LOW-GRADE DYSPLASIA DIAGNOSED BY ENDOSCOPIC BIOPSY

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Introduction: MENBI categorical classification systems were suggested by the Japanese enscopitsts. Vessel plus surface (VS) classification, suggested by Yao et al, was known as useful tool for differential diagnosis between gastric adenoma with LGD and EGC, but few reports have evaluated about the feasibility of this classification system for predicting histologic discrepancy between pre-treatment endoscopic biopsy and post-treatment specimens, especially in other place than Japan.

Aims & Methods: The aim of this study was to evaluate the validity of the parameters of conventional endoscopic and magnifying endoscopy with narrow-band imaging (MENBI) for the prediction of histologic discrepancies between pre- and post-resectional histology in cases of gastric adenoma with low-grade dysplasia (LGD) that were diagnosed based on endoscopically biopsied specimens. The medical records of 149 consecutive patients with gastric LGD and 160 total lesions that were diagnosed based on an endoscopic forceps biopsy were retrospectively reviewed. These patients all underwent a MENBI examination. The incidence of histologic discrepancies and histologic heterogeneity were then analyzed. The relationship between conventional endoscopic/MENBI parameters and the presence of histologic discrepancies were also analyzed.

Results: Histologic discrepancie between the pre- and post-resectional histology were found in 49 cases (30.62%). Among those cases, the histology was upgraded in 47 cases, whereas the histology was downgraded in two cases. Older age, the presence of erythema, positive MENBI findings and the presence of discontinuous lesions were independent factors for the prediction of upgraded histologic discrepancies (p value = 0.046, 0.004, <0.001 and 0.038, respectively). Positive MENBI findings showed the highest predictive value, with a multivariate adjusted odds ratio of 19.812. Histologic heterogeneity in post-resectional specimens was found in 27.7% of cases with upgraded histologic discrepancies. Positive MENBI findings ($p = 0.008$) and the presence of discontinuous lesions ($p = 0.031$) were significant independent factors for the presence of histologic heterogeneity.

Conclusion: Endoscopic resection is recommended in cases of gastric adenoma with LGD that is diagnosed by forceps biopsy that demonstrate (1) surface erythema on conventional endoscopy or (2) a positive finding on the MENBI examination, irrespective of the lesion size. A careful histologic analysis for the presence of discontinuous lesions may be valuable for the detection of histologic heterogeneity.

Disclosure of Interest: None declared

P0532 POSTOPERATIVE NEUTROPHILS TO LYMPHOCYTE RATIO CHANGE IS STATISTICALLY ASSOCIATED WITH OVERALL AND DISEASE-FREE SURVIVAL IN PATIENTS WITH GASTRIC ADENOCARCINOMA

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Introduction: A high preoperative neutrophil-to-lymphocyte ratio (NLR) has been reported to be a prognostic factor for patients with gastric cancer after treatment. However, the clinical implication of postoperative NLR change remains unclear.
Aims & Methods: Three hundred forty-seven patients diagnosed as gastric adenocarcinoma between 2003 and 2014 from two institution (Eulji and hallym hospital) were included. Each subject underwent endoscopic submucosal dissection or gastrectomy. The NLR was recorded within 1 months before and 8 month after surgical procedure. Baseline characteristics, overall survival (OS) and disease-free survival (DFS) were compared according to preoperative NLR and/or postoperative NLR change.
Results: Compared with preoperative NLR, postoperative NLR decreased in 205 patients and increased in 141 patients after surgical treatment. Receiver operating characteristic (ROC) curve exhibited good discriminatory power considering the overall survival for postoperative NLR than preoperative NLR (area under the ROC = 0.744 and 0.54), respectively. Comparing to preoperative NLR, increased postoperative NLR was significantly associated with poor OS and DFS ($p < 0.001$). The 1, 3, 5 years OS was 92.7%, 83.4%, 80.5% for NLR decreased group, and 83.8%, 71.8%, 63.4% for NLR increased group respectively; the corresponding RFS was 92.7%, 85.9%, 33.8% and 83.8%, 69.7%, 63.4% respectively. The survival of patients with lower or higher preoperative NLR can be distinguished more accurate by postoperative NLR change. Multivariate analysis showed that postoperative increased NLR change was an independent prognostic factor for both OS ($P < 0.001$, HR = 2.552, 95% CI 1.744–3.734) and RFS ($P < 0.001$, HR = 2.442, 95% CI 1.609–3.707).
Conclusion: After operation, increased NLR change was an independent prognostic factor for gastric adenocarcinoma undergoing surgical procedure, comparing with decreased NLR change.
Disclosure of Interest: None declared

P0533 ANTITUMOR EFFICACY OF GLV-1H153 FOR PERITONEALLY DISSEMINATED GASTRIC CANCER

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Introduction: Novel therapies are necessary to improve outcomes for patients with peritoneally disseminated gastric cancer. Vaccinia virus has been shown to be an effective oncolytic agent, and genetic manipulations of this virus make it possible to monitor noninvasively therapeutic efficacy and potential toxicity.
Aims & Methods: We examined the therapeutic effects of genetically engineered vaccinia as an oncolytic agtent against peritoneally disseminated gastric cancer. GLV-1h153 was modified from parental vaccinia virus GLV-1h68 to carry hNIS via homologous recombination. GLV-1h153 was tested against human gastric cancer cell line OCUM-2MD3 for replication via viral plaque assays. Viral cytotoxicity and tumore regression of treated OCUM-2MD3 tumor xenografts in nude mice was also determined. Tumor radiouptake in xenograft was assessed via 99mTc pertechnetate scintigraphy and 124I positron emission tomography.
Results: GLV-1h153 infected, replicated within, and killed OCUM-2MD3 cells efficiently. GFP expression conformed viral infection by 24 hours. In vivo, GLV-1h153 was safe and effective in a peritoneal cancer model that simulates clinical disease. A single injection of GLV-1h153 into peritoneal cancer model exhibited intratumoral luciferase activity peaking at days 5-7, with gradual resolution over 10 days. Intraperitoneal injection of GLV-1h153 facilitated imaging of virus replication in tumors via 99mTc pertechnatate scintigraphy and 124I PET.
Conclusion: These results demonstrate significant oncolytic efficacy by gentically GLV-1h153 virus for infecting and lysing peritoneally disseminated gastric cancer both in vitro and in vivo, and support its contined investigation in future clinical trials.

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P0534 ROLE OF STRESS, DIETERY NITRITES AND NITROSO-COMPOUNDS IN TRASFORMATION OF GASTRIC ULCER INTO CANCER OF STOMACH: NITRERGIC AND ADRENERGIC MECHANISMS

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Introduction: Chronic ulcer of stomach is a main risk for gastric cancer. The mechanisms underlying transformation of gastric ulcer to cancer are not well established but there is much epidemiological data suggesting that stress and exogenous N-nitroso-compounds (NOCs) from diet play a major role in these pathological processes. In our previous studies we showed that chronic social stress causes ulcer formation that is associated with pathological changes in local mechanisms of microcirculatory regulation such as nitric oxide (NO) and adrenomediated vasorelaxation. In our clinical work we obtained the abnormal effect of adrenalin on gastric vessels (relaxation) and the hyperteactivity of NO-system in epithelium of stomach in patients with gastric cancer.
Aims & Methods: Here we studied the nitrergic and adrenergic mechanisms of cancerogenic effect of chronic stress (overpopulation, immobilization) and exogenous nitrites/NOCs in rats with gastric stress-related ulcer. The experiments were carried out on six groups of rats: 1) intact (n = 12) and 2) stressed (n = 23) rats without nitrites/NOCs administration; 3) intact (n = 25) and 4) stressed (n = 25) rats with daily administration of N-methylaniline (2g/kg of diet) in the feed with sodium nitrite in the drinking-water (1 g/L); 5) intact (n = 20) and 6) stressed (n = 25) rats with daily administration of N-methylaniline without sodium nitrite. In all groups we analyzed gastric blood flow by LSCI, expression of beta2-adrenoreceptors (B2-AR – a key factor of microcirculatory regulation) by immunohistochemistry and NO/beta-arrestin-1 (co-factors of B2-AR activation) level in epithelium of stomach using spectrophotometry and immunoassay.
Results: Chronic stress (overpopulation) during 5 months was accompanied by primarily erosions in 64% of rats (2d group - stress), 72% (6th group – stress + NOCs) and 93% (4th group – stress + nitrites/NOCs). Additional daily stress (4h immobilization) during 1 month induced development of ulcers in stomach in all rats with stress-related injury of gastric mucosa that was more pronounced in 4th group vs. 2d and 6th groups. The gastric epithelial dysplasia as a sign of pre-cancer formation we found only in 4th group of stressed rats (stress + nitrites/NOCs). In other groups we identified ulcer injures but not mutagenic changes in epithelium of stomach. In intact rats of 1,3,5 groups, gastric tissues were not changed. In all groups of stressed but not in intact rats we observed increase in the level of NO in gastric epithelium. Only stressed rats with gastric epithelial dysplasia demonstrated increase in gastric perfusion that was associated with overexpression of B2-AR, high level of beta-arrestin-1 and more higher level of NO in gastric epithelium that in other groups.
Conclusion: Combination of chronic stress and exogenous nitrites/NOCs are factors for transformation of stress-related gastric ulcer into cancer of stomach. The pathological mechanisms of microcirculatory regulation such as overexpression of B2-AR and the increase in production of co-factors of B2-AR activation – NO and beta-arrestin-1 play an important role in cancerogenic effect of stress and nitrites/NOCs in rats with gastric ulcer.
Research was supported by grant from Russian Ministry of Science and Education (GK-17.488.2014/K).
Disclosure of Interest: None declared

P0535 LONG NONCODING RNA MALAT1 PROMOTES AGGRESSIVE GASTRIC CANCER THROUGH MMP1 OVER-EXPRESSION AND TRANSCRIPTIONALLY ACTIVATED BY C-JUN

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Introduction: Recently long non-coding RNAs (lncRNA) have emerged as new gene regulators and prognostic markers in several cancers including gastric cancer (GC). In this study, we investigated the contributions of the lncRNA MALAT1, a highly conserved long noncoding RNA, in GC and its posttranscriptional regulation.
Aims & Methods: We analyzed MALAT1 expression levels by qRT-PCR and in four GC cell lines compared with epithelial cells. Transient RNAi-mediated knockdown and pcDNA-mediated overexpression of MALAT1 was performed. Stable shRNA-mediated knockdown and lentiviral-mediated overexpression of MALAT1 was to study the role of MALAT1 on in vivo tumorigenicity and metastatic burden in the context of xenograft assays. Proteomic profiling was performed to decipher differential protein expression in cells with different MALAT1 expression levels. One of the differentially regulated proteins, MMP1 was subsequently validated and its function evaluated through xenograft assays.
Results: We found that MALAT1 expression was higher in human GC tissues where it was associated with reduced patients' survival. MALAT1 silencing decreased GC cell proliferation and invasion and increased apoptosis. Mechanistic investigations showed that MALAT1 was transcriptionally activated by c-Jun and that it interacted with MMP1. MMP1 and MALAT1 had a positive relationship, both at expression level and in function. Direct interaction between the two was confirmed through RNA immunoprecipitation coupled with quantitative real time PCR. MMP1 was confirmed to be promoter of GC pathogenesis and as functionally similar to MALAT1 lncRNA.

Conclusion: We found that MALAT1 expression was higher in human GC tissues where it was associated with reduced patients' survival. MALAT1 silencing decreased GC cell proliferation and invasion and increased apoptosis. Mechanistic investigations showed that MALAT1 was transcriptionally activated by c-Jun and that it interacted with MMP1. MMP1 and MALAT1 had a positive relationship, both at expression level and in function. Direct interaction between the two was confirmed through RNA immunoprecipitation coupled with quantitative real time PCR. MMP1 was confirmed to be promoter of GC pathogenesis and as functionally similar to MALAT1 lncRNA.

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P0536 CLINICAL ROLE OF CIRCULATING MIR-223 AS NOVEL BIOMARKER IN EARLY DIAGNOSIS OF CANCER PATIENTS

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Introduction: Current procedures for diagnosis and biomarker examination of cancers are invasive and non-specific. MicroRNAs (miRNAs) have become promising molecular markers for GC predication. However, there have been inconsistencies in the literature regarding the suitability of circulating miRNAs for early detection of cancers.

Aims & Methods: We performed a comprehensive meta-analysis to integrate an evaluation index for diagnostic accuracy of miR-223 in diagnosing cancer patients. Furthermore, we conducted an independent validation set of 50 gastric cancer patients and 50 healthy controls comparing miR-223 expression.

Results: A total of 11 studies met the criteria and included in this meta-analysis. We found that miR-223 yielded a pooled area under ROC curve (AUC) of 0.89 (sensitivity: 81%, specificity: 84%) in discriminating cancer from controls. In our validation analysis, plasma miR-223 levels in GC patients were significantly higher than that in healthy controls ($p < 0.01$). ROC curve analysis showed that AUC was 0.812 with sensitivity of 70% and specificity of 80%. Moreover, the expression trend of miR-223 in plasma samples was in accordance with that of tissue and cell samples.

Conclusion: In conclusion, current evidences suggest that plasma miR-223 could be a reliable and non-invasive biomarker for cancer diagnosis. Further large-scale prospective studies are necessary to validate their potential applicability in human cancer diagnosis.

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P0537 IDENTIFICATION OF THE LONG NON-CODING RNA H19 IN PLASMA AS A NOVEL BIOMARKER FOR DIAGNOSIS OF GASTRIC CANCER

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Introduction: Recent studies have demonstrated that long non-coding RNAs (lncRNAs) are regarded as useful tools for cancer detection, particularly for the early stage; however, little is known about their diagnostic impact on gastric cancer (GC).

Aims & Methods: We hypothesized that GC-related lncRNAs might release into the circulation during tumor initiation and could be utilized to detect and monitor GC. 8 lncRNAs which previously found to be differently expressed in GC were selected as candidate targets for subsequent circulating lncRNA assay. After validating in 20 pairs of tissues and plasma in training set, H19 was selected for further analysis in another 70 patients and 70 controls.

Results: Plasma level of H19 was significantly higher in GC patients compared with normal controls ($p < 0.0001$). By receiver operating characteristic curve (ROC) analysis, the area under the ROC curve (AUC) was 0.838; $p < 0.001$; sensitivity, 82.9%; specificity, 72.9%). Furthermore, H19 expression enabled the differentiation of early stage GC from controls with AUC of 0.877; sensitivity, 85.5%; specificity, 80.1%. Besides, plasma levels of H19 were significantly lower in postoperative samples than preoperative samples ($p = 0.001$).

Conclusion: In conclusion, plasma H19 could serve as a potential biomarker for diagnosis of GC, in particular for early tumor screening.

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P0538 THE INTERACTION BETWEEN MIR-141 AND LNCRNA-H19 IN REGULATING CELL PROLIFERATION AND MIGRATION IN GASTRIC CANCER

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Introduction: Non-coding RNAs including miRNA and lncRNA had been reported to regulate gene expression and were both related to cancer progression. MicroRNA-141 (miR-141) has been reported to play a role in the epithelial to mesenchymal transition (EMT) process and H19 has also been demonstrated to promote malignancy in various cancers.

Aims & Methods: We aimed to determine the correlation between miR-141 and H19 and their roles in gastric cancer in this study. H19 and miR-141 expression were detected by qRT-PCR. By bioinformatic analysis and luciferase assay, we examined the correlation between H19 and miR-141.

Results: H19 expression was found to be inversely correlated to miR-141 expression in gastric cancer cells and tissues. H19 promotes malignancy including proliferation and invasion whereas miR-141 suppresses malignancy in human cancer cells. MiR-141 binds to H19 in a sequence specific manner, and suppresses H19 expression and functions including proliferation and invasion. MiR-141 could also regulate H19 target genes and miR-141 inhibitor restores H19 siRNA function, while H19 regulates miR-141 target gene ZEB1.

Conclusion: These results were the first to demonstrate that H19 and miR-141 could compete with each other and affect their target genes in gastric cancer, which provide important clues for understanding the key roles of lncRNA-miRNA functional network in cancer.

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Disclosure of Interest: None declared

P0539 LONG-TERM COHORT STUDY ON THE RECURRENCE OF BLEEDING AND PROGNOSIS OF PATIENTS HOSPITALIZED FOR ACUTE ESOPHAGEAL VARICEAL BLEEDING

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Introduction: A limited number of studies have reported on the long-term recurrence and mortality in acute esophageal variceal bleeding. This study aimed to elucidate the rates of re-bleeding and mortality and the associated risk factors in patients with esophageal variceal bleeding.
Aims & Methods: A cohort of 174 patients emergently hospitalized for esophageal variceal bleeding was analyzed. All patients underwent endoscopic variceal ligation (EVL) within 12 h of onset. The co-morbidities, drugs use, initial vital sign, laboratory data, follow-up endoscopy were assessed. The Kaplan-Meier method was used to estimate the cumulative re-bleeding and mortality. The Cox proportional hazards model was used to estimate hazard ratio (HR) for mortality. In the re-bleeding risk analysis, we calculated the subdistribution hazard ratio (SHR), treating death without re-bleeding as a competing risk.
Results: Re-bleeding was identified in 49 patients with a mean follow-up of 18 months. The cumulative re-bleeding rate at 1 month, 1 and 5 years was 10.2%, 30.0% and 51.0%, respectively. In univariate analysis, re-bleeding was associated with Child-Pugh class C ($p = 0.03$), alcoholic liver cirrhosis ($p = 0.001$), none follow-up endoscopy ($p < 0.001$), and none follow-up EVL ($p = 0.004$). Multivariate analysis revealed alcoholic liver cirrhosis (SHR, 3.03; $p = 0.003$) and none follow-up endoscopy (SHR, 3.13; $p = 0.001$) as independent risk factors for re-bleeding. During the mean follow-up of 22 months, 69 patients died, 17 due to bleeding. The cumulative mortality rate at 1 month, 1 and 5 years was 12.2%, 26.6% and 63.0%, respectively. In univariate analysis, mortality was associated with age ≥ 65 years ($p = 0.009$), Child-Pugh class C ($p < 0.001$), coexistence of hepatocellular carcinoma (HCC) ($p = 0.013$), none follow-up of endoscopy ($p < 0.001$), and none follow-up of EVL ($p = 0.001$). Multivariate analysis revealed Child-Pugh class C (HR, 2.91; $p < 0.001$), coexistence of HCC (HR, 1.92; $p = 0.013$), none follow-up endoscopy (HR, 25.0; $p < 0.001$) as independent risk factors of mortality.
Conclusion: This study demonstrated more than 50% cumulative re-bleeding and mortality in the 5-year period after hospitalization for acute esophageal bleeding. Alcoholic liver cirrhosis and none follow-up endoscopy increased risk of re-bleeding, whereas Child-Pugh class C, coexistence of HCC, and none follow-up of endoscopy increased risk of mortality.
Disclosure of Interest: None declared

P0540 ENDOSCOPIC VISIBLE LIGHT SPECTROSCOPY IN PATIENTS WITH CHRONIC GASTROINTESTINAL ISCHEMIA AND HEALTHY CONTROLS

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Introduction: Chronic gastrointestinal ischemia (CGI) is the result of decreased mucosal perfusion, in most cases due to atherosclerotic stenosis of the supplying mesenteric arteries. Visible light spectroscopy (VLS) enables direct measurement of mucosal oxygenation saturations during upper endoscopy (1,2). Limited data are available on VLS measurements in patients with CGI compared to a healthy population (2). We aimed to investigate the difference in mucosal oxygen saturation determined by VLS between patients with clinical suspicion of CGI and healthy controls.
Aims & Methods: Consecutive patients with a clinical suspicion of CGI referred to a tertiary care center were prospectively included between September 2014 and April 2015. All patients received the standard work-up for CGI, consisting of assessment of medical history and symptoms, radiological imaging of the gastrointestinal arteries, and VLS measurements. The results were discussed in a multidisciplinary expert panel leading to a consensus diagnosis, which was monitored during follow-up. Healthy, non-smoking volunteers with patent gastrointestinal arteries and unremarkable medical history were after informed consent included as controls. VLS measurements were performed during gastroscopy at three specific locations: gastric antrum, duodenal bulb, and descending duodenum.
Results: We performed 279 VLS measurements in 19 patients with clinical suspicion of CGI (mean age 59.9 (IQR 44.2-66.7) years, 53% male) and 12 controls (33.7 (IQR 29.0-41.2) years, 42% male). CGI was diagnosed in ten (53%) patients and excluded in nine (47%) patients. There was a significant difference in VLS measurements in all locations between patient with CGI and no CGI (antrum 57% (IQR 53-60) vs. 61% (IQR 60-62), $p = 0.04$; duodenal bulb (51% (IQR 47-54) vs. 58% (IQR 54-59), $p = 0.004$; descending duodenum 50% (IQR 45-52) vs. 54% (IQR 52-58), $p = 0.008$, respectively). VLS measurements were significantly lower in the gastric and duodenal bulb of patients with CGI compared to healthy controls (57% (IQR 53-60) vs. 61% (IQR 59-65), $p = 0.04$ and 51% (IQR 47-54) vs. 55% (IQR 53-62), $p = 0.007$, respectively).
Conclusion: Patients with CGI have significantly lower mucosal oxygen saturation levels than patients without CGI as well as healthy controls. VLS can adequately assess mucosal oxygenation. This study confirms the diagnostic value of VLS in distinguishing patients with CGI from patients without CGI and healthy subjects.

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P0541 KAPOSI SARCOMA INVOLVING THE GASTROINTESTINAL TRACT

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Introduction: Kaposi sarcoma (KS) is a low-grade vascular tumour associated with type-8 human herpes virus infection (HHV-8). In pre-antiretroviral therapy era, gastrointestinal involvement was frequent, up to 40% at the diagnosis and up to 80% at the autopsy. In our days, gastrointestinal affection is uncommon.
Objective: Characterization of gastrointestinal involvement by KS.
Aims & Methods: Of 38 biopsies with histologic KS diagnosis, between 2000-2014, it was selected KS cases with gastrointestinal affection. The analysed variables were clinic, analytic, etiologic, endoscopic features, histologic, therapeutic, therapeutic response and mortality.
Results: Nine cases of gastrointestinal KS was identified in fifteen years of study and 25.0% of them happened in 2014. All patients were males, black (22.2%) with diagnosis mean age of 50.4 ± 13.4 years old. The most common type was epidemic/HIV-associated (88.9%), followed by iatrogenic (11.1%). The first type was associated with HIV (100.0%), sexual promiscuity (62.5%), mean CD4+ 136.6 ± 233.1 cells/mm^3 and CDCC3 stage (87.5%). Oral cavity and cutaneous involvement were present in 77.8%, affecting lower limbs in 85.7% and thorax in 71.4%. The main gastrointestinal clinic was dysphagia/odynophagia (44.4%) and nausea/vomiting (33.3%). Esophagogastroduodenoscopy was performed in all patients, with stomach involvement in all cases, mainly in the body (77.8%), followed by duodenum (44.4%) and oesophagus (33.3%). Endoscopy classic features identified were isolated or forming conglomerates violet papules/nodules. Colonoscopy was done in 33.3% of patients with ileocolic lesions in 33.3%. Histopathological features were fusocelular proliferation, storiform pattern, intra-cytoplasmic hyaline globules and vascular slits. Imunohistochemical profile showed CD34 and HHV-8 positivity. Doxorubicin treatment was applied in 66.7% patients (7.8 ± 1.9 cycles). Mortality occurred in 22.2% and was not directly KS-related.
Conclusion: KS is a rare tumour, with male predominance, HIV-associated and CD4+ < 200cells/mm^3. Gastrointestinal involvement was more common in stomach body, with good response to chemotherapy. Diagnosis and treatment should be considered in symptomatic patients.
Disclosure of Interest: None declared

Abstract number: P0542

	Clarithromycin	Nitroimidazole	Clari + Nitro	Quinolone	Amoxicillin
1st line (*naïve*)	19% (16-22%)	29% (26-32%)	11% (9-13%)	14% (10-18%)	1% (0.5-1.5%)
2nd line	52% (45-57%)	45% (38-54%)	32% (26-38%)	16% (9-21%)	0% *
3rd line	64% (59-72%)	60% (52-70%)	53% (48-60%)	44% (39-50%)	0% *
4th line	72% (51-93%)	64% (43-80%)	64% (40-88%)	55% (31-69%)	0% *

* the sample size insufficient to draw conclusionsNumbers represent prevalence of resistant strains and 95% confidence intervals (in parenthesis)

MONDAY, OCTOBER 26, 2015 09:00-17:00
***H. PYLORI* I - HALL 7**

P0542 EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): BACTERIAL RESISTANCE

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Introduction: Antibacterial resistance is one of the main causes of failed eradication attempt in the management of *H. pylori*.
Aims & Methods: To evaluate the resistance rates encountered by European Gastroenterologist in their routine clinical practice. A Local Coordinator was selected from each country with more than 10 *H. pylori* references in PubMed. Each Coordinator selected a representative group of recruiting investigators from his/her country. An e-CRF was created to systematically register all adult patients infected with *H. pylori*. Variables included: *H. pylori* diagnostic test used, use of culture and antibiogram, or molecular tests for the evaluation of antibiotic resistance.
Results: So far 11,272 patients have been included and 9,181 have finished follow-up. Culture was performed in 14% of *naïve* patients (prior to first-line treatment), 14% in second-line, 31% in third-line, and 25% in fourth-line. molecular tests to evaluate resistance were only performed in 0.3% of the cases. Table shows antibiotic resistance per antibiotic and line of treatment.
Conclusion: The mean rate of *H. pylori* clarithromycin resistance in European *naïve* patients reaches the threshold established by consensus conferences (15-20%) in which empirical use of standard triple therapy should be discarded. There is a strong acquisition of antibiotic resistance after failed treatments.
Disclosure of Interest: None declared

P0543 EFFICIENCY OF 14-DAY AND SEQUENTIAL THERAPHY WITH LEVOFLOXACIN IN *HELICOBACTER PYLORI* ERADICATION

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Introduction: *Helicobacter pylori* currently has different antibiotic combinations that are among therapy protocol options. In this study we researched levels of success of the 14-day and sequential therapy methods and whether previous experience of being treated in different combinations and existence of chronic ulcer are effective in eradication.
Aims & Methods: *H. pylori* cases were classified as the 14-day therapy group and the sequential therapy group in a randomized manner. Colloidal bismuth substrate (4x300mg) was used for 4 weeks, Esomeprazole (2x40mg) for 2 weeks, Amoxicillin (2x1000) and Levofloxacin (2x250mg) were used in the 14-day therapy group; and Colloidal bismuth substrate (4x300mg) for four weeks, Esomeprazole (2x40mg) for 2 weeks, Amoxicillin (2x1000) for the first week and Levofloxacin (2x250mg) for the second week and Metronidazole (3x500mg) were used in the sequential therapy group. Eradication success in each group was evaluated by means of a urea breath test conducted 8 weeks after the therapy.
Results: A total of 436 cases were included in the study. The cases were classified into two groups as the 14-day (118 female) and the sequential therapy group (128 female) ($n = 218$). Average age group was 42.24 ± 13.046 in the 14-day therapy groups; while it was 45.10 ± 13.510 in the sequential therapy group. There were no difference of dispersion between groups in terms of gender ($p = 0.407$) or number of previously-received (1,2 or 3) therapies ($p = 0.428$). The ratio of the cases that had received previous therapy was 31.7% in the 14-day group; whereas in was 33.7% ($n = 69$) in the sequential therapy group. The ratio of cases excluded from the study due to the side effects of drugs was determined to be 2.5% in the 14-day therapy group; whereas it was 2% ($n = 4$) in the sequential therapy group; and there were no statistical differences between the groups ($p = 0.719$). Eradication by therapy was 84.2% in the 14-day therapy group; and 80% in the sequential therapy group ($p = 0.274$). Response to the therapy among those that had received previous therapy was 81.3% in the 14-day therapy groups and 72.5% in the sequential therapy group ($p = 0.055$). Moreover; there was no meaningful correlation detected between the number of previous therapies received and response to the therapy [14-day ($p = 0.742$), sequential ($p = 0.077$)]. Non-response to the therapy in cases with ulcer/deformation in bulbus was 34.8% in the 14-day therapy group and 16% in the sequential therapy group. The side effects that were observed more in the sequential therapy in comparison with the 14-day therapy were bad taste in mouth ($p = 0.014$), fatigue ($p = 0.026$), inaccetence ($p = 0.006$) and nausea ($p = 0.046$).
Conclusion: Patient compliance in both therapy protocols was good. Having received standard therapy previously has no effect on eradication success. In spite of the frequent side effects of the therapy, they are well-tolerated and therapy cessation rate is low. High level of success in eradication was achieved in the 14-day and sequential therapies with the therapy combination with Levofloxacin. Nevertheless, eradication success level is lower than expected in quad therapy.
Disclosure of Interest: None declared

P0544 LACTOBACILLUS BULGARICUS GLB44 AND *HELICOBACTER PYLORI* INFECTION – INHIBITION OR POSSIBLE ERADICATION: PRELIMINARY CLINICAL RESULTS

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Introduction: To evaluate the effect of *Lactobacillus delbrueckii subsp. bulgaricus* GLB44 in commercially available form on *Helicobacter pylori* infection in combination with a proton-pump inhibitor.
Aims & Methods: Fourteen patients (57.1% male and 42.9% female) at mean age 42 ± 13.2y were enrolled in our study after esophagogastroduodenoscopy. All patients were *Helicobacter pylori* (HP) positive diagnosed either by rapid urease test, stool antigen test and histology examination, or by a combination of these methods. Every patient was given *Lactobacillus bulgaricus* GLB44 (capsules and tablets) in daily doses of $15x10^9$ living cells together with Rabeprazol 20 mg bid for 7 days, followed by GLB44 alone for 3 days at the same dose. Control stool immunochromatographic antigen tests were performed in all patients after at least 43 days.
Results: After the course of treatment 92.9% of the previously HP positive patients had negative control stool antigen tests. The single case still positive had two unsuccessful antimicrobial eradication courses in the past, while the rest of the group was treatment-naive.
Conclusion: *Lactobacillus delbrueckii subsp. bulgaricus* has in vitro inhibitory properties against H. pylori.[1] Per oral route of administration of adequate probiotic dose in combination with PPI is a promising treatment modality in HP positive patients.

Reference

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Disclosure of Interest: None declared

P0545 RANDOMIZED OPEN LABELED CLINICAL TRIAL: A COMPARATIVE STUDY OF 10-DAY HIGH DOSE PPI TRIPLE THERAPY VS. 10-DAY SEQUENTIAL THERAPY FOR *HELICOBACTER PYLORI* ERADICATION IN FUNCTIONAL DYSPEPSIA PATIENTS

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Introduction: Eradication rates following standard triple therapy for *Helicobacter pylori* (HP) infection are declining worldwide. Studies suggest that high-dose proton-pump inhibitor (PPI)-based triple therapy and sequential therapy for HP infection may yield higher cure rates than standard triple therapy.
Aims & Methods
Objectives: To compare the efficacy and tolerability of high dose PPI-based triple therapy and sequential therapy in adults with *Helicobacter pylori* associated functional dyspepsia.
Methods: One hundred twenty patients with HP positive functional dyspepsia (FD) were prospectively randomized to receive 10-day high dose PPI triple therapy (HD PPI TT) group [60 mg of lansoprazole, 500 mg of clarithromycin, and 1 g of amoxicillin, each administered twice daily for 10 days] or 10-day sequential therapy (ST) group [30 mg of lanzoprazole, 1 g of amoxicillin, each administered twice daily for the first 5 days, followed by 30 mg of lanzoprazole, 500 mg of clarithromycin, and 500 mg of metronidazole, each administered twice daily for the remaining 5 days]. HP status was determined at the 4th week post treatment by the ^{14}C-urea breath test. Eradication rates, antibiotic resistance rates, dyspeptic symptoms, drug compliance, and adverse effects were compared.
Results: The eradication rates in the ST and HD PPI TT groups, were comparable by the ITT analysis [85% (95% CI 73.4-92.9) vs. 80% (95% CI 67.7-89.2), P = 0.471] In the PP analysis, although ST yielded a higher eradication rate than HD PPI TT [94.4% (95% CI 84.6-98.8) vs. 81.4% (95% CI 69.1-90.3), p = 0.035]. Clarithromycin resistance was identified in 10% of isolates. Cure rates with ST were significantly higher than HD PPI TT in patients with clarithromycin-resistant HP strains (100% vs. 33.3%; P = 0.02). Compliance with the treatments was similar (98.3% with HD PPI TT and 93.1% with ST; P = 0.20). Nausea (p = 0.03) and dizziness (p = 0.03) were more common with ST group than HD PPI TT.
Conclusion: In Thailand, ST yielded higher eradication rate than HD PPI TT, in HP associated functional dyspepsia. This was in both in overall FD patients and in a subgroup of clarithromycin resistance. However, the eradication rate of sequential therapy was declined from 94.4% (PP analysis) to only 85% (ITT analysis). The adverse effects of sequential therapy caused lower adherence and might compromise the overall efficacy of ST.
Disclosure of Interest: M. Maneerattanaporn Financial support for research: Pharmaceutical company, C. Auesomwang Financial support for research: Pharmaceutical company, P. kiratisin: None declared, S. leelakusolwong: None declared

P0546 QUADRUPLE THERAPY IN THE ERRADICATION OF HELICOBACTER PYLOTI – THE NEW PARADIGM IN A SOUTHERN EUROPEAN COUNTRY

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Introduction: Empiric triple therapy to eradicate *Helicobacter pylori* (Hp) in Portugal has shown a high failure rate. As such, quadruple regimens should be adopted as first-line therapy. However, due to the simultaneous resistance rate to metronidazole and clarithromycin (5,8%), the efficacy of the sequential therapy may be compromised.
Aims & Methods: Our objective was to evaluate the success rate, in current clinical practice, of the sequential quadruple scheme in *naïve* patients. Additionally, we searched for factors that could influence Hp eradication rates. A total of 250 patients (female – 148; average age – 51.7 ± 15.6 years-old) were treated with sequential scheme (PPI and amoxicillin for 5 days, followed by PPI plus clarithromycin and metronidazole/tinidazole in the next 5 days). Bacterial eradication was checked by Urea Breath Test (UBT). Several clinical and demographic variables that could affect the success rate were analyzed (age, gender, smoking habits, dosage and type of PPI used, metronidazole regimen, use of metronidazole vs tinidazole).
Results: The overall success rate was 90.4% (IC95%: 86.1-93.5%). The most frequent indications for eradication were dyspepsia (58.4%), evaluation before bariatric surgery (12.4%) and peptic ulcer disease (10.8%). Both in the univariate and multivariate analysis, taking metronidazole every 8 hours was more effective than the 12-12 hour regimen (96.5% vs 53.8%, p = 0.002) and the same was noted for full-dose of PPIs when compared to of half-dose (97.8 vs 41.7%, p = 0.002). No other factor had a significant impact on the success rate.
Conclusion: Despite the described high primary resistance rates to both clarithromycin and metronidazole, sequential therapy was quite effective in clinical practice. However, full-dose PPI and an 8-8 hour metronidazole regimen must be adopted to achieve a positive outcome. It is fundamental to conduct another prospective study comparing different quadruple regimens.
Disclosure of Interest: None declared

P0547 COMPARISON OF *H.PYLORI* ERADICATION RATE IN TWO QUADRUPLE REGIMEN "AMOXICILLIN, BISMUTH SUBCITRATE, PANTOPRAZOLE, CLARITHROMYCIN "WITH "AMOXICILLIN, BISMUTH SUBCITRATE, PANTOPRAZOLE AND GEMIFLOXACIN"

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Introduction: *H.pylori* infection is the most bacterial infection in human. Gastritis, peptic ulcer, lymphoma and gastric adenocarcinoma are the outcomes of *H.pylori* infection. According to increase of drug resistance some studies have been done about the role of Floroquinolons in the treatment of *H.pylori* infection. In vitro studies showed the efficacy of Gemifloxacin against *H.pylori* infection.
Aims & Methods: The aim of this study was comparison of *H.pylori* eradication rate in two quadruple regimens "Bismuth subcitrate, Pantoprazole, Amoxicillin, Clarithromycin" with "Bismuth subcitrate, Pantoprazole, Amoxicillin, Gemifloxacin".
In a randomized clinical trial, a total of 182 *H.pylori* positive patients older than 18 years and less than 80 years were enrolled. For all patients information form includes name, age, sex, smoking history was recorded. 91 patients (50%) were treated with BPAC regimen (Bismuth subcitrate 240mg BID, Pantoprazole 20mg BID, Amoxicillin 1gr BID, Clarithromycin 500mg BID) and 91patients (50%) were treated with BPAG regimen (Bismuth subcitrate 240mg BID, Pantoprazole 20mg BID, Amoxicillin 1gr BID,Gemifloxacin 320mg daily) for 10 days. 12 weeks after completion of therapy the eradication was confirmed by a C14 urease breath test.
Results: Three patients were excluded from the study due to drug complications that were a man and a woman due to severe diarrhea, severe Nausea and Vomiting from BPAC group and a woman due to severe Nausea and mouth sores from BPAG group. Thus, 179 patients completed the course of treatment. The eradication rates in the BPAC and BPAG regimens with per-protocol and intention-to-treat analysis was reported 91% vs 77.8%, P-value = 0.015 and 89% vs 76.9%, P-value = 0.03, respectively. No relation between age, sex and smoking with eradication rates was reported, except association of age with BPAG regimen (P-value = 0.03).
Conclusion: In this study, the eradication rates with BPAG regimen in PP and ITT analysis were 77.8% and 76.9% respectively, therefore BPAG regimen was not succeeded in eradication of *H.pylori* infection.
Disclosure of Interest: None declared

P0549 A NEW GENERATION OF COLD-SHOCK EXPRESSION VECTOR DERIVED FROM PCOLD I (PCOLD I-LZ) FOR DIRECTIONAL CLONING AND RECOMBINANT EXPRESSION OF ANTI-HELICOBACTER PYLORI AND ANTI-GASTRIC CANCER STEM CELLS (GCSCS) SMALL PEPTIDES

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Introduction: Current treatment of *Helicobacter pylori* infection has several inherent problems such as the emergence of resistance to the antibiotics used and associated adverse effects, the risk of reinfection or recrudescence, and the high cost of treatment. On the other hand, cancer stem cells (CSCs) have the ability to create tumour and promote its regeneration. These cells are responsible for gastric cancer progression, recurrence, and metastasis. It seems that the use of anti-*H. pylori* and anti-gastric CSCs peptides can provide a new therapeutic strategy for the treatment of this disease. Today, the recombinant expression approach is a useful and economical tool to the high-scale production of therapeutic nano-peptides. However, the short length of the peptides is a limiting factor in the realization of this approach. This is because one or more amino acid residues are added during the cloning process that leads to the loss of the original peptide folding and influences its function.
Aims & Methods: The aim of the present study was to change the structure of the pCold I vector using site-directed mutagenesis in order to do the directional cloning of each target gene and express/purify the small peptides and native proteins with no any additional N-terminus amino acids.
Results: In fact, the structure of the vector was changed such that the cut sites of both the first restriction enzyme at the multiple cloning site (at the nucleotide level) and factor Xa (at the amino acid level) to be the same. The TEE, His6-tag, and factor Xa site were removed by using the factor Xa, leaving no extra N-terminal residues.
Conclusion: The modified vector can be widely used to a fast and more convenient cloning and expression of the native proteins and short peptides, including anti-*H. pylori* peptides (e.g. Magainin 2 and Odorranain-HP) and anti-angiogenesis (e.g. Anginex), gastric anti-CSCs and anti-metastatic peptides.
Disclosure of Interest: None declared

P0550 CLINICAL OUTCOME OF ERADICATION THERAPY FOR GASTRIC MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA ACCORDING TO HELICOBACTER PYLORI INFECTION STATUS

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Introduction: *Helicobacter pylori* (*H. pylori*) eradication is the first-line therapy for *H. pylori*-positive localized gastric mucosa-associated lymphoid tissue (MALT) lymphoma. But the management of the *H. pylori*-negative gastric MALT lymphoma remains controversial.
Aims & Methods: Therefore we assess the efficacy of eradication therapy according to *H. pylori* infection status and find out a predictive factor for resistance to treatment. We retrospectively reviewed the chart with gastric MALT lymphoma between January 2001 and June 2014. The basal characteristics and clinical outcome was compared between *H. pylori*-positive and *H. pylori*-negative gastric MALT lymphoma groups.

Results: Total 54 patients were enrolled and 12 patients were *H. pylori*-negative. *H. pylori*-negative patients were significantly multiple lesion ($P = 0.045$) and the lesion presence of both proximal and distal part of stomach ($P = 0.001$) than *H. pylori*-positive patients. 47 patients received eradication as an initial therapy. 85% (35/41) *H. pylori*-positive patients achieved complete remission and 50% (3/6) *H. pylori*-negative patients obtained regression after eradication therapy. Eradication therapy efficacy was no significant difference between two groups ($P = 0.133$). Multiple lesion was predictive factor for unresponsiveness to *H. pylori* eradication ($P = 0.024$).
Conclusion: In case of *H. pylori*-negative gastric MALT lymphoma eradication therapy could be considered as an initial therapeutic option especially for patients with a single lesion.
Disclosure of Interest: None declared

P0551 CLINICAL OUTCOMES AND INFLUENCING FACTORS OF THE STANDARD TRIPLE THERAPY PLUS PROBIOTICS AND CONCOMITANT THERAPY FOR FIRST-LINE TREATMENT OF *HELICOBACTER PYLORI* INFECTION

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Introduction: Since the efficacy of the standard triple therapy for *Helicobacter pylori* eradication has decreased, there have been attempts to increase the eradication rate by the addition of a potentially helpful drug to the standard triple regimen. Among these, the standard triple therapy plus probiotics (STP) and the concomitant therapy (CT) were introduced and showed encouraging results.
Aims & Methods: We aimed to compare the efficacies and analyze the influencing factors of both regimens. From Mar. 2013 to Feb. 2014, a total of 363 patients who received one of the STP regimen (n = 288, standard-dose proton-pump inhibior + clarithromycin 500mg + amoxicillin 1g + probiotic preparation, b.i.d. for 1 week) and the CT regimen (n = 75, standard-dose PPI + clarithromycin 500mg + amoxicillin 1g + metronidazole 500mg, b.i.d. for 1 week) for *H. pylori* eradication were included. Probiotic bacteria composed of *Bacillus subtilis* and *Lactobacillus rhamnosus*. *H. pylori* status was evaluated at least 4 weeks later, after completion of treatment by ^{13}C-urea breath test.
Results: The intention-to-treat and per-protocol eradication rates were 83.3% (95% CI, 78.8-87.5) and 86.9% (95% CI, 82.6-91.1) in the STP group, and 86.7% (95% CI, 78.7-94.7) and 91.4% (95% CI, 84.5-97.3) in the CT group. There were no significant between-group differences, in regard to the eradication rates and compliance. In the STP group, however, the incidence of side effects was significantly lower than the CT group (13.0% vs 28.2%, $p = 0.002$). The most common side effects were dyspepsia, nausea and dry mouth. In the multivariate analysis, older age in the STP group, and female sex, diabetes and alcohol drinking in the CT group were independent factors associated with eradication failure.
Conclusion: Both treatment regimens showed encouraging efficacies for *H. pylori* eradication. In the aspect of side effects, the addition of probiotics to the standard triple therapy may be a reasonable option. More large sample sized prospective study will be needed.

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Disclosure of Interest: None declared

P0552 FOURTEEN- VERSUS SEVEN-DAY BISMUTH-BASED QUADRUPLE THERAPY FOR SECOND-LINE HELICOBACTER PYLORI ERADICATION

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Introduction: To compare the efficacy of 14- and 7-day bismuth-based quadruple therapies as second-line eradication treatment for *Helicobacter pylori* infection.
Aims & Methods: Between 2004 and 2014, the medical records of 790 patients who had experienced failure of first-line proton pump inhibitor (PPI)-based eradication therapy and were then treated with bismuth-based quadruple therapy were retrospectively reviewed. Those who received bismuth-based quadruple therapy (PPI, bismuth, metronidazole, and tetracycline; PBMT) for either 7 days or 14 days were assigned to a PBMT-7 group (n = 543) or a PBMT-14 group (n = 247), respectively. The eradication rates for both groups were determined by intention-to-treat (ITT) and per-protocol (PP) analyses. ITT analysis compared the treatment groups as originally allocated while the PP analysis including only those patients who had completed the treatment as originally allocated. Successful eradication therapy for H. pylori infection was defined as a negative 13C-urea breath test 4 weeks after the end of eradication treatment.
Results: The overall ITT eradication rate was 69.1% (546/790). Final ITT eradication rates were 67.4% (366/543; 95% confidence interval [CI]: 63.1–71.7%) in the PBMT-7 group and 72.8% (180/247; 95% CI: 67.4–78.2%) in the PBMT-14 group (p = 0.028). The overall PP eradication rate was 80.0% (546/682), and the final PP eradication rates were 78.2% (366/468; 95% CI: 72.1–84.0%) in the PBMT-7 group and 84.1% (180/214; 95% CI: 76.8-90.8%) in the PBMT-14 group (p = 0.009). The *H. pylori* eradication rates in the PBMT-14 group were significantly higher than in the PBMT-7 group according to both ITT (p = 0.028) and PP analysis (p = 0.009). Compliance was similar in both groups (PBMT-7 group: 97.9%; PBMT-14 group: 96.4%). Adverse event rates were 10.7% (51/478) and 17.1% (38/222) in the PBMT-7 and PBMT-14 groups, respectively (p = 0.487).
Conclusion: The *H. pylori* eradication rates in the PBMT-14 group were significantly higher than in the PBMT-7 group according to both ITT and PP analysis. The 14-day bismuth-based quadruple therapy is a significantly more effective second-line eradication treatment for *H. pylori* infection than the 7-day alternative.
Disclosure of Interest: None declared

P0553 PRENEOPLASTIC GASTRIC LESIONS IN PATIENTS WITH MALT LYMPHOMA: COMPARISON WITH DIFFUSE LARGE B-CELL LYMPHOMA AND H PYLORI ASSOCIATED CHRONIC GASTRITIS

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Introduction: Patients with primary gastric MALT lymphoma (GML) are at risk of developing gastric carcinoma GC even after completing remission. The aim of this retrospective study was to assess the prevalence and the course of preneoplastic lesions in patients with GML as compared with gastric diffuse large B-cell lymphoma (GDLBCL) and *H. pylori*-associated chronic gastritis (*Hp*G).
Aims & Methods: From 1990 to 2013, 179 patients with GML, 70 with GDLBCL and 152 patients with *Hp*G, were included. Clinical, biological, endoscopic and histopathological parameters were reviewed. To assess the presence or absence of preneoplastic lesions, we reported the Sydney score in 3 gastric areas (antrum, corpus and lymphoma site). Atrophy $\geq$ 2 was only considered as significant. Preneoplastic lesion-free survival was assessed using Kaplan-Meier method, log-rank test and Cox model. Patients' characteristics were compared using chi^2 and Wilcoxon-Mann-Whitney tests.
Results: The median follow-up of GML patients was 6.5 (0.1-33.7) years. At the time of diagnosis, 119 (66%) patients presented with a *H. pylori* infection. GML was located at the junction of the body with antrum in 43% of the cases with a pseudogastritis appearance in 57%. At the inclusion, atrophy and metaplasia were observed in 35% and 25%, respectively. Both atrophy and metaplasia were more frequently located in the lymphoma site as compared with antrum and corpus. Dysplasia was observed in 3% of the cases. To assess the course of preneoplastic and neoplastic lesion, we analysed a subgroup of 104 patients followed-up for at least five years. Although the overall prevalence of atrophy remained stable over time with the evidence of incidental and regressive atrophy, the prevalence of metaplasia tended to increase at the lymphoma site. In the overall population of 179 patients, the probabilities of atrophy were 24%, 39% and 48% at 1, 5 and 10 years. The probabilities of metaplasia were 12%, 30% and 36% and the probabilities of dysplasia or GC were 9, 16 and 22%, respectively. Nine cases (5 women, 4 males) presented with a gastric cancer during follow-up, all associated with underlying preneoplastic gastric lesions. The median delay before the occurrence of GC was 2.49 (0-16.66) years. At diagnosis, significant atrophy and metaplasia were significantly more frequent in GML group vs. GDLBCL group (19% and 14%) and versus *hp*G (8% and 15%), respectively. No dysplasia was observed in both control groups.
Conclusion: The occurrence of preneoplastic and neoplastic gastric lesions in patients with GML is frequent and still increases overtime at the lymphoma site despite complete remission of the lymphoma. The occurrence of such lesions is higher than in patients with GDLBCL and HpG suggesting a deleterious effect of GML on the gastric epithelia cells that lead to the occurrence of these lesions. Long-term follow-up is warranted to detect gastric neoplasia at an early stage.
Disclosure of Interest: None declared

P0554 PRIMARY GASTRIC LYMPHOMA – EXPERIENCE OF A TERTIARY CENTER

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Introduction: In the immunocompetent patient, the gastrointestinal tract is the most common extranodal site for lymphoma. However, primary gastrointestinal lymphomas are very rare, accounting for only 1-4 % of all gastrointestinal malignancies. The stomach is the most commonly affected site, corresponding to less than 3% of gastric malignancies and 10% of all lymphomas. Approximately 90% of cases of primary gastric lymphomas (PGLs) are either mucosa-associated lymphoid tissue (MALT) lymphoma or diffuse large B-cell lymphoma (DLBCL). Although it's well established the relation between MALT lymphoma and *Helicobacter pylori* (Hp) infection, significant controversy exists regarding the role of Hp infection in the pathogenesis of DLBCL (specially, in those that develop from a MALT lymphoma).

Aims & Methods: (1) To describe the experience of a tertiary center in the diagnosis, management and follow-up of PGLs; (2) To compare clinical, laboratorial, histological (Hp infection) and endoscopic features at presentation, between the MALT and DLBCL subtypes.
All new cases of PGL were retrospectively evaluated between 1996 and 2014. Primary gastrointestinal lymphoma was defined according to Dawson criteria. Staging was established according to Lugano staging system, and for risk assessment International Prognostic Index (IPI) was used. We recorded demographic, clinical, laboratorial endoscopic and radiological data.
Results: We identified 31 patients, with a mean age of 65 years old, a male preponderance (n = 20) and 5 patients had ECOG ≥2. The most common subtype was MALT (n = 18), followed by DLBCL (n = 11). The most frequent symptom was abdominal pain (62%), followed by anorexia (55%), while the classical B symptoms were only present in two patients; 10 patients had Hb < 12.0 g/dL at presentation (none with DLBCL subtype).
At diagnosis, 80% of the cases were classified as limited disease (Lugano: I-II) and 84% as having low or intermediate risk (IPI ≤ 2), with no statistically significant differences between MALT and DLBCL subtypes. The most common endoscopic pattern was ulcerative type (62%), and gastric body was affected in 69%, with no statistically significant differences between the subtypes.
The variables age, Leukocyte count, serum LDH, Albumine, Urine Acid and β-2 microglobuline weren't statistically different between MALT and DLBCL subtypes. Hp infection was present in 11 patients (MALT: 10; DLBCL: 1; p = 0.022). The mean survival was 67 months (MALT: 80.7 versus DLBCL 38).
Conclusion: Although the small number of patients, our data does not support the role of Hp in the pathogenesis of DLBCL lymphoma. Beside anemia, none of the studied variables at presentation, was statistically different between the subtypes. The results agree and strengthen the scarce available literature about PGLs.
Disclosure of Interest: None declared

P0555 *HELICOBACTER PYLORI* VACA GENOTYPES PREDICT RISK OF INTESTINAL- AND DIFFUSE-TYPE ADENOCARCINOMAS IN A VERY HIGH-RISK AREA IN IRAN

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Introduction: Gastric cancer (GC) is the fifth commonest malignant disease throughout the world and the third-leading cause of cancer-related mortality, and histo-morphologically is divided into two groups; intestinal- and diffuse-type carcinomas. *Helicobacter pylori* infection is one of the main risk determinants of both the type of GC. Ardabil in Northwestern Iran has the highest rates of *H. pylori* infection (89%) and stomach cancer, in which it constitutes the 31% of all malignancies seen in this area with the ASRs of 51.8/100,000 for males and 24.9/100,000 for females. In this province, greater than 90% of adults aged 40 or older are suffering from chronic gastritis related to *H. pylori* infection.
Aims & Methods: We aimed to investigate the frequency of the *H. pylori vacA* (vacuolating cytotoxin A) gene polymorphisms and their associations with the intestinal- or the diffuse-type adenocarcinomas in Ardabil. We determined the presence of the *H. pylori 16S rDNA* gene, and also the *vacA* s-, m-, i-, and d-region genotypes in gastric biopsies, and performed histopathological evaluations. Associations between the *H. pylori vacA* allelic variants and whether the intestinal- or the diffuse-type adenocarcinomas were assessed by the $\chi 2$ test or Fisher's exact test where appropriate. Odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) were computed. The Forward Stepwise LR (Likelihood Ratio) multiple logistic regression was used for each genetic variant individually, with adjustment for age and sex.
Results: Of 135 patients, 57 with non-atrophic gastritis and 78 with gastric cancer (GC), 103 were infected by *H. pylori*. In patients with the intestinal-type adenocarcinoma of the stomach, the *vacA* s1, m1, i1, and d1 genotypes were detected in the 47.8%, 63.2%, 84.2%, and 76.5% of *H. pylori* strains, respectively, while in patients with the diffuse-type adenocarcinoma of the stomach, the *vacA* s1, m1, i1, and d1 genotypes were present in the 73.3%, 42.9%, 66.7%, and 76.9% of strains, respectively. The frequency of the *vacA* i1 and d1 genotypes was significantly higher in patients with the intestinal-type adenocarcinoma (84.2%, and 76.5%, respectively) than in those with NAG (47.1% and 45.0%, respectively); the OR was 6.00 (95% CI, 1.47-24.45; P = 0.01) and 3.97 (95% CI, 1.10-14.31; P = 0.042), respectively. However, in multiple logistic regression with adjustment for age and sex, only the *vacA* i1 genotype was significantly associated with an increased risk of the intestinal-type adenocarcinoma (OR = 14.04, 95% CI, 2.15-91.77; P = 0.006). Although the adjusted OR of 4.08 (95% CI, 0.95-17.50) was obtained for d1, the difference did not reach significance (P = 0.058). The presence of the *vacA* d1 genotype was significantly associated with an increased risk of the diffuse-type adenocarcinoma in the multiple logistic regression (OR = 7.71, 95% CI, 1.13-52.28; P = 0.036).
Conclusion: It is proposed that the *vacA* i1 and d1 genotypes might be important for the prediction of the risk of the intestinal- and the diffuse-type adenocarcinomas, respectively.
Disclosure of Interest: None declared

P0556 *H. PYLORI* INFECTION WITH ATROPHIC GASTRITIS IS AN INDEPENDENT RISK FACTOR FOR ADVANCED COLONIC NEOPLASM

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Introduction: *Helicobacter pylori (H. pylori)* infection is a major risk factor for atrophic gastritis (AG) and gastric cancer and can induce various extragastric malignancies, but its relationship to colorectal neoplasm (CRN) remains unclear. The correlation between AG and CRN has been little studied and is inconclusive.
Aims & Methods
Aim: The aim of this study was to investigate the association between *H. pylori* infection status, AG, and advanced CRN.
Methods: This cross-sectional study investigated the relationship between the presence of serum anti-*H. pylori* IgG antibody, AG, and advanced CRN in 6,351 consecutive asymptomatic subjects who underwent screening colonoscopy. Multivariate analysis was performed including clinical variables such as gender, age, family history of colorectal cancer, smoking status, alcohol consumption, presence of metabolic syndrome, and endoscopic findings.
Results: A total of 316 participants (5.0%) had advanced CRN. *H. pylori* seropositivity was found in 61.3% of these cases. In univariate analysis, the presence of *H. pylori* infection was associated with overall CRN (OR 1.33, 95% CI 1.19–1.48; p < 0.001) and advanced CRN (OR 1.49, 95% CI 1.17–1.91; p = 0.001). *H. pylori* infection was associated with an increased risk of advanced CRN after adjusting clinically relevant confounders (OR 1.34, 95% CI 1.04–1.72; P = 0.023). *H. pylori*-related AG was significantly associated with the risk of advanced CRN (OR 1.40, 95% CI 1.03–1.91; p = 0.030), whereas *H. pylori* infection without AG was not.
Conclusion: *H. pylori* infection increases the risk of advanced CRN, especially when combined with AG. Strict colonoscopy screening and surveillance may be warranted in *H. pylori*-positive AG patients.
Disclosure of Interest: None declared

P0557 INCIDENCE OF SECOND CANCERS IN PATIENTS WITH GASTRIC MALT LYMPHOMA

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Introduction: Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is closely associated with *Helicobacter pylori* infection. The incidence of second cancers, namely gastric carcinoma, seems to be increased in this group of patients. However, the evidence is still controversial.
Aims & Methods: To determine the incidence of second cancers in patients with gastric MALT lymphoma who achieved complete remission, we evaluated consecutive patients admitted with gastric MALT lymphoma (1994-2014), staged according to the Ann Arbor staging system modified by Musshoffs. Patients' characteristics, the diagnosis of second cancers and survival were recorded. Standardized incidence ratio (SIR), using age- and sex-specific incidence rates from the Cancer Registry, was calculated.
Results: A total of 143 patients (76 men) were included with a mean age of 56 years (18-83); 103, 24 and 16 patients were diagnosed at stages EI, EII and EIV, respectively. Complete remission was achieved in 128 patients. After a mean follow-up of 109 months (6-246), a second cancer was diagnosed in 14 (9.8%) patients (11 men, mean age of 66 years), in whom complete remission was achieved after eradication therapy (n = 12), surgery (n = 1) and chemotherapy (n = 1). A total of 7 solid (lung (n = 1), brain (n = 1), liver (n = 1), breast (n = 1), pancreas (n = 1), sarcoma (n = 1) and colon (n = 1)) and 7 hematologic cancers (non-Hodgkin lymphoma (n = 4), Hodgkin lymphoma (n = 1), multiple myeloma (n = 1) and chronic myelomonocytic leukemia (n = 1)) were reported. The non-Hodgkin lymphomas diagnosed were diffuse large B-Cell lymphoma (n = 2), chronic lymphocytic leukemia (n = 1) and parotid MALT lymphoma (n = 1). There was an increased incidence of an additional cancer (SIR = 1.4, p = 0.0001) and non-Hodgkin lymphomas (SIR = 9.3, p = 0.04). The 10-year overall survival of the 128 patients that achieved complete remission was 82%. The cause of death was the second cancer in 11/24 (45.8%) patients.
Conclusion: Patients with gastric MALT lymphoma are at an increased risk for a second cancer, particularly non-Hodgkin lymphoma, which highlights the importance of a long-term follow up. There were no patients with gastric

carcinoma. The overall prognosis was good but the occurrence of second cancers, mainly hematologic, were an important cause of death.
Disclosure of Interest: None declared

P0558 APPLICATION OF ABC SYSTEM INTO CLINICAL PRACTICE IN KOREA: IS IT WORTHWHILE?

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Introduction: ABC method, which using a combination of serum *Helicobacter* (Hp) immunoglobulin G (IgG) and pepsinogen (PG) level, has been expected as a promising simple screening tool for gastric cancer. Group A is Hp infection-free subjects, Group B is Hp infected, but has no or minimal changes of atrophy, Group C has both positive result of serum value. Group D is the advanced infected type, which has extensive atrophy and negative Hp IgG which means relatively prior Hp infection.
Aims & Methods: We aimed to validate the ABC method for gastric cancer patients in clinical practice. The presence of Hp infection is determined by serum Hp IgG. The positive PG is defined as PG I level less than 70 ng/ml and the ratio of PG I/II is less than 3.0. According to our strategy for gastric tumor since 2007, we have conducted the serum Hp IgG and PG level for the patients who plan to undergo endoscopic resection. We retrospectively reviewed the patients who underwent serum Hp IgG and PG level between October 2007 and November 2013 in Kyungpook National University Hospital in Korea.
Results: 1,146 cases were possible to be analyzed in ABC method. 717 patients were male and the mean age was 61.4 ± 10.3 years. Among 429 patients with gastric cancer, 82 patients (19.1%) were classified into Group A, 230 (53.6%) into Group B, 89 (20.7%) into Group C, and 28 (6.5%) into Group D, respectively. Group A also occupied considerable portion (15.9%) in gastric tumor including adenoma.
Conclusion: Considering relatively high prevalence of *Helicobacter* in Korea, the ABC method needs reconsideration before application in the screening for gastric cancer. In addition, other gastric cancer risk factors or confounding factors should be revealed, especially for group A patients in further study.
Disclosure of Interest: None declared

P0559 *HELICOBACTER PYLORI* VACUOLATING CYTOTOXIN GENOTYPES AND GASTRIC PRENEOPLASTIC LESIONS OR GASTRIC CANCER RISK: A COMPREHENSIVE META-ANALYSIS

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Introduction: Disease progression to gastric cancer (GC) occurs in only a small proportion of *H. pylori*-infected patients. A considerable differences in the vacuole-creating activities are observed between *H. pylori* strains, which is attributed to the extensive polymorphisms within the vacuolating cytotoxin gene A (*vacA*). These variations may determine the clinical consequences; however, the association evidence is not totally consistent both between and within continents, and thus the actual influence of each allelic variant is still controversial.
Aims & Methods: We examined the strength of this association in adult-infected populations and modeled the impact of mean age-standardized incidence rates (ASRs) of GC as a hypothesized moderator variable. Pooled relative risk (RR) estimates were calculated. Subgroup, sensitivity, and meta-regression analyses were conducted.
Results: Totally, 33 studies, including 1446 cases and 2697 controls, were analyzed. The *vacA* s1 genotype was significantly associated with an increased risk of atrophic gastritis (AG), intestinal metaplasia (IM), and GC (RR = 1.116, 95% CI,1.019-1.222, RR = 1.418, 95% CI,1.035-1.942, and RR = 1.333, 95% CI,1.115-1.593, respectively); however, the *vacA* m1 genotype strongly increased the risk of IM and GC, but not AG (RR = 1.571, 95% CI,1.247-1.980 and RR = 1.431, 95% CI,1.180-1.735, respectively). The *vacA* s1m1 allelic combination was linked to an increased risk of GC. The m1-type of *vacA* was more potent than s1 for predicting the risk of GC within the subgroups with mean ASRs 11/100,000-19/100,000 and less than 10/100,000, which was confirmed either by excluding the studies with the largest variance or by performing a leave-one-out analysis. The meta-regression analysis indicated that the ASR of GC modified the association between *H. pylori* genotypes and GC risk. When the ASRs of GC were used as a moderator variable, the estimated coefficient in predicting the logit was -0.0142, -0.0162, and -0.0160 for the *vacA*-s1, -m1, and –s1m1 genotypes, respectively, indicating that the estimated risk was significantly decreased with increasing the mean ASRs of GC (*P*-values = 0.025, 0.00009, and 0.0005 for s1, m1, and s1m1,respectively).
Conclusion: *H. pylori vacA*-s1 and -m1 allelic variants strongly increased susceptibility to IM and GC; however, only s1 showed an association with AG. This association was largely influenced by geographic variation in the GC incidence rate.
Disclosure of Interest: None declared

P0560 *HELICOBACTER PYLORI* VACUOLATING CYTOTOXIN C1 GENOTYPE STRONGLY PREDICTS RISK OF CARDIA AND NON-CARDIA GASTRIC ADENOCARCINOMA

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Introduction: Gastric adenocarcinomas account for almost 90% of all gastric malignancies that are classified based on the anatomical site of tumor, including cardia gastric adenocarcinoma (CGA) and non-cardia gastric adenocarcinoma (NCGA).
Aims & Methods: We have recently identified a novel polymorphic site in the 3'-end region of *H. pylori* vacuolating cytotoxin gene A (*vacA*), denoted by c1/-c2 (c1: with deletion of 15 bp); thus we aimed to assess its association with the risk of CGA and NCGA in an Iranian population. A total of 593 patients who were of the rural and urban areas of Iran were participated in the study. Gastric biopsy specimens were taken from the antrum and/or the corpus, whether or not positive for rapid urease test, and then were cultured. The colonies were identified based on Gram staining, typical cell morphology, and positive reactions to catalase, oxidase, and urease, as well as PCR amplification of *H. pylori 16S rDNA*. The genotyping of the *H. pylori vacA* gene and histopathological examination and classification of subjects were then performed.
Results: Patients included 496 with non-atrophic gastritis (NAG), 41 with CGA, and 56 with NCGA. Of the 593 patients, 390 (65.8%) were positive for *H. pylori* infection, whereas 203 (34.2%) were negative. Statistical analysis showed no significant associations between the prevalence of *H. pylori* infection and sex, age, rural or urban areas and the risk of the CGA or the NCGA. The NCGA was more prevalent in rural areas [odds ratio (95% confidence interval) = 3.49 (1.86-6.57), $P = 0.00$]. Both the age > = 55 and male gender were significantly associated with the CGA [OR (95% CI) = 17.85 (6.89-47.61) and 4.04 (1.89-8.62), respectively; $P = 0.00$] and the NCGA [OR (95% CI) = 17.24 (7.57-38.46) and 3.75 (1.97-7.19), respectively; $P = 0.00$]. A total of 173 *H. pylori* isolates, including 120 with NAG, 24 with CGA, and 29 with NCGA, were successfully obtained from biopsy cultures and genotyped. The frequency of the c1-type of *vacA* was higher in patients with both the CGA (83.3%) and the NCGA (71.4%) than in those with gastritis (NAG) (24.1%). The results of simple logistic regression analysis showed that this genotype was significantly associated with an increased risk of both the CGA and the NCGA; the OR (95% CI) was 15.71 (4.23-58.26), and 7.85 (3.12-19.78), respectively ($P = 0.00$). Finally, the multiple logistic regression analysis showed that the *vacA* c1 genotype was significantly associated with the age- and sex-adjusted risk for the CGA and the NCGA; the OR (95% CI) was 16.85 (3.83-67.61), and 8.14 (2.83-23.38), respectively ($P = 0.00$).
Conclusion: The present study showed the determinant role of the *H. pylori vacA* c1 genotype in the development of both the CGA and the NCGA in Iran. This is the first report of an association of *H. pylori* genotype with an increased risk of the CGA.
Disclosure of Interest: None declared

P0561 DECREASE OF SERUM TOTAL GHRELIN IN EXTENSIVE ATROPHIC GASTRITIS: COMPARISON WITH PEPSINOGENS IN HISTOLOGICAL REFERENCE

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Introduction: Ghrelin is mainly secreted from the gastric oxyntic mucosa and the production is impaired in chronic atrophic gastritis. This study aimed to evaluate serum total ghrelin levels according to the extent of histological atrophy, and to compare the performance as a serologic atrophic marker with pepsinogen.
Aims & Methods: Data were analyzed from 154 patients with atrophic gastritis. Histological extent of atrophic gastritis was assessed by three paired biopsies from antrum, corpus lesser, and corpus greater curvature. Fasting serum concentrations of total ghrelin, pepsinogen I, and II were measured with enzyme immunoassay. Regression analysis was performed to evaluate factors associated with serum levels of total ghrelin. The serologic performance was compared with pepsinogen using receiver-operating characteristic curves.
Results: *H. pylori* infection rate was 85.1% and extensive atrophic gastritis involving corpus greater curvature was found in 24.0%. Serum total ghrelin concentrations were decreased significantly in patients with extensive corpus greater curvature atrophy (median value, 170.4 pg/mL; vs 201.1 pg/mL in patients without corpus greater curvature atrophy; $p < 0.001$), and the levels were correlated with pepsinogen I and pepsinogen I/II ratio. The decrease of serum total ghrelin in corpus greater curvature atrophy was independent of age, gender, body mass index, and *H. pylori* infection status. Sensitivity and specificity of serum total ghrelin to predict extensive corpus greater curvature atrophy was 56.8% and 78.9%, respectively. The discriminatory ability was similar to pepsinogen I/II ratio ($p = 0.612$) and lower than pepsinogen I ($p = 0.040$).
Conclusion: Serum concentration of total ghrelin is decreased in extensive CGC atrophy. The serologic performance is lower than that of PG I.

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Disclosure of Interest: None declared

P0562 ANALYSIS OF DEREGULATED MICRORNAS AND THEIR TARGET GENES IN GASTRIC CANCER

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Introduction: MicroRNAs (miRNAs) are widely studied non-coding RNAs that modulate gene expression. MiRNAs are deregulated in different tumors including gastric cancer (GC) and have potential diagnostic and prognostic implications. The aim of our study was to determine miRNA profile in GC tissues, followed by evaluation of deregulated miRNAs in plasma of GC patients. Using available databases and bioinformatics methods we also aimed to evaluate potential target genes of confirmed differentially expressed miRNA and validate these findings in GC tissues.
Aims & Methods: The study included 51 GC patients and 51 controls. Initially, we screened miRNA expression profile in 13 tissue samples of GC and 12 normal gastric tissues with TaqMan low density array (TLDA). In the second stage, differentially expressed miRNAs were validated in a replication cohort using qRT-PCR in tissue and plasma samples. Subsequently, we analyzed potential target genes of deregulated miRNAs using bioinformatics approach, determined their expression in GC tissues and performed correlation analysis with targeting miRNAs.
Results: Profiling with TLDA revealed 15 deregulated miRNAs in GC tissues compared to normal gastric mucosa. Replication analysis confirmed that miR-148a-3p, miR-204-5p, miR-223-3p and miR-375 were consistently deregulated in GC tissues. Analysis of GC patients plasma samples showed significant down-regulation of miR-148a-3p, miR-375 and up-regulation of miR-223-3p compared to healthy subjects. Further, using bioinformatic tools we identified targets of replicated miRNAs and performed disease-associated gene enrichment analysis. Ultimately, we evaluated potential target gene *BCL2* and *DNMT3B* expression by qRT-PCR in GC tissue, which correlated with targeting miRNA expression.
Conclusion: Our study revealed miRNA profile in GC tissues and showed that miR-148a-3p, miR-223-3p and miR-375 are deregulated in GC plasma samples. Target gene analysis demonstrated that *BCL2* and *DNMT3B* expression in GC tissue correlated with their targeting miRNA expression.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 09:00–17:00
SMALL INTESTINAL I – HALL 7

P0563 INTESTINAL EPITHELIAL BARRIER DYSFUNCTION IN PATIENTS WITH CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

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Introduction: Chronic intestinal pseudo-obstruction (CIPO) is a rare condition characterized by gastrointestinal (GI) impairment that is so severe to cause a clinical picture suggestive of a mechanical obstruction in the absence of any occlusion. Although degenerative or inflammatory neuro-interstitial cells of Cajal (ICC)-muscular abnormalities are the main pathogenetic mechanisms underlying gut dysfunction, other factors, i.e. intestinal epithelial barrier (IEB) abnormalities, may represent the initial insult contributing to symptoms and clinical manifestations
Aims & Methods: The present study aims to assess the expression of occludin and zonula occludens-1 (ZO-1), two major components of tight junctions (TJs), as markers of IEB integrity in patients with CIPO. A number of $n = 26$ clinically and histopathologically well characterized CIPO pts (15 F; age range: 16 - 75 yrs) were studied. CIPO cases were subdivided according to the histopathological analysis (IHC) in 3 groups: A) apparently normal $n = 7$; B) inflamed $n = 8$; C) degenerative $n = 10$. Patients ($n = 8$; 3 F, age range: 48 - 73 yrs) undergoing elective surgery for uncomplicated neoplastic diseases served as controls. CIPO and control jejunal full thickness biopsies were processed to assess occludin and ZO-1 mRNA and protein expression using q-PCR and WB.
Results: Compared to controls, total occludin protein showed a marked decrease in CIPO pts ($P < 0.05$); also, a tendency to a decreased occludin mRNA expression was found in CIPO vs. controls. Moreover, occludin oligomers, an index of occludin assembly in rafts TJs, were detected only in 19% of CIPO pts while all controls showed normal oligomerization. ZO-1 protein and mRNA expression did not change in CIPO vs controls. Interestingly, the three histologically identified groups of CIPO showed a selective reduction of only one of the two analyzed components. Specifically, in group A and B occludin expression decreased, while in group C only ZO-1 content decreased.
Conclusion: IEB integrity was altered in patients with CIPO as identified by the reduction of at least one of the TJ components. Moreover, the abnormal occludin oligomerization is indicative of TJ dysfunction, which increases the possibility of noxious agents passing through the intestinal wall in these patients. A better knowledge of IEB altered molecular mechanisms is expected to be translated in targeted therapeutic interventions.
Disclosure of Interest: None declared

P0564 LISTERIA MONOCYTOGENES AFFECTS SEROTONIN TRANSPORTER ACTIVITY AND EXPRESSION IN HUMAN INTESTINAL EPITHELIAL CELLS BY TLR10 ACTIVATION

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Introduction: Serotonin (5-HT) is a neuromodulator mainly synthesized in the intestinal epithelium. 5-HT regulates the whole intestinal physiology and it has been shown to be essential in intestinal homeostasis. In fact the excess of extracellular 5-HT has been described to contribute to intestinal inflammation. 5-HT availability is in part mediated by the serotonin transporter (SERT), which is responsible for the 5-HT reuptake inside the enterocytes. Recent results have demonstrated that bacteria resident in the intestinal lumen may affect intestinal pathophysiology by acting on the serotoninergic system. This effect is in part carried out through the activation of Toll-like receptors (TLRs) which regulates SERT in the intestinal epithelium. *Listeria monocytogenes* is a Gram-positive bacteria that causes in humans a serious infection (listeriosis) mainly through the consumption of ready-to-eat foods. Following ingestion, *L. monocytogenes* has been described to cross the intestinal epithelium and to invade intestinal epithelial cells. However, the effect of *L. monocytogenes* on intestinal epithelium activity remains unknown.
Aims & Methods: 5-HT has been shown to be an essential regulator of the intestinal physiology. 5-HT availability has been shown to be modulated by the activity of SERT expressed in intestinal epithelial cells. Therefore, the aim of the present study was to analyze whether the pathogen *L. monocytogenes* affects the intestinal epithelial activity, by focusing on the analysis of SERT in intestinal epithelial cells. In this study human enterocyte-like Caco-2/TC7 cell line was used. These cells express SERT and TLRs. Caco-2/TC7 cells were treated with *L. monocytogenes*, and 5-HT uptake by SERT and transepithelial resistance (TER) were measured. The molecular expression of SERT, TLR2 and TLR10 were analyzed by measuring both, mRNA levels by RT-qPCR, and protein expression by western blotting.
Results: *L. monocytogenes* did not appear to affect TER in the Caco-2/TC7 cells, but the treatment showed to inhibit 5-HT uptake by reducing SERT expression in the cells. However, *L. monocytogenes* inactivated by heat or by pulsed electric fields did not affect SERT activity. Moreover, factors secreted by this bacteria did not seem to be involved in effects on SERT. TLR2 expression in Caco-2/TC7 cells resulted down-regulated by *L. monocytogenes*, however, TLR10 expression appeared to be increased. In this context, TLR10 seemed to be involved in the effect of *L. monocytogenes* on SERT, since the effect disappears by treating the cells with TLR10 specific antibody.
Conclusion: *L. monocytogenes*, a known powerful pathogen bacteria, may induce an alteration of the intestinal homeostasis by inhibiting SERT function and expression. This effect might cause an increase in the level of extracellular 5-HT and, thereby, might contribute to an intestinal proinflammatory effect. Our results demonstrate that *L. monocytogenes* requires be alive to alter SERT, and they show for the first time that this effect may be mediated by TLR10. Moreover, *L. monocytogenes* seemed to yield TLR2 and TLR10 transcriptional effects in intestinal epithelial cells.
Disclosure of Interest: None declared

P0565 MAGNETIC RESONANCE IMAGING-QUANTIFIED SMALL BOWEL MOTILITY IS A SENSITIVE MARKER OF RESPONSE TO ANTI-TNFA THERAPY IN CROHN'S DISEASE

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Introduction: Dynamic imaging in Magnetic Resonance Enterography (MRE) is increasingly used as a non-invasive method of assessing small bowel (SB) motility. The purpose of this study was to determine if improvements in segmental SB motility can detect clinical response to anti-TNFα therapy, both after induction therapy and longer term.
Aims & Methods: ***Patient demographics:*** 46 patients underwent MRE pre- and post-treatment with anti-TNFα agents:
- 11 recruited prospectively (imaged after a median of 12 weeks of treatment, median age 40 years (range 22 to 57), 6 Male, median disease duration 4 years (range 1 to 30)) and,

- 35 identified retrospectively (median = 55 weeks of treatment, median age 23 years (range 15 to 65), 21 Male, median disease duration 16 years (range 6 to 53)).
Scanning protocol: Patients in both groups were prepared with 1-2L oral contrast (2% mannitol) depending on their tolerance. Dynamic motility scans were acquired using a 3T Siemens (prospective cohort) and across 1.5T Siemens and 3T Philips scanners (retrospective cohort). Temporal and spatial resolution across all scanners was standardized prior to analysis.
Motility Analysis: Data was processed using a validated optic-flow registration technique to provide quantitative motility maps describing the deformation from bowel wall motion. A consultant radiologist (4 years MRE experience) assessed the two MRI time points and placed a region of interest over diseased small bowel (identified on the basis of mural thickening), blinded to other imaging sequences. The study coordinator (4 years experience with MRE) performed the quantitative analysis.
Therapeutic response: Response was defined using a composite of all available clinical data for the retrospective group; and by a $\geq$3 point drop in the Harvey-Bradshaw Index for the prospective group.
Statistical analysis: The small bowel motility score took the form of a numerical arbitrary unit value. The higher the score, the greater motility with values typically occurring between 0 (no motility) and 0.6 (high motility). The percentage change in motility score between the two scans was calculated and compared between responders and non-responders using the Mann-Whitney U test. Receiver-operating characteristic (ROC) curves were calculated to assess the sensitivity and specificity of motility as a predicator of therapeutic response.
Results: Anti-TNFα responders had significantly greater improvements in motility (median change = 68.6% increase from baseline) than non-responders (median change = 25% reduction, $p < 0.001$).
Improved MRI-measured motility was 89.7% (95%CI 73.6-96.4%) and 82.5% specific (95%CI 59.0-93.8%) for response to anti-TNFα treatment, in both the prospective (Sn:85.7%; Sp:100%) and retrospective groups (Sn: 90.9%; Sp:76.9%).
The area under the ROC curve for motility changes to discriminate responders from non-responders was 87.9% (95%CI:77.2-98.6%).
Conclusion: Improved MRI-measured SB motility accurately detects response to anti-TNFα therapy for CD, even as early as 12 weeks. MRI may permit early identification of response/non-response to anti-TNFα agents, allowing personalized treatment regimes.
Disclosure of Interest: A. Menys Shareholder: Motilent Ltd, Directorship(s): Motilent Ltd, A. Plumb: None declared, E. Russo: None declared, D. Prezzi: None declared, G. Bhatnagar: None declared, R. Vega: None declared, S. Halligan: None declared, T. Orchard: None declared, S. Taylor: None declared

P0566 EPSILON GERM LINE AND REGULATORS OF IGE-DEPENDENT INFLAMMATION ARE UPREGULATED IN THE DUODENAL MUCOSA OF ATOPIC BUT NOT IN NON-CELIAC GLUTEN SENSITIVITY PATIENTS: A PRELIMINARY REPORT

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Introduction: Gluten-related disorders are activated by the ingestion of gluten-containing grains by individuals with a genetic and/or immunologic predisposition to these conditions. The best-known diseases, wheat allergy (WA) and celiac disease (CD), are mediated by the adaptive immune system. In wheat allergy, immunoglobulin E (IgE) is cross-linked by repeat sequences in gluten peptides (e.g. Ser-Gln-Gln-Gln-(Gln-)Pro-Pro-Phe), inducing the release of immune mediators such as histamine from basophils and mast cells. In contrast, CD has characteristics of an autoimmune disorder. Besides CD and WA, reactions have been reported to gluten-containing grains that involved neither allergic nor autoimmune mechanisms. These are generally termed NCGS. Given the uncertainties about this clinical entity and the lack of diagnostic biomarkers, several reports concluded that NCGS could be defined as a clinical entity induced by the ingestion of gluten-containing grains leading to intestinal and/or extra-intestinal symptoms that resolve once gluten-containing grains are eliminated from the diet, provided that CD and WA have been ruled out. One of the most controversial and highly debated discussions about NCGS concerns the role of gluten in causing NCGS and the hypothesis that some NCGS patients might also have a form of WA that is not detected with conventional serologic or skin tests.
Aims & Methods
Aim: To investigate the local IgE response in the duodenal mucosa of NCGS patients.
Methods: The intestinal mucosa from 7 healthy controls (HC), 13 active CD, 8 active NCGS, and 4 atopic patients was analyzed for the expression of genes involved in class switch recombination to IgE and IgG subclasses, such as ϵ germline transcripts (GLT) and activation-induced cytidine deaminase (AICD), and established regulators of IgE production and IgE-dependent inflammation, such as IL-4, IL-5, and IL-13, by real-time RT-PCR.
Results: The level of ϵ GLT in the mucosa of NCGS patients was significantly lower relative to atopic patients ($p = 0.009$). IL-4, IL-5, and IL-13 mRNA expression was also significantly reduced in NCGS patients ($p < 0.05$), whereas GLT expression for IgG1, IgG3, IgG4, and IgM was similar in all groups of patients. Finally, the level of the B-cell activation marker AICD was also significantly reduced in NCGS compared to the atopic mucosa ($p = 0.04$).
Conclusion: These findings support and extend the idea that the three gluten-associated disorders, CD, NCGS and WA, are different clinical and pathogenetic entities, whereby NCGS is a condition prevalently associated with wheat-induced activation of the innate, rather than adaptive, immune response.

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Disclosure of Interest: None declared

P0567 INCREASED INTESTINAL MUCOSAL PRODUCTION OF IMMUNOGLOBULIN G IN DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME

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Introduction: Enhanced mucosal humoral immunity has recently been implicated in the pathophysiology of diarrhea-prone irritable bowel syndrome (IBS-D). Intestinal barrier dysfunction is associated with mucosal immune activation, likely induced by luminal antigens, however little is known about the antibody response in the intestinal mucosa in functional bowel disorders.
Aims & Methods: We aimed at characterizing the isotype of mucosal immunoglobulins (Ig) being produced in IBS-D. Mucosal jejunal biopsies, stool and blood samples were obtained from healthy volunteers (H; n = 18) and age-matched naïve participants meeting diarrhea-IBS Rome III criteria (IBS-D; n = 20). Bowel movements, stool consistency and abdominal pain were monitored in the prior 10 days to the biopsy. The number and ultrastructure of plasma cells in the jejunal mucosa was determined by transmission electron microscopy, and mucosal IgG^+ cells were quantifed by immunofluorescence. Stool and blood samples were assayed for IgG, IgM and IgA quantification by ELISA technique.
Results: The number of plasma cells was higher in IBS-D patients (IBS-D: $1,257 \pm 966$) respect to H participants (H: 266 ± 199; $P < 0.05$). In both groups, plasma cells displayed signs of activation and Ig production such as massive amount of endoplasmic reticulum and enlarged cisternae, however the presence of plasma cell clusters was more abundant in the IBS-D group. The number of IgG^+ cells was higher in the IBS-D group (H: 240 ± 149; IBS-D: 650 ± 150 cells/mm^2; $P < 0.05$). The amount of IgG in feces was also higher in the IBS-D group (H: 165 [31-1,767]; IBS-D: 553 [76-2,291] ng/mg protein $P < 0.05$), as well as IgA concentration, the later not reaching statistical significance (H: 580 [70-3,565]; IBS-D: 1,455 [201-11,056] µg/mg protein, $P = 0.059$). Differences in mucosal Ig were not detected in systemic circulation. In IBS-D, the concentration of IgG in feces positively correlated with abdominal pain ($r^2 = 0.538$; $P < 0.05$).
Conclusion: IgG production rises as a distinctive marker of mucosal immune activity in association with abdominal pain in IBS-D. Studies aimed at determining IgG subtype and antigens eliciting such responses warrant further investigation.
Disclosure of Interest: None declared

P0568 NOD1 AND NOD2 INTERACT WITH SEROTONIN TRANSPORTER AND TOLL-LIKE RECEPTORS IN INTESTINAL EPITHELIAL CELLS. ANALYSIS IN INTESTINAL TRACT FROM MICE COLITIS MODEL

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Introduction: The intestinal epithelium presents an innate immune system and a serotoninergic system, which interact to contribute to the intestinal homeostasis. The deregulation of this interaction has been described to be involved in intestinal inflammation. Intestinal innate immune system recognizes the microbiota through host recognition receptors, such as Toll-like (TLR) and Nod-like (NOD). These receptors trigger host responses to develop either a tolerant or a defense effect. Inflammatory Bowel Diseases (IBDs) are the result of an inappropriate response to the microbiota, in part mediated by deregulation of NODs and TLRs. Additionally intestinal serotoninergic activity mediated by an increase of extracellular serotonin (5-HT) has been observed to contribute to IBDs. Serotonin transporter (SERT) modulates intestinal 5-HT availability, therefore SERT activity has been considered as an essential tool to be analyzed in intestinal inflammatory processes.
Aims & Methods: The aim of present study was to analyze whether NOD1 and NOD2 alter SERT expression and activity. Furthermore, we aimed to study a possible cross-talk between NOD1 and NOD2, TLR2 and TLR4. Finally, we have assessed NOD1, NOD2, TLR2, TLR4 and SERT expression in a mice colitis model. The human enterocyte-like cell line Caco-2/TC7 was used. Ileum and colon from C57BL6 mice wild type (WT) and Dextran Sodium Sulphate treated (DSS colitis model) were also analyzed. SERT activity was determined by

5-HT uptake measurement. SERT, NOD1, NOD2, TLR2 and TLR4 mRNA were measured by RT-qPCR. Protein expression of SERT, NOD1 and NOD2 were quantified by western blot.
Results: NOD1 and NOD2 activation decreased SERT activity and expression (mRNA and protein) in Caco-2 cells. In this context, TLR2 activation showed to increase both NOD1 and NOD2 mRNA levels, while NOD1 and NOD2 protein expression did not seem to be affected. On the contrary, TLR4 activation showed to decrease NOD1 and NOD2 mRNA and NOD1 protein level with no effect on NOD2 protein level. In relation to the analysis of NODs and TLRs mRNA in mice intestinal tract, the results have shown that in ileum of DSS mice, NOD1, NOD2, TLR2 and TLR4 did not seem to be modified compared with WT. In contrast, in colon of DSS mice, NOD2 and TLR2 mRNA resulted increased, whereas NOD1 and TLR4 mRNA did not show to be affected. Analysis of SERT expression in mice intestine has shown that mRNA and protein expression resulted decreased in both ileum and colon of DSS mice compared with WT.
Conclusion: NOD1 and NOD2 activation seems to regulate intestinal 5-HT level by acting on SERT in the intestinal epithelium. Moreover, the expression of NOD1 and NOD2 in intestinal epithelial cells may be regulated by TLR2 and TLR4 activation, which confirms a cross-interaction between several components of the innate immunity system in intestinal epithelium. Finally, both innate immune and serotoninergic system resulted altered in colitis intestinal tract, thus suggesting a synergy between both systems in intestinal inflammatory processes.
Disclosure of Interest: None declared

P0569 DECREASED PROINFLAMMATORY PROFILE AND INCREASED CORTICOTROPIN RELEASING FACTOR IN MUCOSAL EOSINOPHILS IN ASSOCIATION WITH CLINICAL MANIFESTATIONS DIARRHEA-PRONE IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is characterized by psychological stress and altered intestinal barrier function. Peripheral corticotropin-releasing factor (CRF) and neuropetides such as Substance P (SP) are involved in stress-induced gut dysfunction and CRF has been related to mucosal eosinophils. However, the role of eosinophils in IBS remains unknown.
Aims & Methods: To identify the role of mucosal eosinophils in IBS-D, and to evaluate the mechanisms underlying the stress response using an eosinophil in vitro model.
Methods: Healthy (H) subjects (n = 18) and age-matched, naïve participants fulfilling diarrhea-prone IBS (IBS-D) Rome III (n = 23) were included. Jejunal biopsies were obtained by Watson's capsule in all participants. Mucosal eosinophil ultrastructure, CRF inmunolabelling, activation and secretory activity, were evaluated by transmission electron microscopy or gene expression (microarray and quantitative RT-PCR). Psychological stress, abdominal pain, the number of bowel movements per day, and the stool form were obtained in all participants. The eosinophil cell line 15HL60 was differenciated and stimulated with SP, and secretory activity and CRF content were assessed by RT-PCR, immunofluorescence.
Results: Microarray and IPA analysis revealed eosinophil activity ($P < 0.0001$) in IBS vs H. Array validation revealed decreased eotaxin, EDN and ECP gene expression, but increased synaptosomal-associated protein SNAP-23 ($P < 0.05$) in IBS-D compared to H. CRF was identified only in cytoplasmic eosinophil granules, with increased content in IBS-D (IBS-D = 7,3 [2,99;11,4]; H = 1,9 [0,75; 4,10] particles/granule; $P < 0.01$). Notably, the amount of CRF significantly correlated with baseline level of stress ($r_s = 0.70$; $P = 0.018$), depression ($r = 0.61$; $P = 0.037$), the number of bowel movements ($r_s = 0.78$; $P = 0.007$) and the stool consistency ($r_s = 0.67$; $P = 0.027$). In vitro, eosinophils expressed NKR1 and responded to SP by relocation of SNAP-23, VAMP2 and CRH from the cytoplasm to the plasma membrane, without changes in gene expression profile of pro-inflamatory proteins.
Conclusion: CRF is stored in jejunal mucosal eosinophils and its increase correlates with clinical symptoms in IBS-D. Similarity between mucosal eosinophils and in vitro response to SP, suggests eosinophil contribution to IBS through neuroimmune mechanisms.
Disclosure of Interest: None declared

P0570 GLIADIN EFFECT ON THE OXIDATIVE BALANCE AND DNA DAMAGE IN CACO2 CELL LINE

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Introduction: Recently, gluten and gliadin have been identified as a key environmental factor in different human disorders (celiac disease, food allergies and non celiac gluten sensitivity).
They induce different biological alterations into the cell. In particular, the gluten-cell interaction increases the expression and the cellular content of transglutaminase type 2 enzyme (TG2) and altering the pro-oxidant–antioxidant balance in the intestinal mucosa, accompanied by ROS overproduction.
Aims & Methods: Evaluation of gliadin effect on oxidative/reductive balance and assessment of the possible genotoxic damage caused by free radicals
Caco2 cells were treated with gliadin (digested according to the method: S. Friis, *Gut* 1992; 33:1487-1492) at different concentrations (range 15 μg/mL-1mg/mL) for 24h. We investigated: i) cytotoxicity (MTT test); ii) oxidative stress through the evaluation of reactive oxygen species (ROS, flow cytometry with DCFDA); iii) DNA damage by means of comet test, to detect single, double strand breaks and alkali labile sites; iv) TG2 activity in different cellular compartment (colorimetric assay).
Results: After 24h of gliadin treatment we observed a decrease in cell viability of about 50% at the dose of 1mg/mL. ROS levels showed a 30% increase also using low gliadin doses (30μg/mL). A DNA damage was observed at comet assay as demonstrated by an increase of tail moment particularly visible at 1mg/mL of gliadin concentration. Following the doses indicated by ROS, the activity of TG2 was increased after gliadin treatment (30μg/mL) with a translocation from the cytoplasm to the nucleus, suggesting an apoptotic phenomenon.
Conclusion: Gliadin induces a cellular oxidative stress. Moreover, our findings demonstrate a DNA damage and a TG2 activity translocation from the cytoplasm to the nucleus.
Disclosure of Interest: None declared

P0571 THE DEPLETION OF MURINE MICROBIOTA BY BACITRACIN AND NEOMYCIN REDUCES THE INTESTINAL PERMEABILITY BY INCREASING THE LEVELS OF ZO-1, JAM-A AND OCCLUDIN

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Introduction: Oral bacitracin has been used for the treatment of *Clostridium difficile*-associated diarrhoea and colitis. Oral neomycin is indicated for suppression of intestinal microbiota in patients undergoing colorectal surgery. Antibiotics may alter the intestinal microbiota and affect the intestinal permeability. The intestinal epithelial permeability is regulated by the tight junctions (TJs) proteins. The TJs complex consists of transmembrane (occludin, junctional adhesion molecule (JAM), claudins) and intracellular scaffold (ZO-1) proteins[1].
Aims & Methods: The aim was to investigate the effects of the oral administration of bacitracin and neomycin on murine intestinal permeability and the expression of TJs proteins.
Female C57BL/10 mice of 5-7 weeks old were divided into two groups: control and treated with antibiotics. Mice were gavaged for 7 consecutive days with water (controls) or a combination of antibiotics (bacitracin 20 mg and neomycin 20 mg) per mouse and day (treated mice). This combination of antibiotics has been shown to deplete the intestinal microbiota[2]. *In vivo* paracellular permeability assay to assess barrier function was performed using an FITC-labelled dextran method. Mice were gavaged with 60 mg per 100 g body weight of FITC-dextran and at 4 h serum samples were obtained. Fluorescence intensity was measured (excitation, 485 nm; emission, 535 nm) and FITC-dextran concentrations were determined. TJs protein gene expresion (mRNA) was determined in ileum and colon by quantitative RT-PCR.
Results: Control mice showed levels of FITC-dextran of 378.45 ± 60.20 ng mL^{-1} of blood. In comparison, there was a reduction to the half in FITC-dextran levels in antibiotics treated mice (208.09 ± 25.84 ng mL^{-1}), suggesting increased barrier function in these mice. The treatment with bacitracin and neomycin increased the expression of ZO-1, JAM-A and occludin in mice ileum and colon. However, the treatment with these antibiotics reduced the levels of claudins-3, 4 and 7 in ileum, but increased the levels of claudins-3 and 4 in colon.
Conclusion: Microbiota may regulate the intestinal permeability. The oral treatment with bacitracin and neomycin enhances the barrier function by increasing the levels of the tight junction proteins ZO-1, JAM-A and occludin.

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P0572 NON-INVASIVE MONITORING OF REGIONAL TISSUE OXYGENATION IN NEWBORN USING NEAR-INFRARED SPECTROSCOPY

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Introduction: Near-infrared spectroscopy (NIRS) is a noninvasive method for monitoring in real time regional tissue oxygenation status. NIRS has the ability to continuously and simultaneously monitor tissue perfusion in various organs, without interrupting daily care. Research has demonstrated its usefulness in monitoring cerebral, intestinal and renal perfusion, in detection of potential ischemic episodes.
Aims & Methods: NIRS was used in comparation, through somatic regional oxygen saturation (rSO2S), cerebral saturation(rSO2C) and cerebro- somatic oxygenation ratio (ROCS) in a group of 30 newborns with gestational age(GA) between 24-39 weeks, birth weight 600- 3100 grams, from day 3 until day 21 of life, over a 1-5 day, period required for causal diagnosis, in which we clinically presumed a decrease in mesenteric blood flow. The group included 12 newborns with ulceronecrotic enterocolitis (NEC), 6 newborns with intrauterine growth retardation (IUGR), 6 newborns with congenital heart malformation (CHM) and 6 infants with sepsis. rSO2-S and ROCS were compared with each other to determine which of the two parameters are faithful for detecting changes in tissue perfusion. To verify statistical hypothesis which states that there are significant differences regarding rSO2S value and ROCS depending on the type of the disease were used ANOVA statistical tests, Bonferroni option and Pearson correlation
Results: In the NEC group the rSO2S average was 40.37 compared with 44.94 for CHM group, 51.86 in IUGR group and 53.08 for the sepsis group. The ROCS average achieved was 0.59 for NEC, 0.68 in CHM group, 0.97 in sepsis group and 0.73 for IUGR. No statistically significant differences were found for rSO2S ($F = 1.69$, $p = 0.18$, p?0.05) inside the group and between groups values but were significant for ROCS ($F = 2.82$, $p = 0, 04$, $p < 0.05$).
Conclusion: The study shows that continuous noninvasive monitoring with NIRS technology can show that impaired intestinal perfusion increases with decreasing GA. Decreases of the two parameters are influenced by GA (rSO2S: $p = 0.008$; ROCS: $p = 0.03$). The lowest values of intestinal perfusion are in NEC (rSO2 = 40.37, ROCS = 0.59), followed by CHM (rSO2S = 44.94, ROCS = 0.68), IUGR (rSO2S = 51.86, ROCS = 0.73) and sepsis (rSO2S = 53.08, ROSC = 0.97). rSO2S value is less statistically significant ($F = 2.82$, $p = 0.18$) compared with ROCS ($F = 2\ 82$ $p = 0.04$) in patients with NEC compared to those with CHM, sepsis or IUGR.
ROCS is the most accurate parameter in determining intestinal perfusion changes and the use of NIRS remains a very good method for early detection of lower intestinal perfusion in various diseases.
Disclosure of Interest: None declared

P0573 RIFAXIMIN PREVENTS ENTERIC BACTERIA ALTERATIONS AND INFLAMMATION IN A RAT MODEL OF DICLOFENAC-INDUCED ENTEROPATHY

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Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs), besides exerting detrimental effects on the upper digestive tract, can also damage the small and large intestine. Although the underlying mechanisms remain unclear, there is evidence that enteric bacteria could play a prominent role. In particular, NSAIDs increase mucosal permeability, thus facilitating the entrance and action of bacteria, which trigger the inflammatory cascade *via* activation of Toll-like receptors (TLRs).
Aims & Methods: The present study examined the effects of rifaximin, a poorly absorbed antibiotic, on enteric bacterial load and composition as well as small bowel inflammatory responses in a rat model of diclofenac-induced enteropathy. Enteropathy was induced in male rats (40-weeks old) by intragastric diclofenac administration (4 mg/kg BID) for 14 days. Control animals received drug vehicle (0.3 ml of 1% methylcellulose). A group of rats received Rifaximin-EIR (enteric coated microgranules of rifaximin), (50 mg/kg BID), 1 hour before diclofenac ($n = 6$-7 per group). At the end of treatments, feces were collected to quantify calprotectin content by ELISA. Ileum was excised and processed for the evaluation of: 1) tissue myeloperoxidase levels (as an index of neutrophil infiltration); 2) bacterial total load and quantitative analysis of strains, *via* 16S real-time PCR; 3) expression of TLR-2/4 and activation of downstream signaling as phosphorylated nuclear factor kB subunit p65 (NF-kB p65) and myeloid-differentiation primary response-gene 88 (MyD88), by Western blot.
Results: In control animals, myeloperoxidase and calprotectin levels were 6.0 ± 1.1 ng/mg and 2.5 ± 0.2 ng/mg, respectively. These parameters were significantly increased (by 290% and 52%) in diclofenac-treated rats. Ileal specimens from control animals were found to contain a total bacterial load of $4.66 \pm 1.01 \times 10^{10}$. In particular, the Bacteroidetes phylum was $0.14 \pm 0.05 \times 10^{10}$ and the Firmicutes phylum was $0.26 \pm 0.03 \times 10^{10}$. All these bacterial loads increased after treatment with diclofenac. The expression of TLR-2/4, NF-kB p65 and MyD88 in diclofenac-treated animals was higher, as compared with control animals (+104%, +23%, +147% and +71%, respectively). In rats treated with diclofenac plus Rifaximin-EIR, myeloperoxidase and calprotectin levels were lower in comparison with diclofenac alone (-74% and -89%, respectively). In this setting, the bacterial total load decreased by 88%, with a significant reduction of Bacteroidetes and Firmicutes, while the increased expression levels of TLR-2/4, NF-kB p65 and MyD88 returned towards control values.
Conclusion: In the small bowel, treatment with diclofenac leads to quantitative and qualitative alterations of enteric bacteria that are associated with increased expression/activation of TLR-2/4 and consequent tissue inflammation. Under these conditions, Rifaximin-EIR counteracts the bacterial changes and promotes a normalization of related inflammatory responses. These peculiar pharmacological actions of rifaximin may represent the underlying mechanism(s) of its preventive activity against NSAID-induced intestinal damage, recently shown in rats[1] and humans[2] in our Institutions.

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P0574 WHEAT ALPHA-AMYLASE/TRYPSIN INHIBITORS (ATIS) EXACERBATE AUTOIMMUNE ENCEPHALOPATHY IN MICE

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Introduction: We identified wheat alpha-amylase/trypsin inhibitors (ATIs) as main activators of innate immunity by engaging the toll like receptor 4 (TLR4)-MD2-CD14 complex in cells of the mononuclear phagocyte system. ATIs play a fundamental role in the pathogenesis of celiac disease (CD) and other autoimmune diseases.
Aims & Methods: The aim of this study is to evaluate the effects of dietary ATIs on murine experimental autoimmune encephalitis (EAE), a preclinical model of human multiple sclerosis (MS). Female mice (C57BL/6) were fed with a gluten/ATI-free diet for 4 weeks and thereafter EAE was induced by injecting 50 µg of MOG 35-55 peptide emulsified in CFA and supplemented with heat-inactivated *M. tuberculosis* (day 0) in the tail base and 200 ng pertussis toxin i.p. on day 0 and 2. On day 0 the protein (casein) adjusted diet was continued as follows: 1) gluten/ATI-free; 2) 25% gluten (ATIs equivalent to the human wheat based diet); 3) 25% gluten de-enriched of ATIs; 4) purified ATIs. Mice were monitored daily for clinical signs of EAE (graded on a scale from 0 to 5) and euthanized at the peak of EAE for molecular, histological and immunohistological studies on gut, brain, spinal cord, lymph nodes and spleen. In addition, lymphoid organs were harvested for analysis of immune cell specific markers using flow cytometry.
Results: Mice on a gluten/ATI-free diet and on a diet containing 25% gluten de-enriched of ATIs had a significant lower clinical score compared to animals on a diet containing 25% gluten (and ATIs) or purified ATIs. We also observed that both intestinal and CNS-infiltrating total and encephalitogenic T cells ($CD4^+IFNg^+IL\text{-}17^+$) were significantly increased in the ATI fed groups, paralleled by significantly increased tissue and circulating levels of MCP-1, IL-8 and IL-6.
Conclusion: 1) Nutritional wheat ATIs exacerbate EAE in mice; 2) a gluten/ATI-free diet ameliorates the course of EAE; 3) gluten depleted from ATIs fails to exacerbate the development of EAE, indicating that ATIs are important nutritional activators of innate immunity in EAE.
Disclosure of Interest: None declared

P0575 THE AUGMENTED EFFECT OF REBAMIPIDE ON MUCIN PRODUCTION BY INTESTINAL GOBLET CELLS

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Introduction: The prophylaxis and treatment for acetyl salicylic acid (ASA)-induced small intestinal injury is urgently required. Recently, we found that rebamipide (Reb), a gastro muco-protective drug, protects small intestinal mucosa from ASA-induced injury in human clinical trial using a capsule endoscopy (PLoS ONE 2015). However, the precise mechanism by which Reb protects ASA-induced small intestinal injury is not clear yet. Although MUC2, a main component mucin secreted by goblet cells, has been reported to play an essential role in the protection of epithelial cells, the effect of Reb on MUC2 production has not been investigated.
Aims & Methods
Aim: In this study, we investigated whether Reb affects on mucin secretion of goblet cells.
Materials and Methods: We used LS174T cell as a goblet cell line. The concentration of Reb (1-100µM for 24hrs) we used in this study did not affect cell viability. After Reb addition to LS174T cells, samples were taken for the following analysis at 6hr and 24hr. Subsequent mucin production was assessed by PAS staining, and MUC2 expression was assessed by PCR and WB (whole cell). Since, the mucin secretion is hard to detect by WB, we used dot-blot for the detection of secreted MUC2.
Results: Reb strongly up-regulated the positivity of PAS staining in LS174T, suggesting the increased production of intracellular mucin production. To confirm this phenomenon we assessed the MUC2 expression by PCR and WB and found that Reb significantly increased MUC2 mRNA and its protein expression in whole cell lysate of LS174T. In order to assess the subsequent secretion of mucin by LS174T, we assessed MUC2 protein expression in the supernatant of

Reb conditioned LS174T using dot-blot method, and found that Reb significantly increased the secretion of MUC2 in a concentration dependent manner.
Conclusion: Taken together, the protective effect of Reb on ASA-induced mucosal injury in small intestine might depend on its ability to increase mucin secretion by small intestinal goblet cell.

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P0576 RISK OF AUTOIMMUNE DISEASES AND FREQUENCY OF SERUM ANA POSITIVITY IN NON-CELIAC WHEAT SENSITIVITY

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Introduction: Non-celiac wheat sensitivity (NCWS) has raised great interest but little is known about the risks linked to this condition. We evaluated the frequency of autoimmune diseases (AIDs) and of serum anti-nuclear antibodies (ANA) in NCWS patients.
Aims & Methods: A group of NCWS patients, composed of 131 subjects (121 F, mean age 39.1 years), belonging to a historical cohort retrospectively evaluated, was studied. These patients had been recruited at two Internal Medicine Institutes. Two groups of age- and sex-matched controls, respectively composed of celiac (CD) and irritable bowel syndrome (IBS) patients, were also chosen. A pre-structured questionnaire was used to record any co-existent AIDs. ANA titers were evaluated by immuno-fluorescence.
Results: An associated AID was observed in 29% of NCWS patients (Hashimoto's thyroiditis 29 cases, psoriasis 4 cases, type 1 diabetes 4 cases, mixed connective tissue disease 1 case, ankylosing spondylitis 1 case), in 21% of CD (not statistically significant) subjects and in 4% of IBS controls ($P < .0001$). Serum ANA were positive in 46% of NCWS (median titer 1:80), in 24% of CD ($P < .0001$) and in 2% of IBS ($P < .0001$) cases. An association between ANA positivity and the presence of the DQ2/DQ8 haplotypes and with the presence of duodenal lymphocytosis was found.
Conclusion: Our data showed a strong tendency towards autoimmunity in the NCWS patients, characterised by both associated AIDs and serum ANA positivity and raised the question of an overlap between NCWS and CD.
Disclosure of Interest: None declared

P0577 ROUTINE SMALL BOWEL BIOPSIES IS A COST EFFECTIVE STRATEGY IN THE INVESTIGATION OF IRON DEFICIENCY ANEMIA

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Introduction: Iron deficiency anemia (IDA) is a common disorder. Half of the celiac disease (CD) patients have IDA at diagnosis. There is no consensus regarding the need for routine small bowel biopsies (SBB) in IDA patients.
Aims & Methods: To compare two strategies; strategy A- routine SBB during EGD in any patient with IDA regardless celiac serology status vs. strategy B- SBB only in IDA patients with positive serology. The main outcomes were quality adjusted life years (QALY), average cost and the incremental cost effectiveness ratio (ICER).
We used a state transition Markov model. Patients were placed into 5 health states in each cycle; No CD, undiagnosed CD, potential CD, CD under normal diet, CD under gluten-free diet, death. One way sensitivity analyses was performed on all variables and two way sensitivity analyses on selected variables were done.
Results: Performing SBB regardless the serological results yielded 19.888 QALY in strategy A compared to 19.887 if performed only in patients with positive serology. Prevalence of CD in IDA patients, utility of CD and probability of identifying CD due to symptoms were the most influential parameters. The average cost of strategy A was 218.10$ vs. 234.17$ in strategy B. As long as the cost of SBB is less than 67$, performing SBB to all patients with IDA dominates the strategy of strategy B, performing SBB only in positive serology patients. These results are independent of the costs of serological test (within a range of 60-80). However, when the cost of SBB is higher than 67$, the dominant strategy depends on both the cost of SBB and the cost of the serological tests. In terms of ICER, as long as the cost of biopsy stays under 77$, conducting routine SBB in all patients with IDA is still the preferred strategy. Monte Carlo simulation demonstrated that SBB to all IDA patients yielded the same QALY but with lower costs than the strategy of selected SBB.
Conclusion: Our model suggests that EGD with routine SBB appears to be a cost-effective approach with improved QALYs in patients with IDA when the prevalence of CD is 5% or greater. SBB should be a routine screening tool for CD among patients with IDA, regardless of their celiac antibody status.
Disclosure of Interest: None declared

P0578 AND WHEN IS NOT CELIAC DISEASE?: DIAGNOSIS DILEMMA IN SERONEGATIVE VILLOUS ATROPHY

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Introduction: Celiac disease is an immune-mediated pathology in individuals with genetic susceptibility to gluten that leads to variable degrees of villous atrophy. However the villous atrophy seronegative to celiac disease (SNVA) implies a diagnosis and therapy dilemma in clinical practice.
Aims & Methods: Retrospective study of all biopsies with villous atrophy, performed between 2000 and 2015. That was conducted a research of the words 'villous/villousity atrophy' in pathology database. Of the total of 374 results, were excluded biopsies with extra-duodenal histology (126), absence of duodenal villous atrophy (97), no search/positive serology for celiac disease (79), no medical records (26) and multiple biopsies for the same patient (17). Of the remaining 29 patients with villous atrophy and negative serology for celiac disease were recorded clinical and analytical characteristics, diagnosis and therapy.
Results: Patients with SNVA had a mean age 50.1 ± 17.2years, without gender differences (15♂:14♀). Approximately 86.2% ($n = 25$) had symptoms, mainly diarrhea, weight loss and anorexia. The malabsorption syndrome occurred in 72.4% (21/29) with microcytic anemia in 71.4% (15/21). Twelve patients had other autoimmune diseases (41.4%). Endoscopic findings consistent with celiac disease were present in 62.1% ($n = 18$). The villous atrophy were mild-moderate in 75.9% (22/29) and severe in 24.1% (7/29). The villous atrophy associated with intraepithelial lymphocytosis occurred in 37.9% (11/29). Only 2 patients did HLA DQ2/8, both positive. The main identified etiologies were drug iatrogenic ($n = 6$), seronegative celiac disease and common variable immunodeficiency ($n = 5$), refractory celiac disease, duodenal Crohn's disease, Whipple's disease and unclassified sprue ($n = 2$). Therapy was made in 26 patients, with response in 69.2% (18/26), being complete in 61.1% (11/18).
Conclusion: Duodenal villous atrophy is the final common event to several aggressor agents. Excluding celiac disease, differential diagnosis must be made with multiple pathologies, in order to establish the appropriate directed therapeutic, with clinical and histologic improvement in the most cases.
Disclosure of Interest: None declared

P0579 RISK OF COMMUNITY-ACQUIRED PNEUMONIA AMONG PATIENTS WITH COELIAC DISEASE COMPARED TO THE GENERAL POPULATION: A POPULATION BASED COHORT STUDY

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Introduction: Our aim was to quantify the risk of community-acquired infective pneumonia (CAP) among patients with coeliac disease (CD), vaccinated and unvaccinated against pneumococcus, compared to the general population.
Aims & Methods: We identified all subjects with diagnosed CD within the Clinical Practice Research Datalink linked with Hospital Episodes Statistics between 1st April 1997 and 31st March 2011 and up to 10 controls per CD patient by frequency matching within 10-year age bands. We calculated rates per 1000 person-years of the first CAP among all patients with CD and controls, separately in those vaccinated and unvaccinated against pneumococcus, and in CD patients before and after their diagnosis. We used a Cox regression model to estimate the hazard ratio (HR) of pneumonia among CD patients compared to the controls.
Results: Among 9,803 CD patients and 101,755 controls, respectively there were 179 (1.82%) and 1864 (1.83%) CAP events. The overall rate of CAP in CD was 3.42 per 1000 person-years and 3.12 per 1000 person-years in controls. We found an increased risk of pneumonia among the unvaccinated CD patients compared to unvaccinated controls (HR 1.28, 95% CI 1.02-1.60), but not in vaccinated CD patients compared to vaccinated controls (HR 0.88, 95% CI 0.70-1.10). The increased risk in unvaccinated CD subjects was limited to those younger than 65 years, was particularly increased around the time of diagnosis (HR 2.31, 95% CI 1.03-5.19 within 1 year after diagnosis) and was maintained for more than 5 years after diagnosis (Table).

Table. Pneumonia risk: timing from CD diagnosis (unvaccinated subjects younger than 65 years old)

Time period	N events in CD	Rate in CD per 1000	UnadjustedHR	Adjusted HRa
Before diagnosis				
+1 year	**21**	1.43	1.45 (0.93-2.24)	1.62 (1.04-2.53)
within 1 year	**13**	4.62	4.66 (2.68-8.10)	4.69 (2.69-8.18)
After diagnosis				
within 1 year	**6**	2.28	2.33 (1.04-5.21)	2.31 (1.03-5.19)
1-4 years	**19**	2.12	2.14 (1.35-3.39)	2.11 (1.39-3.35)
+ 5 years	**31**	1.59	1.60 (1.11-2.31)	1.63 (1.13-2.36)

a: adjusted for gender, calendar year; body mass index; smoking; Charlson index; socioeconomic status; Reference is controls group

Conclusion: Unvaccinated people with CD under the age of 65 have a higher risk of CAP compared to the general population around the time of diagnosis and subsequently. Pneumococcal vaccination in people with CD following diagnosis and treatment would appear to be good medical advice.
Disclosure of Interest: None declared

P0580 REVISITING DIAGNOSTIC FEATURES OF REFRACTORY CELIAC DISEASE OF TYPE I

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Introduction: A small group of celiac patients becomes refractory to a gluten-free diet (GFD). In contrast with refractory celiac disease of type II (RCDII), characterized by clonal expansion of intraepithelial lymphocytes with abnormal phenotype, RCDI can be scarcely distinguished from active celiac disease at diagnosis.
Aims & Methods
Aim: We aimed to assess RCDI for its clinical, biological, histopathological features and precise phenotype of intestinal lymphocytes at diagnosis.
Patients and Methods: 202 patients, with intestinal villous atrophy refractory to a GFD, were investigated in European Georges Pompidou Hospital between 2000 and 2013. Clinical and histopathological study allowed diagnosis of RCDI in 20 patients.
Results: In our institution, diagnosis of RCDI is performed in 10% of patients with intestinal villous atrophy refractory to a GFD. Main patients (17/20) with RCD I (15F/5M; mean age at diagnosis of celiac disease (CD): 41 years) were primary refractory to a GFD. Three patients were secondary refractory to a GFD within 25 years [14-35 years] after diagnosis of CD. At diagnosis of RCDI, persistent positive serology was found in 8 patients. One third of RCDI patients had severe malnutrition with low albuminemia and iron deficiency. Except one patient HLA-DQ8, all others were HLA-DQ2 and six patients (30%) were HLA-DQ2/DQ2. Seven patients (35%) had extra-intestinal autoimmune diseases, mainly autoimmune thyroiditis, 44% (7/16) of patients had serum auto-antibodies mainly, anti-nuclear antibodies. At diagnosis, half RCDI patients (10/20) had severe intestinal villous atrophy with increased count of IEL (CD3 + CD8+: 69 %) and thickened collagenous subepithelial layer was found in duodenal mucosa of 25% of them (5/20). Increased frequency of CD3 + CD4+ IEL (10.5%) was found in comparison with active celiac patients (4.5%; $p = 0.01$) or CD patients under GFD ($p < 0.05$). Microscopic colitis, of collagenous or lymphocytic type, was observed in 86% (6/7) of patients investigated with colonoscopy.
Conclusion: Increased intestinal CD4+ IEL count, collagenous sprue (25%) and microscopic colitis (86%) are histopathological and phenotypic features of diagnosis of RCDI. High frequency of HLA-DQ2 homozygosity (30%) and associated extra-intestinal autoimmune diseases (35%) suggest an autoimmune mechanism.
Disclosure of Interest: None declared

P0581 SMALL INTESTINE DIGITAL HISTOMORPHOMETRY FOR CELIAC DISEASE

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Introduction: Digital image analysis of small intestinal biopsies, allowing quantitative villus height crypt depth ratios measurements (VH:CrD) and CD3-positive cell counts, holds promise in celiac disease research. We validated our morphometric procedures using virtual microscopy of small intestinal biopsy sections and compared the results to those of conventional microscopy.
Aims & Methods: Standard H&E stained biopsy specimens ($n = 144$) from adult celiac disease patients and non-celiac disease controls were scanned and analyzed using a dedicated virtual microscopy platform - Celiac Slide Viewer. The specimens, which comprised different grades of mucosal injury, were evaluated morphometrically on computer screen by two accredited evaluators. Specimens with tangential cutting were included. The intra- and interobserver variations for VH:CrD and CD3+ densities (IELs/100 epithelial cells) were analyzed with the Bland-Altman method and intraclass correlation.
Results: Both observers measured 93 samples out of 144 (65 %) for VH and CrD readings. The rejected samples were evaluable neither for morphometry measurements or Marsh-Oberhuber classes because of tangential biopsy cuttings. CD3+ stained specimens were available from 107 patients. The intraobserver analysis of VH:CrD showed a mean difference of -0.019 with limits of agreement from −0.394 to 0.432; the standard deviation (SD) was 0.211. The mean difference in interobserver analysis was 0.0047, limits of agreement −0.544 to 0.554, and SD 0.280. The intraclass correlation coefficient in intraobserver variation was 0.985 and that in interobserver variation 0.970. $CD3^+$ IEL density showed a SD of 18.5% and an intraclass correlation coefficients of 0.957.
Conclusion: The results indicate that digital morphometry is a powerful tool for measuring even small injury changes of small intestinal mucosa. Virtual microscopy allows image sharing via internet, saving and tracking of measurements. A conversion table between Marsh-Oberhuber grouped classification and quantitative morphometry is shown.
Disclosure of Interest: None declared

P0582 FLOW CYTOMETRY OF INTRAEPITHELIAL LYMPHOCYTES INCREASES CELIAC DISEASE DIAGNOSTIC SENSITIVITY

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Introduction: Celiac disease diagnosis can be difficult in patients with minimal histologic changes (Marsh 0-1) or when there is disagreement between serology and histology. Celiac disease is characterized by an increase in the total number of intraepithelial lymphocytes (IELs) in the small bowel mucosa, with an increase in the subset of γ/δ T-cell receptor-bearing IELs along with a decrease in the subset of CD3-CD103+ IELs (celiac immunophenotype).
Aims & Methods: Our aim was to assess the role of the analysis of IELs by flow cytometry in the diagnosis of celiac disease, both in adults and children.
Material and Methods: 317 patients with suspicion of celiac disease (194 adults and 123 children) were included in the study. In all patients serum IgA tissue transglutaminase antibody levels were determined and six biopsy samples from the second part of duodenum were obtained during an upper gastrointestinal endoscopy. Four biopsies were fixed in 10% formalin for histologic assessment and two biopsies were placed in cold 0.9% saline solution for flow cytometric analysis of IELs. Celiac disease diagnosis was based in a positive serology and compatible changes in duodenal biopsy (Marsh 2-3). In doubtful cases, diagnosis of celiac disease was supported by a positive clinical and serological response to a gluten-free diet.
Results: 68 adults (45 female; median age: 35 years; range: 14-74 years) and 96 children (54 female; median age: 7 years; range: 0–13 years) were diagnosed of celiac disease. Histology had a 89% sensitivity and a 97% specificity for the diagnosis of celiac disease. The presence of a compatible celiac immunophenotype in the flow cytometric assessment of IELs had a 93% sensitivity and a 96% specificity. Considering the presence of either Marsh 2-3 in duodenal biopsies and/or a compatible immunophenotype as diagnostic of celiac disease, we obtained a sensitivity of 99% and a specificity of 97% (Table 1). Flow cytometry allowed us to diagnose celiac disease in 10 adults and 6 pediatric patients with mild histologic changes (Marsh 0-1).**Table 1:** Diagnostic accuracy of the combination of histology and flow cytometry of IELs in suspected celiac disease.

Marsh 2-3 and/or celiac immunophenotype	Celiac disease	No celiac disease
Positive (%)	162 (98.8%)	4 (2.6%)
Negative (%)	2 (1.2%)	149 (97.4%)
Sensitivity (95%CI)	99% (96-100%)	
Specificity (95%CI)	97% (93-99%)	
PPV (95%CI)	96% (94-99%)	
NPV (95%CI)	97% (95-100%)	

CI: confidence interval. PPV: Positive predictive value. NPV: Negative predictive value.

Conclusion: In patients with suspicion of celiac disease the combined use of histology and flow cytometry of IELs increases diagnostic sensitivity without decreasing specificity.
Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 09:00–17:00
NUTRITION I – HALL 7

P0583 THE CORRELATION BETWEEN INCREASED LEPTIN CONCENTRATIONS AND PECULIARITIES OF GASTRIC MUCOSA IN PATIENTS WITH PROLONGED USE OF NSAIDS

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Introduction: Leptin is a hormone produced primarily by adipocytes and plays important role in nutritional status and in obesity. Recently, the presence of leptin as well as the expression of its receptors was detected in rat and human stomach. It is known that the level of leptin in males with DU is increased. Data about the correlation between the leptin levels with severity of gastritis, *H. pylori* (Hp) and sex are controversial (Roper J.L. et al. 2008; Khudlur S. et al. 2011).
Aims & Methods: The aim of our study was to determine a correlation between leptin levels with sex, Hp status, BMI and histological features of gastric mucosa (GM) in patients with prolonged use of non-selective NSAIDs. We examined 94 patients who regularly during the last month used non-selective NSAIDs. Excluded from this study were those who had used proton pump inhibitors or antibiotics in the previous month, patients with prior history of gastroduodenal surgery and pregnant or lacting women. The mean-age of these patients was 63.2 ± 6.0. For all of these individuals gastroscopy with further morphological examination, laboratory examinations were performed. All patients were divided in two groups: with erosive gastropathy and without visible changes of GM. The serum leptin levels were determined in all patients using sandwich leptin solid phase ELISA (DRG-instrument GmbH-Germany). Endoscopically obtained biopsies were stained with hematoxylline and eosine. Severity of inflammation was graded according to modified Sydney classification. The presence of Hp was determined by rapid urease test/CLO test. Normal distribution of studied parameters for each sampling was checked using Shapiro-Wilka's criteria. Average value (M) error and standard deviation (SD) were calculated to discover significant changes of investigated indices. Sampling comparison was performed using the paired t-test and ANOVA. Differences among values were considered statistically significant if $p < 0.05$. Correlations were analyzed using the Pearson test.
Results: NSAIDs-gastropathy was detected in 63 patients, in 31 patients visible changes of GM were absent. As expected, leptin correlated significantly with BMI ($r^2 = 0.43$) and it was higher in women (15.59 ± 6.69) vs men (11.05 ± 6.6), $p = 0.023$. Serum leptin level was increased on 25 % in patients with erosive changes of GM ($p = 0.04$). Of the 63 subjects 17 were Hp+ and 46 were Hp-. Of 31 subjects 18 were Hp+ and 13 were Hp-. The groups were not significantly different in terms of gender, height, weight or BMI. Serum leptin levels were significantly lower in Hp+ (9.78 ± 4.83) vs Hp- (16.57 ± 6.19) patients with NSAID gastropathy ($p = 0.004$). The changes between Hp+ vs Hp- patients without visible changes of GM were not statistically valid ($p = 0.891$). Correlation between the level of leptin and the severity of gastritis was not observed in our study ($p = 0.86$).
Conclusion: Serum leptin correlates with BMI, sex and presence of erosions. Hp colonization is associated with reduced serum leptin levels, independent of BMI. An increase in serum leptin in patients with NSAIDs-gastropathy may be a defense mechanism that can be used as prognostic factor for the prediction of the erosive NSAIDs-gastropathy in patients with prolonged use of NSAIDs.
Disclosure of Interest: None declared

P0584 SOCIAL PHOBIA AND QUALITY OF LIFE IN MORBIDLY OBESE PATIENTS BEFORE AND AFTER BARIATRIC SURGERY

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Introduction: Morbidly obesity is characterized by physical and psychological comorbidities which are associated with reduced quality of life. Bariatric surgery has been linked to a reduction of psychopathology other than to a reduction of weight and improvement in physical functioning
Aims & Methods: Aim of the present study was to compare psychological features of morbidly obese patients, before and after bariatric surgery, assessing social phobia and quality of life. A total of 46 morbidly obese patients were enrolled in the study. 20 patients were waiting for bilio-pancreatic diversion (group A), while 26 patients had already undergone surgical procedure (group B). Social phobia, fear for the body-shape and quality of life were assesed using appropriate psychometric tests.
Results: The percentage of patients showing social phobia was significantly higher compared to a sample of healthy controls ($p = 0.004$), both in group A ($p = 0.003$) and in group B ($p = 0.029$). No differences in percentage of patients affected by social phobia were found between two groups. A significantly higher percentage of patients affected by distress about the body ($p < 0.0001$) was found in group A with respect to group B. A reduction of quality of life was found in both groups.
Conclusion: The present study shows a high prevalence of social phobia in a population of morbidly obese patients, both before and after surgery. A general reduction of quality of life was also observed, with a partial improvement after surgery. Future studies are needed to clarify the relationship between social phobia and quality of life in surgically-treated morbidly obese patients.
Disclosure of Interest: None declared

P0585 INCREASED EXPRESSION OF PPARΓ IN CD24 KNOCKOUT (KO) MICE AND GENDER-SPECIFIC METABOLIC CHANGES: A UNIQUE MODEL OF INSULIN-SENSITIVE OBESITY

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Introduction: Background: The heat stable *(HSA)/CD24* gene encodes a heavily-glycosylated cell surface protein. CD24 expression is high in immature precursor cells and low/absent in terminally differentiated cells. It plays an important role in the adaptive immune response and homeostasis in autoimmune diseases. CD24 is highly expressed in a large variety of human cancers. The association between cancer, diabetes, and obesity is not clear. Peroxisome proliferator-activated receptor gamma (PPARγ) is a nuclear receptor and regulator of adipogenesis that plays a role in insulin sensitivity, lipid metabolism, and adipokine expression in adipocytes.
Aims & Methods
Aim: To assess gender-dependent changes in *CD24/HSA* KO mice fed with normal and high-fat diet (HFD).
Methods: Body weight (BW), water and food consumption were closely monitored from birth in $HSA^{+/+}$ and $HSA^{-/-}$ mice for one year. The trial was repeated twice). Insulin (0.5IU/kg) sensitivity and glucose (1gr/kg) tolerance was determine thrice**.** Adipose tissue from kidney (KF), testicular (TF), and liver (LF) were isolated from KO and WT mice. High-throughput sequencing of stool 16S rRNA genes was assessed in the enteric microbial populations of the KO and WT mice, male and female, normal and HFD consumers. $N = 10$ in each group. Taxa analysis was performed on the core taxa prevalent in more than >25% of samples. Extraction of vascular fraction from adipose tissues was performed and primary cultures of adipocytes were established.
Results: Water and food consumption was similar for the KO and WT mice in normal and HFD. Mean BW of the KO was higher than that of their WT littermates, particularly in males and surprisingly with greater insulin sensitivity (10-20%) and glucose uptake (30%). It remained valid for mice fed with HFD. No such differences were observed among females. Significant differences in BW, KF, TF and LF were demonstrated between *CD24* KO and WT mice. Aadipocytes size of the KO (8258 ± 2359 uM^2) was significantly higher than that of the WT (5471 ± 2030 uM^2) mice ($P < 3.51E\text{-}09$). PPARγ expression was higher (x1.5) in *CD24* KO mice. Enteric bacterial populations were significantly different between KO and WT mice (normal diet) by unweighted ($R = 0.32$, $P < 0.01$) β-diversity analysis. These differences became much more apparent when mice were kept on HFD by weighted ($R = 0.43$, $P < 0.01$) and un-weighed β-diversity analysis ($R = 0.31$, $P < 0.01$) as well as by specific bacterial taxa.
Conclusion: 1. CD24 negatively regulate PPARγ expression in male mice. 2. The association between CD24 and insulin sensitivity, and the oncogenic potential of CD24, suggest a possible mechanism for diabetes as a cancer risk factor. 3. *CD24* KO male mice may serve as a model of male early obesity and insulin sensitivity.
Disclosure of Interest: None declared

P0586 ENDOSCOPIC REVISION WITH ARGON PLASMA COAGULATION FOR FAILED ROUX-AND-Y GASTRIC BYPASS (RYGB). FIRST LARGE SERIES

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Introduction: The weight regained has been a described growing problem in patients after bariatric surgery, especially at long term. This weight regained is multifactorial and often associated with dilation of Gastrojejunostomy (GJ), allowing a faster gastric emptying and therefore greater food intake. For the patients with significant weight regain after failed conservative approach, some revisional procedures are attempted and more recently endoscopic revisional procedures have been described.
Aims & Methods: To evaluate the safety and effectiveness of argon plasma coagulation (APC) decreasing the diameter of the gastro-enteric anastomosis in patients who have undergone Roux-and-Y Gastric Bypass (RYGB) for morbid obesity and regained weight associated to dilation of the GJ.
From jan-2014 to jan-2015 215 RYGB subjects with weight regain, a dilated anastomosis (more than 18mm in diameter) and at least 2 years from procedure were submitted APC application at GJ had their data reviewed from a prospective designed databank. Interval between an APC session applications was 60 days, with a maximum of 03 applications. APC set was at 2-3L/m with 65-75W. GJ diameter target was to reduced it up to 8-12mm estimated with premeasured open grasper. At first APC session pre-op weight and BMI, post-op weight nadir, actual weight and BMI and estimated diameter of GJ were the

Abstract number: P0589 Table 1: Average and standard deviation or median, minimum and maximum of adipokines, inflammatory and insulin resistance markers of patients who underwent liver transplantation according to metabolic syndrome

Characteristic	Adiponectin (mg/mL)	Resistin (ng/mL)	TNF-a(pg/mL)	MCP-1(pg/mL)	IL-6(pg/mL)	HOMA IR	FFA (mEq/L)
Metabolic syndrome							
Yes	6.7 ± 4.5**	5.0 ± 1.1	40.5 (16.6-170.2)	342.6 ± 251.8	10.4 (4.6-244.3)	4.9 ± 3.8**	0.8 ± 0.3*
No	3.2 ± 1.2	5.3 ± 2.3	40.0 (16.7-495.9)	260.9 ± 208.5	18.2 (2.0-305.2)	1.6 ± 0.8	0.5 ± 0.3

*$p < 0.05$; **$p < 0.01$.

variables collected. At each following session weight, BMI and estimated GJ diameter were taken. Complications during treatment were also collected. Data were analyzed with descriptive statistics, student's t test and Spearman correlation.

Results: Of the 215 patients, 82.8% were women and 17.2% were men. Average time between bariatric surgery and the first APC was 97.42 months (±41.64. Range: 25–175) and average weight regained in this interval was 20.25kg (±9,95. Range: 3-63). The mean diameter of the anastomosis was 24.81mm (±5,34. Range: 16-40) and the average number of APC sessions were 1.36 times (±0.52. Range: 1-3). The average reduction of anastomotic diameter was 13.52mm (±6,19. Range: 4-34) and the final average diameter was 11,3mm (±3,32. Range: 5-28). The average weight loss between the first and last APC was 13,77kg (±6,99. Range: -4,55-35,62) and the average decrease of BMI was 4,66kg/m^2 (±2,55. Range: -1,69-11,07). 69 patients (32,1%) did not achieve the target GJ diameter and 01 patient (0.5%) did not lose weight even with the desired GJ diameter. From the 27 subjects followed up to 6 months no regain weight was noted. Of the 215 patients APC, 35 (16.27%) required dilatation balloon due to symptomatic stenosis at least once. No further complications were reported.

Conclusion: Argon Plasma Coagulation (APC) has been shown to be an effective and safe endoscopic technique for the reduction of gastro enteric anastomosis in patients undergoing bariatric surgery who have regained weight with dilation of the anastomosis.

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Disclosure of Interest: None declared

P0587 INTRAGASTRIC BALLOON TO TREAT EXCESS WEIGHT: A LARGE BRAZILIAN EXPERIENCE

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Introduction: Endoscopic methods, especially the intragastric balloon (IGB), have been shown to be effective for the treatment of excess weight.

Aims & Methods

Objective: To assess the efficacy and complications of excess weight treatment with an IGB in patients seen at the Endogastro Med Service clinic and Sander clinic.

Methods: A total of 2727 patients were analyzed. A liquid-filled IGB with a volume of 600 to 700 ml was used. The patients had a minimum initial body mass index (BMI) of 27 kg/m2 and were followed up by a multidisciplinary team consisting of a nutritionist, a doctor and a psychologist. For statistical analysis, the patients were divided into groups according to sex and degree of excess weight (overweight and grade I, II and III obesity). Data were analyzed using descriptive statistical methods, the Student t-test, and analysis of variance followed by the Tukey post-test. The level of significance was set at $p < 0.05$.

Results: 188 patients were excluded from the analysis: 114 (4.18%) due to early IGB removal, 27 (0.99%) due to absence of weight loss or weight gain, 9 (0.33%) due to incomplete data. The incidence of contamination of the balloon liquid filling was 0.22% (n = 6) and the incidence of leakage was 0.55% (n = 15); pregnancy was 0.33% (n = 9); Wernick Korsakoff syndrome due to excessive vomiting was 0.03% (n = 1), pancreatitis, early removal due to intake non steroidal anti inflammatory drugs necessity, gastric perforation and upper digestive bleeding was 0.03% each (n = 1). 0.11% (n = 3) removed balloons were from other teams' patients. Of the 2539 remaining patients, 1908 were women and 631 were men. Mean age was 37.56 years. The patients showed a significant weight loss, with a significantly lower final BMI (mean: 28.91 ± 7,83 kg/m2; range: 18.98-58) than the initial BMI (mean: 36.23 ± 5.70 kg/m2; range: 27-74.74) ($p < 0.0001$). Mean BMI reduction was 7.38 ± 3.99 kg/m2 (range: 0.25-29.79). Mean percent weight loss was 20.09 ± 7.61% and mean percent excess weight loss (EWL) was 74.23 ± 36.71% (range 3.99-336.14). The treatment success rate (%EWL > 25) was 94,7%. Percent EWL was higher in the overweight group (147%EWL), followed by obesities grades I (82.91%), II (62.12%) and III (51.44%) sequentially ($p < 0.0001$). Percent EWL was also higher in women (76.31%EWL) than in men (68.08%EWL) ($p < 0.0001$).

Conclusion: Endoscopic treatment of excess weight with an IGB has been established as an excellent therapeutic option for patients of both genders with overweight or different degrees of obesity.

Disclosure of Interest: None declared

P0588 A NEW APPROACH IN THE TREATMENT OF WEIGHT REGAIN AFTER BARIATRIC SURGERY: THE ARGON PLASMA COAGULATION OF THE ANASTOMOSIS

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Introduction: The weight regain is a problem after bariatric surgery, it is multifactorial, and occurs, in part, by dilatation of the gastro-jejunal anastomosis, which causes a faster gastric emptying and increased food intake.

Aims & Methods

Objective: To evaluate the efficacy of endoscopic argon plasma coagulation (APC) of the anastomosis and of the gastric pouch aiming to reduce the diameter thereof.

Methods: We analyzed 40 patients. 35 of them underwent at least 03 sessions of APC. Two patients underwent only one session and three patients underwent only two sessions, due to an immediate reduction of the anastomosis to a diameter smaller than 12 mm after the first or the second session, which is the procedure target. The APC was held at the anastomosis and in gastric pouch. 80w power was used in the 1st session, and 70w power APC in the following, with an Argon flow of 2L/min. The time interval between sessions was eight weeks. The objective is to obtain an anastomosis with a diameter between 8-12 mm. The patient's weight had been evaluated in each APC session and six months after the latest APC session. Data were analyzed with descriptive statistics, student's t test and Spearman correlation.

Results: Of the 40 patients, 87.5 % were women (n = 35). The mean regained weight in relation to the maximum weight lost (Nadir) after bariatric surgery was 46.60 % (16.45-123.68). There was a significant reduction in body mass index (BMI) at the end of the analysis (30.78 ± 4.81 kg/m2) compared to the initial mean BMI (mean BMI = 36.34 ± 4.78 kg/m2) ($p < 0.0001$). The average loss of the regained weight was 71.44% (12.09-169.57). The average weight loss in Kg was 15.47 (4-40.5). The average diameter of the anastomosis in the beginning of the treatment was 36,18 mm (25-50mm) and at the end of the treatment 11.02 (6-12mm).

Conclusion: The APC has demonstrated great efficacy in the treatment of weight regain after bariatric surgery of gastric bypass in Roux-Y.

Disclosure of Interest: None declared

P0589 ADIPOKINES, INFLAMMATORY AND INSULIN RESISTANCE PARAMETERS: CAN THEY BE GOOD MARKERS OF METABOLIC SYNDROME AFTER LIVER TRANSPLANTATION?

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Introduction: Metabolic syndrome (MS) and obesity are widely prevalent among liver transplant (LTx) recipients. Although there is lot of data on the role of adipokines in these diseases, studies after LTx are scarce.

Aims & Methods

Aim: To investigate the concentrations of adipokines, inflammatory and insulin resistance markers among liver recipients according to MS and its components.

Methods: This was a cross-sectional study in which serum samples from 34 patients (55.9% male; average age 54.9 ± 13.9 years; average time of 7.7 ± 2.9 years after LTx) were evaluated for analysis of adiponectin, resistin, tumor necrosis factor-alpha (TNF-a), monocyte chemoattractant protein-1 (MCP-1), interleukin-6 (IL-6), C-protein reactive (CPR), HOMA-IR and free fatty acids (FFA) in 2012/2013. The dosages were uni and multivariate analyzed considering metabolic syndrome (using the Harmonizing the MS criteria) and its components.

Results: Half of the patients evaluated had MS (n = 17). Higher concentration of adiponectin was observed among liver recipients that had MS (6.7 ± 4.5 mg/mL versus 3.2 ± 1.2 mg/mL; $p < 0.01$). Low HDL and high waist: hip ratio were considered independent predictors of adiponectin concentrations. Lower amounts of resistin were observed in those patients with high blood pressure (4.5 ± 1.6 ng/mL versus 6.2 ± 2.3 ng/mL; $p < 0.01$) and higher, in those with abdominal obesity (5.5 ± 4.2 ng/mL versus 4.3 ± 1.6 ng/mL). Increased FFA

(0.8 ± 0.3 mEq/L *versus* 0.5 ± 0.3 mEq/L, $p < 0.05$) and HOMA-IR (4.9 ± 3.8 *versus* 1.6 ± 0.8) were observed in patients with MS. Independent risk factors were not identified for TNF-a, MCP-1, IL-6 and FFA.
Conclusion: MS and its components are related to increased FFA concentration and HOMA-IR. Adiponectin, resistin and inflammatory markers, such as TNF, IL-6, MCP-1 and CRP, were not good markers of metabolic syndrome in this sample of patients who underwent liver transplantation.

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Disclosure of Interest: None declared

P0590 THE IMPACT OF VEGETARIAN AND VEGAN DIET ON THE INCIDENCE OF GASTROINTESTINAL SYMPTOMS

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Introduction: More than a million of Polish citizens and about 420 millions of people worldwide use vegetarian diet.
Aims & Methods: To assess the impact of a vegetarian and vegan diet on the incidence of gastrointestinal symptoms.
Material: The study involved 1209 persons (73% from Poland and 27% from US), 702 (58%) used vegetarian diet, 365 (30%) vegan diet and 142 (12%) non-restrictive diet.
Methods: All participants replied to online questionnaire comprising 31 questions.
Results: People using exclusive diets were older than those without dietary restrictions (28.3 vs. 23.8 yrs, $p < 0.001$). American responders had higher BMI than Polish subjects (25.6 vs. 22.0 kg/m^2, $p < 0.001$), but vegetarian diet had reducing effect on body weight only in Polish population ($p < 0.001$). Participants from USA remained on vegetarian diet longer (81.5 vs. 63.4 months, $p = 0.001$) and their monthly diet-related supplementary expenses were higher (199.8 vs. 111.0 €, $p < 0.001$) than in Polish population. 57% of vegetarians and 66% of vegans introduced their diets for healthy motives. Vegetarians and vegans reported improvement (74% and 84%), deterioration (4% and 3%) or no change (22% and 13%) in prevalence of gastrointestinal symptoms ($p = 0.002$). In the respective groups the incidence of bloating and/or abdomen fullness decreased from 52% to 13% and from 60% to 12%, of heartburn, nausea and vomiting from 25 to 2% and from 32% to 4%, of constipation from 35% to 8% and from 44% to 4%, and taste alterations or anorexia from 11% in both groups to 2% and 3%, respectively. By contrast, after introduction of vegetarian or vegan diet the incidence of skin lesions increased from 2% to 16% and from 3% to 10%.
Conclusion: More than half of responders introduced vegetarian/vegan diet for healthy reasons and in the majority these diets reduced severity of gastrointestinal symptoms.
Disclosure of Interest: None declared

P0591 MOTIONS IN ICU: A PROSPECTIVE STUDY ON THE PREVALENCE OF DIARRHOEA IN A TERTIARY ICU

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Introduction: Diarrhoea is a frequently reported problem in Intensive Care Units (ICU). Little is known about diarrhoea prevalence and the role of different risk factors in ICU at Queen Elizabeth Hospital Birmingham (UHB) – a large tertiary centre with one of the largest single-floor ICUs in Europe.
Aims & Methods: To identify prevalence of diarrhoea in intensive care patients with a length of stay (LOS) greater than 24 hours receiving any type of enteral nutrition, in addition to determining its clinical impact i.e. on length of stay in ICU, timing of diarrhoea onset, and risk factors for diarrhoea focusing on its association with hypoalbuminemia.
A prosective study of 109 patients consecutively admitted into a mixed medical-surgical ITU during a 2-month period (October 2014- December 2014) were included into the study according to the following criteria:
1. Length of stay > 24 hours
2. No diagnosis or evidence of diarrhoea on admission
3. Absence of parenteral nutrition
4. No recent admission to ICU at UHB.

Diarrhoea was defined as 3 or more liquid stools per day, or that which warranted Clostridium Difficile Toxin to be sent for microbiological analysis (such patients were presumed to have had diarrhoea).
Results: A total of 109 patients were analysed. Diarrhoea was observed in 35 patients (32%). The median day of diarrhoea onset was on the ninth day, and 66% of those had diarrhoea for four days or more. The incidence of *C. Difficile* infection was 3%, this occurred in a patient who was previously known to have had *C. Difficile* infection on a previous admission. Those with diarrhoea had double the length of stay in ICU than there non-diarrhoea counterparts (44.7 vs 22.6 days), with just under a third (31%) of their stay ICU stay being with ongoing diarrhoea. Of those with diarrhoea 29% died on ICU compared to 16% of its non-diarrhoea counterparts.
If all those with acute or chronic liver disease were excluded- 100% of patients with an albumin level of less than or equal to 26 g/L had diarrhoea. Furthermore it was noted that diarrhoea occurred in all patients with an albumin level less than 30 g/L except for those with known acute or chronic liver disease, in fact one patient with chronic liver disease awaiting liver transplant had an albumin level as low as 14 without evidence of diarrhoea.
Conclusion:
Diarrhoea was common in our ICU, its prevalence (32%) being consistent with established literature. It was associated with significantly increased ICU LOS and mortality, although any single direction of causality still remains to be established. A low stool investigation yield and low prevalence of *C. difficile* suggests that other non-infective causes of diarrhoea need excluding. The results from this study conclude that there may indeed be a causal link between hypoalbuminemia and prevalence of diarrhoea in ICU, with hypoalbuminemia-related diarrhoea being significantly higher in patients with an albumin level of less than or equal to 26 g/L. It remains unexplained why those with acute or chronic liver disease are not as susceptible to diarrhoea despite low albumin levels. Further research is required to establish the prevalence and pathogenesis of diarrhoea on UK ICUs, in order to develop evidence-based management plans for reducing its incidence, and its clinical and financial impact.
Disclosure of Interest: None declared

P0592 SIGNIFICANT GASTROINTESTINAL PATHOLOGY AND THE INCIDENCE OF SUBSEQUENT ANEMIA IN YOUNG MALES PRESENTING WITH IRON DEFICIENCY WITHOUT ANEMIA

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Introduction: The etiology of iron deficiency (ID) without anemia in young males is unclear, and there are no evidence-based recommendations for the required gastrointestinal (GI) evaluation
Aims & Methods: To examine the incidence of significant GI pathology and the development of anemia during the follow-up of young males presenting with ID, but without anemia.
All young males (18-30 years) who served in the Israel Defense Forces during the years 2005-2013 and had at least a single laboratory test indicative of ID without anemia were followed until the diagnosis of significant GI pathology or discharge from military service.
Results: The study population included 2061 young males (mean age 20.7 ± 1.8 years). During follow-up of 3150 person years, significant GI pathologies were diagnosed in 39 patients: inflammatory bowel disease in 25 (1.2%), celiac disease in 8 (0.4%) and peptic disease in 4 (0.1%). No cases of gastrointestinal related cancer were diagnosed. Iron deficiency anemia developed during follow-up in 203 (9.8%). Lower baseline hemoglobin levels, lower ferritin levels and younger age at diagnosis were more common among those who developed anemia. The development of anemia was a predisposing factor for diagnosis of GI pathology (RR = 3.60, 95%CI 1.34-8.32, $p = 0.012$)
Conclusion: Significant GI pathology is very uncommon in young males presenting with ID. Overt anemia developed in close to 10% of the study cohort. Therefore, we advise simple GI evaluation (celiac serology, CRP and urease breath test) as well as follow-up in this population.
Disclosure of Interest: None declared

P0593 PREBIOTIC EFFECT OF FODMAPS IN PATIENTS WITH CROHN'S DISEASE: A RANDOMISED CONTROLLED TRIAL

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Introduction: A low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet is commonly used in patients with Crohn's disease and functional gut symptoms, however, its putative negative effects on microbiota[1] is concerning in a population at high risk of dysbiosis.
Aims & Methods: This study aimed to investigate the effects of altering FODMAP intake on markers of colonic health in patients with Crohn's disease. Nine patients with clinically quiescent Crohn's disease underwent evaluation of their habitual diet followed by randomisation to 21 days of provided diets containing low or typical amounts of FODMAPs ('Australian diet') and matched for other nutrients in a cross-over design with >21-day washout. Five-day faecal samples were collected and pooled during each diet and analysed for calprotectin, pH, short-chain fatty acids (SCFA) and bacterial abundance. Gastrointestinal symptoms were recorded daily using 0-100mm visual analogue scale.
Results: Eight participants collected faeces and were adherent to the diets. FODMAP intake differed across the 3 diets with mean daily oligosaccharide and polyol content 1.8g on low FODMAP, 4.8g on habitual (lower than previous estimations of typical intake) and 9.7g on Australian diet. Calprotectin, SCFA, pH, and total bacterial abundance remained unaltered, but the Australian diet increased relative abundance of butyrate-producing *Clostridium* cluster XIVa by 7-fold and mucus-associated *Akkermansia muciniphila* by 10-fold compared to the other diets and reduced *Ruminococcus torques* compared to the low FODMAP diet (Table). These changes were similar to a similarly studied IBS/healthy cohort[1]. Symptoms were increased by the Australian diet (mean[95%CI] 24.8 [12.6-37]mm compared to low FODMAP 13.5 [5.9-21.1]mm and habitual diet 12.5 [8.7-16.3]mm; $P < 0.001$ repeated measures ANOVA).

Table: Relative abundance of faeces. Differences between provided diets are shown in bold and between habitual diet indicated with an asterisk ($P < 0.05$; Wilcoxon matched-pairs signed rank test)

Bacteria	Australian diet	Low FODMAP	P-value	Habitual diet
Clostridium cluster IV	2.70 [0.63-4.78]	2.69 [0.93-4.46]	0.383	3.02 [0.77-5.26]
Faecalibacterium prausnitzii	0.47 [0.21-0.72]	0.66 [0.14-1.19]	0.250	0.81 [0.09-1.54]
Clostridium cluster XIVa	**19.2* [11.2-27.3]**	**2.81 [1.88-3.74]**	**0.008**	**2.90 [1.80-4.01]**
Roseburia	0.94 [0.21-1.68]	0.81 [0.18-1.44]	1.00	0.68 [0.23-1.13]
Akkermansia muciniphila	**0.15* [-0.05-0.35]**	**0.01 [-0.02-0.04]**	**0.016**	**0.01 [-0.01-0.03]**
Ruminococcus gnavus	1.17 [-0.25-2.59]	1.39 [-0.38-3.17]	0.461	2.26 [-1.51-6.03]
Ruminococcus torques	**0.10 [-0.04-0.24]**	**0.16 [-0.03-0.34]**	**0.039**	0.15 [-0.05-0.35]

Conclusion: The increase in FODMAPs on the Australian diet induced a prebiotic effect in patients with Crohn's disease, but increased symptoms. No 'anti-prebiotic' effect was seen on a low FODMAP diet compared to the habitual diet, which was lower in FODMAPs than expected. The promotion of increased FODMAPs for gut health may be at the cost of inducing functional symptoms and caution should be taken in reducing FODMAP intake below an estimated typical diet.

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Disclosure of Interest: E. Halmos: None declared, C. Christophersen: None declared, A. Bird: None declared, S. Shepherd Conflict with: Published a book on food intolerances and several cookbooks related to the topic, J. Muir: None declared, P. Gibson Conflict with: Published a book on food intolerances

P0594 CHANGES IN GASTRIC AND GALLBLADDER DYNAMICS AFTER A GLUTEN-CONTAINING VERSUS GLUTEN-FREE MEAL: AN ULTRASONOGRAPHIC STUDY

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Introduction: Gluten ingestion has been reported to be involved in a broad spectrum of gastrointestinal symptoms even in absence of a detectable immunologic response. However, data concerning the pathophysiological effects of gluten on the upper gastrointestinal tract are limited.
Aims & Methods: Aim of the study was to assess the effect of gluten ingestion on gastric emptying or gallbladder contraction and relaxation.
Between June and October 2014, 10 healthy subjects underwent ultrasound (Philips iU22, Bothell, WA, USA) evaluation of gastric emptying dynamics and gallbladder contraction at base line and at 30 minutes intervals after a standard solid meal (250 kcal, 70% carbohydrates), until the antral area returned to the basal value. The evaluation was performed in all subjects both after a gluten-containing and a gluten-free meal.
Results: Overall, the pattern of gastric emptying was similar after both types of meal, but differed in terms of postprandial filling peak, which was significantly wider (median area 5.1, range 3.7-7.9 vs 3.7, range 2-6.3 cm^2, $p = 0.006$) after the gluten-containing than the gluten-free meal. Gastric emptying time was longer after the gluten-containing meal (median 225 min, range 90-360 vs 180 min, range 60-230, $p = 0.2$) although this finding did not reach statistical significance. The pattern of gallbladder contraction was different after the gluten-free meal ($p < 0.05$), with higher gallbladder volumes observed in the late refilling phases.
Conclusion: The present data support the hypothesis of a relevant effect of gluten intake on both gastric and gallbladder motility. Although the underlying pathophysiological mechanism is still unknown, these results could account for some of the gluten related symptoms.

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Disclosure of Interest: None declared

P0595 CYSTIC FIBROSIS CHILDREN WITHOUT GASTROOESOPHAGEAL REFLUX DISEASE HAVE FUNCTIONAL IMPAIRMENT OF OESOPHAGEAL MUCOSA AS DETERMINED BY COMBINED OESOPHAGEAL IMPEDANCE-PH MONITORING

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Introduction: CF patients are prone to gastrooesophageal reflux disease (GORD). Main pathogenetic mechanism is stronger gastrooesopgaheal reflux during transient lower oesophageal sphincter relaxations due to a larger pressure difference between abdominal and thoracic cavity. It is not clear if there are additional pathogenetic mechanisms apart from gastrooesophageal reflux affecting oesophageal mucosa.
Aims & Methods: The aim of this study was to compare functional parameters measured by combined oesophageal impedance-pH (MII-pH) monitoring in CF patients without GORD with a group of non-CF children without GORD.
The study was retrospective re-analysis of stored MII-pH recordings. In the study group were included children with CF who underwent combined oesophageal impedance-pH (MII-pH) monitoring due to the signs of GORD but had a normal investigation result. As the control group we included children who underwent MII-pH due to extraintestinal symptoms of GORD but who had a normal MII-pH, too. We compared standard MII-pH parameters (No. of acid, weakly acid and non-acid refluxes, total acid exposure index, DeMeester score) and recently proposed additional parameter of epithelial integrity called baseline impedance. Groups were compared with nonparametric Mann-Whitney U test was used (small sample, not-normal data distribution).
Results: We identified 13 children with CF (1-18 y, median age 10 y, 5 males) and 17 children without oesophageal disease (1-15y, median age 8 years, 6 males) who underwent MII-pH (Ohmega measurement system, MMS, Netherlands) between 2009 and 2014 and re-analysed recordings using same analysis strategy. There were no differences between the groups regarding age ($p = 0.645$), weight ($p = 0.965$), height ($p = 0.908$), and body mass index ($p = 0.447$). According to the inclusion criteria, impedance and pH parameters were normal and equally distributed in both groups (No. of acid refluxes ($p = 0.057$), non-acid refluxes ($p = 0.085$), total acid exposure index ($p = 0.530$), DeMeester score ($p = 0.722$)), except from weakly acid refluxes ($p = 0.011$) which were more prevalent in the cystic fibrosis group. The baseline impedance between upper two (Z1; $p = 0.023$) and lower two (Z6; $p = 0.006$) electrodes were significantly lower in CF group.
Conclusion: Despite not having GORD and having the same standard MII-pH parameters except weakly acid refluxes, in the group of children with CF and without GORD we measured lower baseline impedance in Z1 and Z6. This indicates either greater importance of weakly acid refluxes than previously thought or an additional, probably local factor influencing membrane integrity which is reflected in the baseline impedance. The exact pathogenetic mechanism and the importance of this finding have yet to be determined.
Disclosure of Interest: None declared

P0596 *HELICOBACTER PYLORI* RESISTANCE TO ANTIBIOTICS IN CHILDREN

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Introduction: Increased *H. pylori* resistance to antibiotics is observed in many countries, especially in children. The amount of antibiotic consumption influences their resistance to microbes (1). Clarithromycin consumption in Lithuania from 2009 to 2014 has increased from 1,375 to 1,514 (the average daily therapeutic dosage/1000 citizens/per day).
Aims & Methods: To evaluate *H. pylori* primary resistance to antibiotics in children and to compare this data with previous results. *H. pylori* susceptibility to antibiotics were tested in children to whom *H. pylori* eradication has not been applied before. From 2013 until 2015 March at tertiary Vilnius University Children's Hospital, Lithuania upper gastrointestinal tract endoscopy with antrum biopsies were performed in children with abdominal pain, dyspepsia symptoms or anemia. Biopsies from 137 children (80 girls, 57 boys) with positive urease test were sent for *H. pylori* micriobiological investigation. Samples were grown microaerobically at 37°C on horse agar. The E-tests were performed for amoxicillin (Amo) (MIC $\geq$0.125 mg/l), clarithromycin (Cla) (MIC $\geq$0.5 mg/l), metronidazole (Met) (MIC $\geq$8 mg/l), levofloxacin (Lev) (MIC $\geq$1 mg/l).
Results: *H. pylori* grew in 82 (60.4%) of 137 microbiological samples. Resistance to at least one antibiotic was in 41 (50%) cases. Resistance to Cla in 33 (40.2%) cases, to Met - 18 (22%), to Lev 2 (2,4%). Combination of Cla and Met in 11 (13,4%) cases. No cases of Amo resistance have been detected. We compared this data with the previous study results performed in 2007-2008 in Lithuania (2). The

results revealed that resistance to Cla has increased from 16,8% to 40.2% ($p < 0.05$), to Met - from 20.7% to 22% ($p = 0.88$), resistance to both antibiotics from 4,2% to 13,4% ($p = 0.089$).
Conclusion: 1. From 2007-2008 to 2013-2015 *H. pylori* resistance to Cla has increased 2,4 times and to Met increase was statistically not significant. Resistance to Lev was observed in isolated cases.
2. The increased resistance to Cla could be associated with increased consumption of Cla in the country.

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Disclosure of Interest: None declared

P0597 PECULIARITIES OF IRON DEFICIENCY ANEMIA ASSOCIATED WITH HELICOBACTER PYLORI INFECTION IN CHILDREN

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Introduction: Iron deficiency anemia (IDA) is the most common nutritional disorder in children, but little information is available about peculiarities of course of the IDA and approaches in treatment in children with *Helicobacter pylori* (Hp) infection.
Aims & Methods: This study is aimed at assessing the role of *Helicobacter pylori* infection in children with iron deficiency anemia and effectiveness of the eradication of Hp in treatment of IDA.
For this purpose were examined 67 children with IDA aged 11-15 years, separated into 2 groups: 22 children Hp (+) (1st group) and 45 Hp (-) children (2nd group). Diagnosis of IDA was based on follow parameters: level of Hb, RBC, MCV, RDW, serum iron and ferritin level. Presence of Hp was confirmed by rapid urease test and/or gastric biopsy. As eradication therapy patients received 10 days of triple therapy (proton pump inhibitor plus amoxicillin and nifuratel in age dependent dosages).
Results: Hp was found in every third children with IDA. Initial ferritin and Hb level was lower in children with Hp infection (9.4 ± 0.1 g/dl vs 10.6 ± 0.47 g/dl, $P < 0.001$; 87.4 ± 10.56ng/ml vs 118.12 ± 16.38 ng/ml, $P < 0.001$). In this group IDA had refractory course of the disease and not respond on the basis treatment of IDA compare with children of the 2nd group. The level of Hb in 1 month after using of iron supplementation wasn't changed compare with the 2nd group (increase in Hb > 4 g%). Successful eradication was received in 81.8% children with Hp infection. In 1 month after eradication and basis therapy the mean Hb level was increased more than 4 g/% in 52.9% children, more than 2 g/% in 29.4%, the rest – less than 2 g/%.
Conclusion: *H. pylori* infection was found in 32.8 % children with IDA. In this group of children anemia characterized by refractory course of disease, lower level of Hb and ferritin compared to children without Hp infection. After successful eradication of *H. pylori* infection in children with IDA significantly increase the level of Hb.
Disclosure of Interest: None declared

P0598 MUCOSAL MORPHOMETRY AND INFLAMMATION OF DUODENAL BULB BIOPSIES IN COELIAC DISEASE

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Introduction: Recent coeliac disease guidelines recommend including duodenal bulb specimens in the diagnostic evaluation. However, previous studies exploring the value of bulb in diagnostics have shown inconsistent results. Further, clinical experience suggest that bulb might be more difficult to interpret than distal duodenum due to inferior specimens and differences in the mucosal morphology. We addressed these issues in a prospective pediatric cohort with our validated histological methods.
Aims & Methods: 133 consecutive children with positive serum transglutaminase 2 (TG2) and/or endomysial antibodies were evaluated in clinical centers in Finland and Romania. Upon gastrointestinal endoscopy 6-8 biopsies were taken from anatomic duodenal bulb and distal duodenum irrespective of the macroscopic findings. Special attention was devoted to representative biopsies and correct orientation and cutting of the paraffin-embedded specimens. Quantitative villous height: crypt depth (VH:CrD) ratio was used for the morphometric measurements (normal ratio > 2.0). Further, density of mucosal CD3+ and $\gamma\delta$+ intraepithelial lymphocytes (IEL) and presence of TG2 targeted IgA-deposits were evaluated in frozen mucosal samples.
Results: Altogether 118 (88%) out of the 115 children had diagnostic mucosal lesion in at least one biopsy site (median age 7 years, range 1.6 -17.9, 67% girls). Although several samples were taken, in 45% of the patients the bulb specimens were of inadequate quality for accurate morphometric measurements; altogether reliable evaluation was possible from both bulb and duodenum biopsies in only 75 (63%) patients. Four patients (3.4%) showed mucosal damage only in bulb specimens and 3 (2.5%) only in the distal duodenal specimens. There was no significant difference in the mean VH:CrD ratio between the bulb and duodenum (0.4 vs 0.6, $p = 0.281$) but the crypts were deeper in bulb ($p = 0.020$). Also, no differences were observed in the mean density of either CD3 + IELs (76.5 vs 70 cells/mm, $p = 0.678$) or $\gamma\delta$+ IELs (23.6 vs 23.3 cells/mm, $p = 0.339$) between the bulb and duodenum. All coeliac disease patients showed TG2 targeted mucosal IgA deposits in both bulb and distal duodenum samples.
Conclusion: We confirmed previous observations that coeliac patients may have lesions only in the duodenal bulb. However, diagnosis based solely on bulb histology should be used with caution because the samples are often more difficult to interpret and may also differ morphologically from the distal duodenum. Markers of mucosal inflammation and coeliac disease-specific IgA deposits are valuable in both biopsy sites. $p = 0.020$). Also, no differences were observed in the mean density of either CD3 + IELs (76.5 vs 70 cells/mm, $p = 0.678$) or $\gamma\delta$+ IELs (23.6 vs 23.3 cells/mm, $p = 0.339$) between the bulb and duodenum. All coeliac disease patients showed TG2 targeted mucosal IgA deposits in both bulb and distal duodenum samples.
Disclosure of Interest: None declared

P0600 HOW VALUABLE IS "10-TIME ULN THRESHOLD" FOR IDENTIFYING VILLOUS ATROPHY IN SCREENING-DETECTED PATIENTS?

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Introduction: In 2011, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) has released its updated guidelines on coeliac disease (CD) diagnosis. According to these new guidelines, symptomatic children with anti-transglutaminase (anti-tTG) antibody levels ≥ 10 times upper limit normal (ULN) coul avoid duodenal biopsies if the HLA test and serum anti-endomysial antibodies (EMA) are positive. So far, both symptomatic patients with anti-tTG2 titer < 10 times ULN and those asymptomatic should undergo upper endoscopy with "multiple" duodenal biopsies to confirm a suspected CD.
Aims & Methods: The aim of the study was to calculate the positive predictive value (PPV) of anti-tTG levels ≥ 10 ULN in discovering a severe mucosal damage in asymptomatic children, identified by salivary screening. From March 2007 to February 2014, 11698 children (age range: 5-10-years) were enrolled in Rome and Civitavecchia. A total of 8871 salivary samples were collected and tested for anti-tTG, using a fluid-phase radioimmunoassay (RIA). Salivary anti-tTG-positive children were analyzed for serum antibodies (EMA and enzyme-linked immunosorbent assay (ELISA) anti-tTG). Positive children underwent upper gastrointestinal endoscopy; histological lesions were graded according to the Marsh-Oberhuber (MO) criteria.
Results: Among the 8871 screened children, 68 (0.76%) had positive anti-tTG antibodies both in serum and salivary samples. Among them, 57 (83.82%) had anti-tTG titers ≥ 10 times ULN; of these, 56 (98.24%) showed severe lesion degree (3a, 3b, 3c MO) and 1 (1.75%) received a diagnosis of potential CD (MO1). On the contrary, 11 out of 68 (16.17%) children had anti-tTG titers < 10 times ULN; 10 (90.90%) of them had severe mucosal damage (3a,3b, 3c MO) and 1 (9.09%) was classified as potential CD patient (MO 0).These results suggest that anti-tTG ≥ 10 times ULN are remarkably reliable of severe histological damage in asymptomatic children (PPV = 98.2% CI: 90.0% > 100%)
Conclusion: If proved in larger and multi center studies, our results suggest the possibility to apply the "biopsy-sparing" protocol also in asymptomatic patients with anti-tTG titer ≥ 10 times ULN.
Disclosure of Interest: None declared

P0601 SOLUBLE SYNDECAN-1: A POTENTIAL NOVEL BIOMARKER OF SMALL BOWEL MUCOSAL DAMAGE IN CHILDREN WITH CELIAC DISEASE

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Introduction: Syndecan-1 (SDC1) is essential for maintaining normal epithelial barrier. Shedding of SDC1 ectodomain, reflected by serum soluble syndecan-1(*S*SDC1) levels, is highly regulated by inflammation. Increased intestinal

permeability plays a central role in celiac disease (CD). The association between *S*SDC1 level and mucosal damage in CD has not been evaluated.
Aims & Methods: Our objectives were to compare serum levels of *S*SDC1 in children with CD to healthy controls and to determine its relationship with histological grading classified by modified Marsh criteria.
Cross-sectional, pilot study, in which serum concentrations of *S*SDC1 were analyzed by ELISA in a cohort of 50 consecutive untreated children with CD, 11 children with latent CD and 11 healthy controls. CD was diagnosed based on positive celiac serology and classical small intestinal histology. *S*SDC1 levels at the day of biopsy were compared with the intestinal damage of the biopsy.
Results: *S*SDC1 levels were significantly higher in pediatric CD, compared to healthy controls (107.2 ± 150 vs. 44.5 ± 21.1 ng/ml, respectively, $p < 0.01$). *S*SDC1 levels were significantly higher in patients with Marsh 3c lesion compared to patients with latent celiac (153.1 ± 186.9 vs. 48.9 ± 34.6 ng/ml, respectively, $p < 0.05$). *S*SDC1 concentrations correlated significantly with mucosal injury defined by Marsh ($r = 0.28$, $p = 0.027$).
Conclusion: This is the first study demonstrating elevated levels of serum *S*SDC1 in patients with celiac disease compare to healthy controls. Our results suggest that *S*SDC1 is a potentially novel marker of intestinal mucosal damage in patients with CD. Its applicability as a diagnostic and a surrogate biomarker in CD remains to be determined.
Disclosure of Interest: None declared

P0602 DIAGNOSIS OF COELIAC DISEASE AMONG CHILDREN WHOSE MOTHERS HAVE COELIAC DISEASE: A UNITED KINGDOM GENERAL POPULATION-BASED COHORT

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Introduction: Our aim was to quantify the risk of clinically diagnosed coeliac disease (CD) in children of mothers with coeliac disease to assess this burden in the general population of the United Kingdom.
Aims & Methods: We used a large population-based general practice database (The Health Improvement Network) to obtain data pertaining to all children born between 1990 and 2010 registered with general practices whose records were linked to their mothers' medical records. We identified all mothers and children diagnosed with CD and assessed the maternal-child CD association using logistic regression with generalised estimating equation modelling, adjusting for potential confounders.
Results: There were 708 children diagnosed with CD in the study population of 798,343 children up to 16 years of age. Among children with CD, 10.3% had mothers who also had CD whereas maternal CD diagnoses were 0.3% among the children without CD. This equated to offspring CD risks of 3.2% versus 0.1% among mothers with CD versus those without. The odds ratio for offspring CD associated with maternal CD was 36.7, 95% confidence interval 28.2-47.7 after adjusting for child sex, socioeconomic deprivation, year of birth, caesarean delivery, and maternal age.
Conclusion: A child born to a woman with CD is almost 40 times more likely to be diagnosed with CD than if the mother does not have CD. In absolute terms, 3.1% more children will receive a diagnosis, considerably raised from the average population risk. This could be due to genetics, shared environmental risk factors within families or ascertainment bias.
Disclosure of Interest: None declared

P0603 GUT MICROBIOTA IN CELIAC DISEASE PATIENTS AND ITS CORRELATION WITH SYMPTOMS

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Introduction: The inflammatory response in celiac disease (CD) is mediated by mechanisms of adaptive immunity and of innate immunity. The activation of the innate immunity takes place by the binding of toll-like receptor (TLR). The inflammatory response is generated only with the initial activation of innate immunity. In CD patients an increased expression of TLR was also found. The intestinal microbiota regulates the intestinal immune system homeostasis through TLR. Recent researches have shown an altered gut microbiota in CD patients compared with healthy controls (HC). On these basis a role of gut microbiota in the pathogenesis of CD and of its symptoms has been hypothesized.
Aims & Methods: To evaluate the composition of the microbiota on duodenal biopsy of CD patients, to compare CD patient faecal microbiota with that of HC and to correlate clinical data with bacterial levels in CD patients.
Subjects were enrolled as outpatients from Pediatric Gastroenterology Unit referring suspected symptoms for CD. At enrolment a sampling of stool and, in patients with suspected CD, of a fragment of the duodenal mucosa during upper endoscopy was performed. Microbiota evaluation was performed by HTF-Microbi.Array [1-2].
Results: Thirty-two (32) subjects enrolled: 21 CD patients and 11 HC. HTF-Microbi.Array of duodenal biopsy specimen revealed a total dominance of Enterobacteriaceae in CD patient biopsies (in 50% of samples belonging to the genus Proteus) and a subdominance of Bacteroidetes and/or Streptococcus. In stools there was a significantly greater abundance of the cluster of Lactobacillaceae ($p < 0.01$) and Streptococcaceae ($p < 0.02$) and a lower abundance of Bacteroides-Prevotella cluster ($p < 0.01$), Akkermansia ($p < 0.01$) and Staphylococcaceae ($p < 0.01$) in CD patients compared to HC. Correlating clinical data with faecal bacterial abundance, an inverse correlation was found between Clostridium cluster XIVa and the presence of diarrhea ($p = 0.04$) and the presence of growth failure ($p < 0.02$). Diarrhea was directly associated with Clostridium cluster IX ($p < 0.01$), Bacillaceae ($p = 0.03$) and of Fusobacterium ($p < 0.05$). The presence of abdominal pain was associated with the abundance of Bacillaceae ($p < 0.01$) and of Enterobacteriaceae ($p = 0.01$). Furthermore, the abundance of Enterobacteriaceae was associated with IgA anti-tTG antibody levels($p < 0.05$).
Conclusion: The intestinal microbiota of CD patients is different from that of HC. In CD there is a particular abundance of potentially pathogenic species such as Enterobacteriaceae and Streptococcaceae. A depletion of Akkermansia, which has a mucosal barrier-protective function and a decrease of Bacteroides-Prevotella, which has an immunomodulatory function, has been demonstrated in CD patients. Moreover, the presence of gastrointestinal symptoms was associated with a decrease of 'healthy' species and an increase in potentially harmful species.

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Disclosure of Interest: None declared

P0604 HIGH PREVALENCE OF COELIAC DISEASE AMONG PRE-SCHOOL CHILDREN IN VAS COUNTY, HUNGARY

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Introduction: Celiac disease (CD) remains underestimated in many regions of Europe. Rapid point-of-care tests (POCT) have been previously described to enable detection of new cases at primary care or community-based screening studies.
Aims & Methods: It was our aim to evaluate the prevalence of CD in pre-school children in Vas County in SW Hungary.
1062 pre-school children (age 6-7 years, 462 girls) from 25 kindergartens in Vas County were invited to participate in CD screening using commercially available rapid finger prick test for detection of CD specific antibodies in capillary blood. 62 parents refused testing. All children tested positive and all IgA deficient children were referred for further confirmatory tests to Vas county teaching hospital. Tissue transglutaminase antibodies ELISA based serological tests and total IgA determination was performed and all children also were offered intestinal biopsy to confirm CD.
This study was a part of LQ-CELIAC project partially EU financed by the Operational Programme of Cross-border Cooperation Slovenia-Hungary.
Results: Among 1000 tested children 19 (1.9%) were detected positive with rapid test and another 9 (0.9%) were IgA deficient. Among positive children 7 (43%) had unspecific gastrointestinal symptoms. They had not been tested for CD previously. The remaining 12 positive children were asymptomatic.
CD was confirmed serologically and histological in 16 children (1.6%). Serology was negative in two positive children, and in one histology was negative. This child was HLA DQ2 positive. All three will be further followed.
Conclusion: Rapid testing for CD in young children in Vas County in Hungary has detected unexpectedly high number of affected children, with figures similar to those from a previous study in Jasz-Nagkykun-Szolnok County in Hungary. To our surprise almost half of detected children were symptomatic, and could have been detected earlier.
Rapid testing for CD has shown to be a valuable tool for community-based screening even in young children. At the same time the awareness about CD must increase in order to detect symptomatic children before the onset of preventable complications of the disease.
Disclosure of Interest: None declared

P0605 PRIMARY PREVENTION OF TYPE-1 DIABETES MELLITUS BY CHILDHOOD MASS SCREENING FOR COELIAC DISEASE

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Introduction: Coeliac disease and type-1 diabetes mellitus (T1D) are often associated but a causative relationship is not yet confirmed.
Aims & Methods: Aim of this study was a prospective intervention to investigate whether undetected coeliac disease can cause T1D diabetes mellitus. The prevalence of T1D was studied in 2014 in a county among schoolchildren (n = 21724) in five school year birth cohorts born between 1.6.1996 and 31.5.2001 using local school nurse registries and data from diabetes centres. The middle birth cohort born between 1.6.1998-31.5.1999 received screening for anti-transglutaminase and anti-endomysial antibodies in 2005, at the age of 6 years (BMJ 2007;335:1244-7), where 78% of the total population took part. Screen-detected coeliac disease cases were confirmed by small bowel biopsy, treated by a gluten-free diet and followed by regular serology monitoring at the local gastroenterology unit. The screened and not screened children used the same schools and were exposed to identical other environmental factors.
Results: None of the screen-detected & treated coeliac cases (n = 45) developed T1D. The prevalence of T1D was 2.69/1000 children (95% confidence intervals [CI] 1.92-3.46) in the not screened control birth cohorts comprising children 1&2 years older as well as 1&2 years younger than the screened cohort. The prevalence of T1D was 0.93/1000 children (95% CI 0.02-1.85) in the screened/treated cohort, odds ratio 0.35 (95% CI (0.13-0.96). Half of the T1D cases in the birth cohort where the screening took place actually did not participate in the screening due to lack of parental consent. Eighty-two percent of all paediatric T1D cases in the population appeared after the age of 6 years.
Conclusion: Early detection and treatment of coeliac disease is able to prevent a substantial fraction of paediatric-onset T1D cases.

Reference

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P0606 A NOVEL MOUSE MODEL FOR MICROVILLUS INCLUSION DISEASE IDENTIFIES A ROLE FOR MYOSIN VB IN APICAL AND BASOLATERAL RECYCLING

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Introduction: Microvillus inclusion disease (MVID) is a rare intestinal enteropathy with an onset within a few days to weeks after birth, resulting in persistent watery diarrhoea. Mutations in the myosin Vb (*MYO5B*) gene have been identified in the majority of MVID patients. However, the exact pathophysiology of MVID still remains unclear.
Aims & Methods: To address the specific role of MYO5B in the intestine we generated and analysed an intestine-specific conditional *Myo5b*-deficient deficient (*Myo5b$^{fl/fl}$;Vil-CreERT2*) mouse model. We analysed intestinal tissues and cultured organoids of *Myo5b$^{fl/fl}$;Vil-CreERT2* mice by electron microscopy (EM), immunofluorescence and immunohistochemical methods.
Results: *Myo5b$^{fl/fl}$;Vil-CreERT2* mice developed severe diarrhoea within 4 days after tamoxifen induction. Periodic Acid Schiff (PAS) and alkaline phosphatase (ALP) staining revealed subapical accumulation of intracellular vesicles in villus enterocytes. Analysis by electron microscopy (EM) showed an almost complete absence of apical microvilli and the appearance of microvillus inclusion bodies in induced *Myo5b$^{fl/fl}$;Vil-CreERT2* intestines. In addition, we showed that MYO5B is involved in not only apical, but also basolateral recycling of proteins. The analysis of the intestine during the early onset of the disease revealed that subapical accumulation of secretory granules precedes entrapment of recycling endosomes, indicating involvement of MYO5B in early differentiation of epithelial cells.
Conclusion: Our mouse model completely recapitulates the intestinal phenotype of human MVID, including severe diarrhoea, loss of microvilli, microvillus inclusions and accumulation of secretory granules. Our data indicate a novel mechanism for MYO5B in regulating polarity of epithelial cells, which might explain the secretory component of diarrhoea in MVID due to disturbed barrier function. We conclude that loss of MYO5B disturbs both apical and basolateral recycling of proteins and causes MVID.
Disclosure of Interest: None declared

P0607 SYSTEMATIC REVIEW ON FEEDING DISORDERS IN CHILDREN DIAGNOSED WITH AUTISM

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Introduction: Autism spectrum disorder (ASD) is a neurodevelopmental disorder diagnosed according to defined criteria set out in the DSM-5. Feeding disorders are a major concern of parents caring for children with ASD. Since recent evidence-based guidelines fail to address this issue we conducted a systematic review (SR) on the subject.
Aims & Methods: Medical databases (Medline Ovid and Pubmed, Psychinfo Ovid, Embase & Cochrane) were searched using Mesh terms and keywords referring to 'autism' and 'feeding disorders' with no time limits. All studies on children, with any study design, were included. We adhered to the PRISMA recommendations.
Results: Four SR and 17 primary studies reached our selection criteria. One SR confirmed the higher prevalence of eating disorders in ASD [1]. Two SRs described selective eating patterns [2, 3]. One meta-analysis was retrieved on treatment outcomes to improve feeding [4]. Additional primary studies were published from 1978 onwards. They reported on diagnosis (n = 1), feeding behaviour (n = 4), breastfeeding (n = 1), nutritional deficiencies (n = 5) and feeding programs (n = 6).
Conclusion: Despite their frequency, current guidelines fail to address feeding difficulties experienced by children with ASD. Recent SR focus on (behavioural) interventions to improve oral intake in autistic children. Studies on underlying physiological mechanisms, deglutative function, sensory or motor function of the upper gastrointestinal (GI) tract are lacking. Since autism is currently considered a neurodevelopmental disorder it may be advisable to explore GI function.

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P0608 DIETARY MODIFICATIONS OF THE MATERNAL DIET AMONG BREASTFEEDING MOTHERS

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Introduction: Fussing and colicky infants are challenging to the breastfeeding mother and multiple actions are taken in attempt to improve infant behaviour. One apparently common technique is for mothers to adjust their own habitual diet. Changes instituted have stemmed from 'old-wives tales' and popular beliefs. A major concern of dietary change is that nutritional adequacy may be compromised. The frequency and types of manipulation used and the success of such adjustments are poorly documented.
Aims & Methods: To explore the dietary practices of breastfeeding mothers, to define the frequency of dietary change, reasons for such action, and to gauge whether they are at risk of nutritional inadequacy.
An on-line survey was developed using Qualtrics software application. Survey questions were designed to collect both quantitative and qualitative data. The survey was anonymous and volunteers were invited to participate through websites and social media such as Facebook and Twitter.
Results: Of the 1203 respondents, 1,046 (87%) completed the survey. 780 (75%) modified their usual diet while breastfeeding. The most common reasons were 'baby was unsettled' (33%), 'baby had lots of wind/gas' (29%), 'baby wasn't sleeping well' (18%), 'baby had reflux' (18%) and 'baby had colic' (11%). The most common dietary modifications were minimisation of the intake of alcohol (79%), coffee (43%), cow's milk (24%), milk chocolate (21%), and cabbage, chilli and onion (each 20%). Information was sourced from the internet (46%), maternal and child health nurses (44%), the Australian Breastfeeding Association (37%), and books and mother's groups (each 21%). Sourcing information from paediatricians was less common (9%) and 89% of respondents who had modified their diet had never seen a dietitian. 25% of respondents who had removed dairy did not replace it with other calcium-rich foods nor did they take a calcium supplement. 44% that modified their diet did not take a suggested breastfeeding multi-vitamin for when the nutrition guidelines are difficult to meet.
Conclusion: Dietary modification among breastfeeding mothers is common practice (3 out of four) and a variety of food and drink sources are avoided placing them at risk of deficiencies such as calcium. This together with the fact that the majority of information is sourced from the internet and not experts in nutrition suggest this group is at risk of nutritional inadequacies in general.
Disclosure of Interest: None declared

P0609 MANIPULATING THE DIET OF BREASTFEEDING MOTHERS TO RELIEVE THE SYMPTOMS OF INFANTILE COLIC: A PROOF OF CONCEPT STUDY

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Introduction: Infantile colic is the most common complaint for which parents seek professional advice during the first months of life, and occurs in both breastfed and formula-fed infants. Mothers are often advised to avoid certain 'gas-forming' foods (e.g., onions or legumes) although the scientific evidence supporting this advice is poor. A recent placebo-controlled study of probiotics showed a mean improvement of 49 minutes over one month, in symptoms of infantile colic (cry-fuss) in both arms. Anecdotal reports of relief of infantile colic when the mother reduced dietary FODMAPs (Fermentable Oligo- Di- and Mono-saccharides And Polyols) have been received by our group. The low FODMAP diet is known to reduce bloating and abdominal pain in adults with irritable bowel syndrome. This prompted our assessment of the concept that maternal low FODMAP diet might be efficacious for infantile colic.
Aims & Methods: To perform a proof-of-concept study of the effect of a low FODMAP diet in breastfeeding mothers, on the behaviour of their infants with colic.
An open-label study of infants with colic, as defined by the Wessel Criteria, was undertaken. Mothers, who were exclusively breastfeeding, were supplied with a low FODMAP diet for seven days. Using the validated Barr diary, the behavioural patterns of infants were captured for seven days at baseline and daily during the dietary intervention. The mothers were followed for 14 days.
Results: 18 infants, aged 2-16 weeks (mean 8 weeks), were studied. The mothers were aged 29-40 y (mean 34 y), 85% of mothers with the first child. The duration of crying times reduced from mean (SD) of 142 (70) to 90 (60) min/d representing a reduction of 35% ($p = 0.0001$; paired t-test). Crying episodes reduced from 12 (5) to 8 (4) per day, a reduction of 33 % ($p = 0.0018$) and crying-fussing time combined reduced from 232 (69) to 161 (56) min/d, a reduction of 31% or 71 mins ($p = 0.0006$). In the weeks following the intervention, 16 mothers continued on a low FODMAP diet.
Conclusion: Consuming a low FODMAP diet was associated with a reduction of infantile colic that was greater than the anticipated clinical significance of >25%, as deemed by previous colic studies. Since infantile colic does spontaneously improve with time, a controlled evaluation of the low FODMAP diet in mothers is needed and mechanisms by which such an effect might occur require investigation.

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Disclosure of Interest: None declared

P0610 THE ROLE OF TNF ALFA 308 A/G GENE POLYMORPHISMS IN NUTRITIONAL DISORDERS OF CHILDREN

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Introduction: Obesity and malnutrition are diseases with increasing incidence lately, they becoming important health problems. Multiple factors proved that these two impair growth, an important role being played by inflammation, as well as by the inadequate nutritional intake. Inflammation, anorexia and weight loss are all manifestations of the circulating TNF-alfa. On the other hand, the adipocytes secrete hormones, growth factors, prostaglandins, pro-inflammatory cytokines, among which, the tumor necrosis factor (TNF) -α that has a pro-inflammatory effect.
Aims & Methods: The aim of the current study was to establish the role of TNF alfa 308 G/A gene in the determination of nutritional diseases such as obesity and malnutrition in child, and to establish the correlations between the polymorphisms of the gene TNF alfa 308 and antropometric and laboratory parameters.
Methods: We assessed 290 hospitalized children regarding TNF alfa 308 A/G polymorphisms, anthropometric parameters (mid-upper arm circumference / MUAC and tricipital skin fold thickness/TST), which we correlated with the laboratory findings (proteins). The patients were divided according to their nutritional status into three groups: control group (I) 112 children with normal nutritional status, the group of malnourished children, 100 children (II) and the group of obese children (III) 78 children.
Results: We observed that the genotype GG and GA of the TNF alfa 308 gene was more frequent in the malnourished group [($p = 0.01$, OR 1.73, 95% CI (1.28-2.36)], while the genotype GG was more frequent in the obese group ($p = 0.01$, OR 2.21, 95% CI (1.37-4.40). The G allele is also more frequent in the malnutrition group ($p = 0.02$) BMI, MUAC and TST were significantly correlated with the genotypes GG and GA of the TNF alfa 308 gene ($p = 0.001$), in malnutrition group ($p = 0.01$). The same correlation was found for the low serum albumin levels. Serum TNF alfa was correlated with the TNF alfa 308 gene polymorphism in the case of the malnourished children group for genotypes GG ($p = 0.02$) and GA ($p = 0.001$), while serum IL 6 was correlated with TNF alfa 308 gene polymorphism in case of genotype GG ($p = 0.001$).
Conclusion: TNF alfa 308 is an important parameter of inflammation, correlated with nutritional disorders. Malnutrition is more frequently encountered in children who have the GG and GA genotype of the TNF alfa 308 gene, while GG genotype is correlated with obese group inclusively with the form of severe obesity.

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Disclosure of Interest: None declared

MONDAY, OCTOBER 26, 2015 09:00–17:00

ADVANCES IN GI SCIENCE USING OMIC TECHNOLOGIES – HALL 7

P0611 TCAB1 MUTATIONS ARE ASSOCIATED WITH AN ACCELERATED PROGRESSION OF LIVER CIRRHOSIS

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Introduction: Telomerase Cajal body protein 1 (TCAB1) is a stable component of the telomerase holoenzyme that plays a major role in telomere synthesis. TCAB1 missense mutations have recently been shown to cause dyskeratosis congenita by the disruption of telomerase trafficking. Whether TCAB1 mutations are associated with liver cirrhosis formation is currently unknown and the hypothesis of the present study.
Aims & Methods: The TCAB1 gene was sequenced in 144 individuals (48 patients with hepatitis C-induced cirrhosis, 48 patients with alcohol-induced cirrhosis and 48 non-cirrhotic controls). In total, 3.744 DNA sequences were analysed and compared to the wildtype TCAB1 form in order to determine the incidence of mutations. Patients with nucleotide variants within the TCAB 1 gene were screened for demographic and clinical characteristics, such as progression of disease, overall survival or tumorigenesis.
Results: We detected 9 different nucleotide variants within the TCAB1 gene, including a newly identified c.663G > A p.V221V mutation in the group of hepatitis C-induced cirrhotics (allele frequency 0.010). The frequency of single nucleotide polymorphisms in African patients was significantly increased compared to Caucasian patients (p value <0.0001). Furthermore, the group of homozygote mutation carriers in the alcohol-induced cirrhosis group was found to significantly correlate with a more rapid progression of liver cirrhosis (p value 0.0139). Survival data of this group showed a significant correlation between the presence of homozygote TCAB1 nucleotide variants and liver failure (p value 0.0352).
Conclusion: Taken together, these data provide the first experimental evidence that TCAB1 gene mutations are present in a subset of liver cirrhosis patients. Furthermore, we were able to show that TCAB1 mutations lead to an accelerated cirrhosis formation in chronic liver disease and a decreased survival of affected patients with alcohol-induced liver cirrhosis. These data provide a potential starting point for the development of new therapeutic strategies for the treatment or prevention of liver cirrhosis.
Disclosure of Interest: None declared

P0612 AN EVIDENCE-BASED SOFTWARE TOOL FOR PERSONALIZED CANCER MEDICINE TO RECOMMEND THERAPEUTIC OPTIONS AND AVOID TOXICITY

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Introduction: For many tumors, therapy is sparse beyond the guidelines. More treatment relevant biomarkers are known for targeted therapy. DNA analysis with next generation sequencing (NGS) is becoming a routine. However, to analyse the vast amount of data and provide concrete, evidence-based treatment recommendations is a challenge.

Aims & Methods: To demonstrate the feasibility of personalised cancer medicine by applying NGS in a quality controlled set-up together with the newly developed evidence-based software tool TreatmentMAP (CE-marked).

Results: From Oct 2013 to April 2015, 51 patients were analysed with TreatmentMAP. In 4 cases, more than one tumor was investigated. NGS was performed (WXS = 33; panel/paired = 15, panel = 3). Sequencing could be performed in all but one patient (Whole Exome; bone metastasis). Sequencing quality was insufficient for analysis in 3 cases (paired panel), leaving 47 patients. The indication was: Pancreatic = 20; Colorectal = 10; Breast = 3; CUP = 2; NSCLC = 2; and 1 case each for Adenocarcinoma, Common Bile Duct, Endometrial, Glioblastoma, Liver, Lung, Leukemia, B-Cell Lymphoma, Mantle-Cell Lymphoma, Meningioma, Multiple Myeloma, Prostatic, Sigmoid, Uveal melanoma.

In 44/47 patients, drugable targets (response biomarkers) could be identified (range 0-8; median 3). In 28/47 patients (range 0-5; median 1) biomarkers indicated lack of efficacy (e.g. KRAS mutation in CRC). In 42/47 patients, biomarkers indicated increased toxicity (range 0-7; median 2), in 14/42 patients FDA-approved biomarkers for toxicity were detected (22 biomarkers).

Of the positive biomarkers, 32 biomarkers in 20 patients indicated drugs approved in the indication, 55 biomarkers in 29 patients indicated approved drugs, and 44 biomarkers in 28 patients indicated experimental drugs (preclinical and phase II - III). Six patients have already received drugs recommended by TreatmentMAP. In 9 patients, toxicity markers explained observed toxicity during previous treatment.

Conclusion: In 93 of the evaluable patients, at least one drugable target could be identified using this evidence-based software. In less than 50% of the patients, these were approved in the indication. In 89% of the cases, a biomarker indicating increased toxicity was detected, in 20% FDA-approved. In conclusion, application of personalised csancer medicine has to take into account that many drugs approved may not be available for the required indication.

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P0613 METHYLATION OF NEUROG1 IN SERUM CAN COMPLEMENT THE FECAL IMMUNOCHEMICAL TEST FOR COLORECTAL CANCER SCREENING IN FAMILY-RISK INDIVIDUALS

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Introduction: *NEUROG1* (Neurogenin1) is frequently found methylated in colorectal cancer (CRC) and has been included as a criteria to classify tumors as CIMP (CpG island methylator phenotype)[1-2]. Individuals with first-degree relatives with CRC are at increased risk for developing advanced neoplasia [AN; CRC and advanced adenomas (AA)][3]. Therefore, new non- invasive screening methods for this population are still necessary.

Aims & Methods: To determine the diagnostic yield of *NEUROG1* methylation for the detection of AN in asymptomatic individuals with first-degree relatives with CRC. All individuals were recruited from "Complexo Hospitalario de Ourense" and underwent a colonoscopy, a fecal immunochemical test (FIT) and a blood extraction. Methylation of *NEUROG1* in serum samples was assessed using pyrosequencing in 33 individuals with no neoplasia, 36 AA and 8 CRC cases (44 AN). The promoter region analyzed included the 12 CpG sites reported by Herbst *et al.* (2011)[4] for CRC diagnosis.

Results: Mean methylation levels for each of the 12 CpG sites analyzed were increased in individuals with AN compared to no neoplasia, though no statistically significant differences were found. The area under the curve (AUC) for discriminating AN resulted between 0.467-0.621, with the highest AUCs corresponding to CpG site 7, 8 and 9. Based on this optimal combination the AUC was 0.619 (95% CI 0.491-0.747). Given the importance of a high specificity for a screening test, a sensitivity of 27.3% was reached with a 93.9% specificity for detecting AN.

In relation to FIT (cut-off $\geq$100 ng/mL), all CRC cases were detected and 33.3% of the AA cases. Among FIT negative individuals, CpG sites 7-9 from *NEUROG1* showed an AUC of 0.620 (95% CI 0.474-0.766) for the diagnosis of AA. One-fourth (25%) of the AA not diagnosed by FIT were detected, with a 93.9% specificity (cut-off $\geq$10.6% methylation).

Conclusion: Methylation analysis of *NEUROG1* by pyrosequencing revealed that its diagnostic performance for AN may be maximized including only 3 of the 12 CpG sites (CpG sites 7-9). Based on our study, methylation of *NEUROG1* in serum seems valuable to complement FIT for the detection of AA in CRC screening.

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Disclosure of Interest: None declared

P0614 A NOVEL SAMPLING METHOD FOR ANALYSIS OF THE HUMAN GUT MICROBIOME

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Introduction: The gut microbiome is the most complex bacterial community in the human body. Alterations in the composition of intestinal microbiota are associated with various disease states including inflammatory bowel disease, obesity and colon cancer.

The majority of studies of the human gut microbiome have analysed stool samples although mucosal biopsy specimens have also been used in numerous studies. In this study, we investigated the utility of OriCol™, a novel sampling device, for profiling the human gut microbiome.

Aims & Methods: This study was undertaken to compare the microbiome profile collected in human stool, rectal swab and rectal mucosa. The purpose of the study was to examine the differences and relationships in gut microbial abundances using the different sampling techniques, and to validate the degree to which the OriCol™ sampling technique can accurately replicate trends in microbial diversity using stool samples as a microbial reference.

The OriCol™ device is a simple, convenient method for sampling the rectal mucosa without the need for prior fasting or bowel preparation. Sampling can be performed by a trained healthcare professional in less than 5 minutes. The device incorporates a nitrile membrane, which after insertion into the rectum via a standard proctoscope, is inflated to make contact with the rectal mucosa. The membrane is then deflated and retracted into the device prior to removal from the patient. Upon retraction the material sampled from the rectal mucosa is retained on the inverted membrane. The device can either be stored frozen or a suitable buffer added to preserve the material for subsequent analysis.

Samples from the rectal mucosa (obtained using the OriCol™ device) and stool were obtained from 5 healthy volunteers on three discrete occasions. A single rectal swab sample was taken from each volunteer immediately before the final OriCol™ sample. The microbial community of samples was profiled via 16S V4 sequencing.

Results: OriCol™ and stool samples have comparable diversity measures, while samples taken using a rectal swab show lower diversity. Whole microbiome abundance profiles were significantly different between OriCol™ and stool samples when grouped by subject ($p < 0.001$) or sample type ($p < 0.001$). These differences were attributable to shifts in abundance rather than the presence or absence of bacteria. Significantly higher levels of Proteobacteria were observed in OriCol™ over stool. The OriCol™ device is able to capture differences between donors, but the microbial community is different to that from stool samples.

Conclusion: The OriCol™ device offers a novel, simple and convenient method for physician-led sampling of the gut microbiome represented in the rectal mucosa. Samples using the OriCol™ device contain the same spectrum of bacteria as stool samples but there are differences in the abundance of certain groups, with mucosal organisms such as Proteobacteria relatively enriched in the OriCol™ samples. We hypothesise that this may be due to the capture of bacteria closer to the mucosa by the OriCol™ device.

Disclosure of Interest: J. Booth Directorship(s): Origin Sciences, A. Llewelyn Shareholder: Origin Sciences, C. Collins: None declared

P0615 MINIMUM CURVILINEARITY: AN INNOVATIVE NONLINEAR MULTIVARIATE ANALYSIS REVEALS PROTON-PUMP-INHIBITOR-RELATED PATTERNS IN GASTRIC METAGENOMIC DATA

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Introduction: Unsupervised discovery of patterns that segregate groups of samples in omic datasets is a pivotal task that is useful in many metagenomic case-control studies. Principal Component Analysis (PCA) and many other linear multivariate methods are the first resort, routinely used for this purpose (Dinsdale et al, 2013). However, they often lack the ability to reveal complex, nonlinear data patterns.
Aims & Methods: We introduce Minimum Curvilinear Embedding (MCE) - a machine learning for nonlinear multivariate analysis (Cannistraci et al, 2010) - in order to detect complex patterns in metagenomic data. Minimum Curvilinearity (MC), the principle behind MCE, suggests that curvilinear distances between samples (e.g. case-control individuals) can be estimated as pairwise distances over their Minimum Spanning Tree (MST), constructed according to a selected norm (Euclidean, correlation, etc.) in a high-dimensional feature space (e.g. the metagenomic space). The collection of all nonlinear pairwise distances forms a distance matrix called MC-distance matrix or MC-kernel, which can be used as an input in algorithms for dimensionality reduction, classification and generally in machine learning (Cannistraci et al, 2010). In MCE, the MC-kernel can be centred or non-centred, and its singular value decomposition is used to favour a sample projection onto a two-dimensional space for visualisation and analysis. Thus, MCE is a form of nonlinear and parameter-free kernel PCA.
Results: Does proton pump inhibitor (PPI) treatment significantly modify the gastric microbiota? In order to answer this question, we collected 24 gastric biopsy samples from subjects: 12 under PPI treatment, 4 untreated *Helicobacter pylori* positve (HP+), 4 untreated *Helicobacter pylori* negative (HP-) and 2 untreated undefined. Amplicons were sequenced on a Roche 454 plataform.
Using PCA (and other linear methods) we found that our samples do not appear to differentiate according to treatment. This could be a normal conclusion that researchers would draw by applying classical multivariate analysis on case-control metagenomic datasets, such as ours, in many labs across the world. However, we decided to test whether the presence of nonlinear relations between the samples would represent a cause for the linear multivariate approach to fail. In fact, our further analysis showed that MCE can clearly separate samples according to the different conditions and treatments in cases in which PCA fails to reveal any clear structure. We were also able to use MCE to perform reverse engineering of the discriminant bacterial 'social networks' responsible for the separation between the different conditions.
Conclusion: The juxtaposition of PCA and MCE visualisations can provide a novel standard of multivariate analysis for discovering and validating significant linear/nonlinear complementary patterns in metagenomic data and, in general, in case-control omic studies.

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P0616 CHARACTERIZATION OF VESICLE-ENCLOSED AND MEMBRANE-BOUND RNA AND DNA CONTENT IN CANCER-DERIVED EXTRACELLULAR VESICLES

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Introduction: Extracellular vesicles (EVs) have recently emerged as mediators of intercellular communication both in normal physiological and pathological processes, including cancer. They have been shown to carry mRNAs, non-coding RNAs, proteins and even gDNA fragments harbouring specific mutations, therefore EVs in biological fluids may serve as a "liquid biopsy" of cancer. Nevertheless, controversy regarding nucleic acid (NA) location has arisen two possible scenarios: the first suggests that all NAs are selectively sorted inside EVs, while the second suggests that NAs are randomly attached to the surface of EVs.
Aims & Methods: The aim of the current study was to characterize the vesicle-enclosed and surface-bound RNA and gDNA content in EVs isolated from colorectal (SW480), breast (MDA-MB231) and lung (A549) cancer cell cultures and plasma samples from cancer patients and healthy controls (n = 12). EVs were isolated using size-exclusion chromatography and characterized by electron microscopy and Western blot analysis using specific EV markers (CD9, CD81, CD63, Alix), H3 as a marker for apoptotic bodies and GM130 as a negative control. Then, EVs were treated with RNaseI or DNaseI followed by total NA extraction from the treated and non-treated samples. NA amount was measured by Qubit and 2100 Agilent Bioanalyzer and expression levels of 5S and 28S rRNAs and selected miRNAs were quantified by RT-qPCR.
Results: Treatment of EVs with RNAse showed that 30 to 60% of EV RNA content was attached to the surface of EVs obtained from various cell cultures. Further expression analysis revealed that rRNA fragments were predominantly located on the surface of EVs, while the majority of miRNAs were enclosed within the vesicles. The total amount of RNA tended to lower in plasma-derived EVs than in cell culture-derived EVs, yet the proportion of vesicle-enclosed and surface-bound RNA was 90% vs 10%. Regarding gDNA content, we found that DNA amount varies significantly among the cell lines and 20 to 40% of DNA fragments were attached to surface of cell line-derived EVs, while plasma EVs contained 50-fold lower amounts of gDNA than EVs derived from the cell lines.
Conclusion: This study showed that miRNAs are predominantly packed inside EVs derived from cancer cell lines and patients' plasma, while rRNA and gDNA fragments are found in the vesicle-enclosed and surface-bound form. Furthermore, the NA yield tends to be lower in plasma-derived EVs than those produced by cancer cell lines suggesting that either cancer cells secrete EV-associated NAs more efficiently than normal cells or the enhanced NA secretion is an *in vitro* phenomenon. (Financed by project 625/2014)
Disclosure of Interest: None declared

P0617 VIABLE CYTOGENETIC BIOMARKERS FOR ADVANCED COLORECTAL NEOPLASIA IN AVERAGE RISK PATIENTS

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Introduction: Loss of genetic stability seems to be one of the main pathogenic key processes appearing early in carcinogenesis of colorectal carcinomas (CRC). We used the Cytokinesis-Bloked Micronucleus Assay (CBMN) technique for detecting DNA damages. The aim of our study was to predict the presence of significant colorectal lesions by specific biomarkers detected by this method in average risk persons.
Aims & Methods: We designed a prospective study including patients undergoing diagnostic or opportunistic screening colonoscopy. A blood sample was obtained from each patient to to be analyzed by CBMN technique for specific biomarkers: presence of micronuclei (MN), nucleoplasmic bridges (NPB) and the Nuclear Division Index (NDI).
Results: 98 patients met the inclusion criteria, 57 of them assimilated to average-risk persons (age between 50-75 years, with no personal or familial CRC history). The mean age of our group was 55.36. The advanced neoplasia rate was 34.68% for the entire group. In the average-risk group 21.05% had advanced adenoma and 26.31% adenocarcinomas. MN frequeny and NPB presence were not significanty different in patients with neoplastic lesions compared to normal population or non-neoplastic colorectal lesions. NDI was significant lower in patients with adenoma or adenocarcinoma versus individuals with normal colonoscopy or non-neoplastic lesions, in the whole group but also in average-risk group (AUC ROC = 0.668, $p = 0.005$ and AUC ROC = 0.715, $p = 0.006$ respectively). For a cutt-off value of NDI = 1.8, the sensitivity in detecting any neoplasia was 97.7% for all patients and 97% for medium-risk patients. NDI was significantly lower in patients with advanced neoplasia compared with individuals with normal colonoscopy or with non significant colorectal lesions (AUC ROC = 0.636, $p = 0.029$ for all patients, AUC ROC = 0.672, $p = 0.029$ for average-risk group). For the same cut-off value of NDI of 1.8, the sensitivity in detecting advanced neoplasia was 97% for all patients and 96% for average-risk group. When predicting only carcinomas, an NDI value of < 1.8 will predict it with a sensitivity of 94.4% for all patients and 93.3% for average-risk group.
Conclusion: We found a significantly low Nuclear Division Index in patients with advanced colorectal neoplasia in average risk individuals. NDI score may have a certain value in colorectal cancer screening.
Disclosure of Interest: None declared

P0618 VALIDATION OF SMARTPILL WIRELESS MOTILITY CAPSULE FOR GASTROINTESTINAL TRANSIT TIME

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Introduction: Normal values for gastrointestinal transit time were quantified in healthy Swedish volunteers using SmartPill® wireless motility capsule (WMC). This ambulatory method, permits motility recordings (transit time and luminal pressure) in real time, by 5 days, without exposing to radiation, and it possible study the response to food intake, bowel movements, normal daily activity, periods of pain and discomfort. We wanted establish WMC normal values for gastric emptying, small bowel, colon and whole gut transit. Furthermore, evaluated the stability of recordings upon repeat recordings and estimated the fidelity of naked-eye inspection of transit values vs software-aided values; and finally comparison of gastric emptying and small bowel transit as measured by video capsule endoscopy (VCE) was made.
Aims & Methods: Seventy-two healthy volunteers ingested a 260 kcl meal, and SmartPill® with 100 ml of water, after which food intake ad libitum was permitted. Data obtained from the WMC was transferred to a receiver carried; values presented were regional (gastric, small bowel, colon), and total transit time, and other group of 75 subject taked the under fasting conditions.
Results: Using the SmartPill in 72 healthy subjects we obtained the following normal values displaying a Gaussian distribution (hours): Gastric emptying time (GET) 2.87-3.38, Small bowel transit time (SBTT) 4.82-5.67, colon transit time

(CTT) 18.50-23.27, and whole gut transit time (WGTT) 27.03-32.20. The variation coefficient varied between 33 to 48% indicating a certian spread of values. The maximum GET was 6.1, Max SBTT 11.2, max CTT 54.9 and max WGTT 68.1. Comparison between software and physician evaluation we obtained a correlation of r = 0.99 for WGTT. The Bland-Altman plot analysis exhibited only one single outlier in repeated measurements after 1 and 2 weeks. The comparison of SmartPill and PillCam GET and SBTT regularly showed shorter transit times with PillCam, most likely as a result of the fasting condition with PillCam as compared with SmartPill ($P < 0.05$).

Conclusion: The SmartPill WMC gave robust data of transit times for passage through different regions of the gastrointestinal tract. Our results suggest that the SmartPill technology is able to detect transit times for passage through different regions of the gastrointestinal tract. Estimates of transit are reliable with little differences from physicians "true" estimates by visual readings. Furthermore, capsule endoscopy may not substitute for WMC for estimates of transit as done under other conditions and defined by anatomical landmarks rather than functional divides in the gut. The feasibility of the recordings as well as the useful interpretation softare makes the SmartPill a strong competitor for use in the clinical setting where its use is comparable to that of the PillCam. Swift and easy trustful values of gastric emptying, small bowel transit and colon transit values can be obtained in order to verify gastroparesis, constipation and possibly also high amplitude contractions causing painful discomfort in patients with enteric dysmotility.

Disclosure of Interest: None declared

P0619 METABOLITE PROFILING IN HUMAN COLORECTAL CANCER BY GAS CHROMATOGRAPHY / MASS SPECTROMETRY (GC/MS) REVEALS BACTERIAL METABOLITES AND CHANGES IN ENERGY METABOLISM

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Introduction: Colorectal cancer (CRC) is a common malignancy worldwide. Numerous parameters including genetic alterations, lifestyle factors as well as the composition of colonic microflora are relevant in CRC development. Tumour-specific metabolic changes progressively attract interest in the perpetuation of a malignant phenotype since they provide a chance to understand the tumour's biology.

Aims & Methods: We investigated paired samples of normal colon tissue and colorectal cancer tissue of 53 CRC patients. The samples were gained during endoscopy, thus, avoiding long ischemic time usually coming along with tumour surgery. Gas chromatography / mass spectrometry (GC/MS) was performed to analyse differences in metabolic profile of normal and tumourous tissue of CRC patients.

Results: Several differences in metabolic profile of normal and malignant transformed tissue were revealed. These included changes in energy household and cell turnover in tumorous tissue like dysregulation of tricarboxylic acid (TCA) cycle, increase of glycolysis, and augmented protein formation. Furthermore, several metabolites arising in microbial metabolism were found at heightened levels in cancer tissue.

Conclusion: In conclusion, GC/MS metabonomics revealed interesting differences in the metabolic profiling of human CRC and normal colon mucosae. Especially, the significant disparity in abundance of bacterial metabolites reflecting the importance of composition of colonic microflora in the development of CRC is worth further investigation. A better understanding of tumours biology has a great potential in the development of personalized therapeutic strategies in the treatment of this common neoplasia.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00-17:00
LIVER & BILIARY II - HALL 7

P0620 H63D/H63D GENOTYPE AND H63D ALLELE PREDISPOSE PATIENTS WITH HYPERFERRITINEMIA TO DEVELOP METABOLIC SYNDROME

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Introduction: Nearly 25% of adult population in western countries have the metabolic syndrome (MS). Hyperferritinemia (HF) is frequently present in patients with this clinical entity (dysmetabolic hyperferritinemia). The presence of mutations in the HFE gene, like the H63D/H63D mutation, may induce MS in these patients.

Aims & Methods: A Prospective study of 132 consecutive patients with HF (> 200µg / L women, > 300µg / L men) was conducted from January to December 2010. The Metabolic syndrome was defined by the presence of waist circumference ≥94cm men; ≥80 cm women. And two of the following factors: Triglycerids ≥ 150 mg/dL or treatment for this dislypemia; HDL < 40 mg/dL women, < 50 mg/dL men or treatment for this dislypemia; glucose ≥ 100 mg/dL or Type 2 diabetes; hypertension: blood pressure ≥130 mm Hg/ ≥85 mm Hg. or treatment for arterial hypertension. DNA was extracted from the blood samples and *HFE* gene analysis was performed by multiplex real-time PCR using LightCycler technology (LC 1.0). Simultaneous detection of the *HFE* C282Y, H63D and S65C mutations was carried out in a single capillary using LC-Red 640, LC-Red 705 and fluorescein-labelled hybridization probes (Tibmolbiol, Berlin, Germany). Melting curve analysis was used to distinguish wild type and mutant alleles in each case. The results were compared with a control group of blood donors from the same geographical area.

Results: In 97 from 132 patients we have all the data to determine the MS presence: 44/80 men (55%) and 10/17 women (59%) presented MS. The HFE mutations from 51/54 patients with MS were: 2 C282Y/wt (3.92%); 11 H63D/H63D (21.56%); 15 H63D/wt (29.41%); 3 C282Y/H63D (5.88%); 19 wt/wt (37.25%); 1 S65C/ wt (1.96%). The genotype frequency of the H63D/H63D mutation in MS cases was significantly higher than in controls (7) - 21.56% vs 7.76% > ($p = 0.011$); the H63D allelic frecuency was 42.15% in MS group and 31% in controls ($p = 0.027$).

Conclusion: The H63D/H63D genotype and H63D allele predispose individuals with HF to MS.

Disclosure of Interest: None declared

P0621 A1166C AGTR1 AND I/D ACE GENETIC POLYMORPHISMS DETERMINE REGULATION OF CHEMOKINES AND FORMATION OF THE VICIOUS CIRCLE INVOLVING ENDOTHELIAL DYSFUNCTION OF MESENTERIC VESSELS AND INTESTINAL DYSBIOSIS IN HEPATIC STEATOSIS

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Introduction: Fatty liver disease or Hepatic Steatosis (HS) is frequently observed in patients with arterial hypertension (AH) as they both have common systemic pathogenesis realized through metabolic and immune mechanisms involving vascular and digestive system injury. Moreover, chronic vascular damage influences intestinal byocenosis causing further damage to liver. We hypothesized that the combination of vascular and metabolic changes may have detectable genetic background.

Aims & Methods: The aim is to evaluate the endothelial function and mesenteric vessels remodeling depending on I/D polymorphism of angiotensin-converting enzyme (ACE) gene and A1166C polymorphism of angiotensin II type 1 receptor (AGTR1) gene in patients with HS and AH.

Study included 104 patients with HS combined with AH (50 female, 54 male, age 53.2 ± 8.7). Intimae-media thickness (IMT) of abdominal aorta (AO) and other flow mediated parameters of mesenteric vessels status were evaluated by sonography. Nitric oxide (NO) and nitrite/nitrate plasma concentrations, vascular adhesive molecule (sVCAM-1) levels were defined by ELISA. ACE (I/D) and AGTR1 (A1166C) genes polymorphisms assessed with PCR.

Results: High risk of endothelial dysfunction is associated with D-allele of ACE gene ($p < 0.001$) and C-allele of AGTR1 gene ($p = 0.02$). Flow-mediated parameters of mesenteric vessels were higher in DD-genotype patients. IMT of abdominal aorta was higher in CC-genotype of AGTR1 gene ($p = 0.039$-0.01) and no dependence was found on I/D genotypes of ACE gene. sVCAM-1 level was significantly higher in D-allele of ACE gene ($p < 0.01$) than in II-genotype and not depending on A1166C polymorphism of AGTR1 gene. Nitric oxide plasma level does not depend on ACE (I/D) and AGTR1 (A1166C) genes polymorphisms. Vascular remodeling in HS patients (AO IMT enlargement for more than 0.9 mm) is associated with III-IV grades intestinal dysbiosis and 1.3-1.6 times growth of sVCAM-1 plasma levels ($p < 0.05$-0.001). AO IMT strongly positively correlates with dysbiosis severity ($r = 0.69$-0.83), presence of HS and sVCAM-1 level ($r = 0.64$-0.87) and is not dependent on arterial hypertension severity.

Conclusion: Risk contingents for endothelial dysfunction and mesenteric vessels remodeling in HS patients include DD-genotype carriers of ACE gene because of increased sVCAM-1 plasma levels and diameter of mesenteric vessels; and CC-genotype carriers of AGTR1 gene due to significant enlargement of Intimae-media thickness of abdominal aorta ($p \leq 0.02$-0.001).

Disclosure of Interest: None declared

P0622 NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) AS POTENTIAL RISK FACTOR OF CARDIOVASCULAR DISEASE AND ONCOLOGICAL DISEASE IN DIABETIC TYPE 2 PATIENTS

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Introduction: NAFLD is an increasingly cause of liver damage in western countries associated with obesity, hypercaloric diet and the sedentary lifestyle. The increasingly high prevalence of NAFLD and its possible damage on several organs due to its inflammatory effects (cardiovascular risk and oncological risk) will lead to a prioritary health care problem in the next future. Validated prognostic scores for NAFLD and for cardiovascular risk in diabetics patients were respectively Fatty liver index (FLI) and UK Prospective Diabetes Study (UKPDS risk engine)

Aims & Methods: The aims of our study are to assess the real correlation between FLI and UKPDS risk with cardiovascular (CE) and oncological events (OE) in a cohort of diabetic type 2 patients, in order to identify with accurancy the best predictor. 2004 patients referred to our Diabetics Center Ambulatory and in a regular follow-up were retrospectively tested. UKPDS risk and FLI were calcolated for each patient. Data such as CE, OE,

anthropometric, biochemical and metabolic features were also collected. T test for unpaired data and Pearson Chi-squared test were performed.
Results: 304/2004 pt (15%), 211 M and 93 F, were FLI >60; in this group we observed 14 (5%) OE (7 M and 7 F) and 81 (27%) CE (64 M and 17 F). 743/2004 pt (37%), 638 M and 17 F), were FLI < 20; in this other group we observed 9 (1%) OE (6 M and 3 F) and 74 (10%) CE (47 M and 27 F). The statistical analysis showed that patients with FLI > 60 have a higher risk of OE ($p = 0.0006$) or CE ($p = 0.0001$) compared to patients FLI < 20. We identified also two peculiar profiles of cardiovascular risk, in fact male gender patients with FLI > 60 presented a significant higher risk of developing CE than female ($p < 0.05$); instead female gender patients with FLI < 20 presented a significant higher risk of developing CE than male ($p < 0.001$). No statistical significance was found between FLI > 60 +UKPDS >20 and CE ($p = 0.754$). FLI > 60 and FLI < 20 patients also significantly differed respectively for mean age 62.2 vs 68.4 y ($p = 0.02$), duration of diabetes 4.9 y vs 13.24 y ($p = 0.002$) and mean glycated hemoglobin 8.7y vs 7.9 ($p = 0.009$).
Conclusion: An early and aggressive program of follow-up and treatment could be established in diabetic type 2 patients with FLI > 60 and so with reasonable suspicion of NAFLD because this population have higher risk to develop CE and OE in comparison to FLI < 20 (or FLI negative and not suspicion of NAFLD). The simultaneous UKPDS and FLI positivity doesen't improve accuracy in predicting CE.
Disclosure of Interest: None declared

P0623 HIGH BODY MASS INDEXES PRESERVE BONE MINERAL DENSITIES IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: The effect of non-alcoholic fatty liver disease (NAFLD) on bone mineral density (BMD) is poorly understood. NAFLD is more prevalent with higher body mass indexes (BMI).
Aims & Methods
Aim: We aimed to evaluate the effect of different classes of BMI on BMD in adult patients with NAFLD.
Methods: Adult patients diagnosed with NAFLD on liver imaging in 2013 were enrolled in the study. Patients with concomitant liver pathologies were excluded. Patient demographics were obtained from the medical notes and the BMI was calculated and classified using the WHO classification (underweight (<18.5), normal (18.5-24.9), overweight (25-29.9) and obese (≥30)). BMDs of the femur and lumbar spine were measured in all patients by dual energy X-ray absorptiometry. Age and gender-matched Z scores and T scores were calculated and analysed against the different BMI classes using the ANOVA model.
Results: 197 NAFLD patients were enrolled in the study (178 females, 90.3%; mean age 63.5, range 35-82; mean BMI 32.8, range 22-48.6). No underweight patients were present in the study. Obese patients had higher BMD T scores (-0.38 ± 1.12) of the whole femur than overweight patients (-0.82 ± 1.074) and normal BMI patients (-1.53 ± 0.89) (*p 0.001*). This was also true for the femoral neck (-0.97 ± 1.14, -1.41 ± 1.00, -1.77 ± 0.95, respectively, *p 0.007*) and lumbar spine (-0.71 ± 1.38, -1.06 ± 1.16, -1.80 ± 1.62, respectively, *p 0.017*). Likewise, obese patients had higher BMD Z scores of the whole femur (0.71 ± 1.09, *p 0.002*), femoral neck (0.59 ± 1.1, *p 0.005*) and lumbar spine (0.46 ± 1.36, *p 0.008*) compared to overweight patients (0.26 ± 1.15, 0.16 ± 1.03, 0.04 ± 1.15 respectively) and normal BMI patients (-0.25 ± 0.79, -0.25 ± 0.84, -0.65 ± 1.31 respectively). On subgroup analysis of obese patients, obese class 3 patients (BMI >40) had higher BMD T scores of the whole femur (*p 0.002*) and lumbar spine (*p 0.003*) but not of the femoral neck (*p 0.321*) when compared to obese class 2 (BMI 35-39.9) and obese class 1 (BMI 30-34.9) patients.
Conclusion: In NAFLD patients, obesity was associated with stronger bone mineralisation, demonstrating a linear relationship with increasing BMIs. NAFLD patients with normal BMI should undergo BMD to screen for osteopenia. Weight loss in NAFLD obese patients might have deleterious effects on bone health.
Disclosure of Interest: None declared

P0624 URSODEOXYCHOLIC ACID INFLUENCE ON EFFICACY AND SAFETY OF STATIN THERAPY IN PATIENTS WITH HIGH RISK OF CARDIOVASCULAR EVENTS AND NONALCOHOLIC FATTY LIVER DISEASE: THE RACURS STUDY (POST-HOC ANALYSIS)

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Introduction: The RAKURS study included 62% of patients with a history of nonalcoholic fatty liver disease (NAFLD).
Aims & Methods: To assess the ursodeoxycholic acid (UDCA) influence on efficacy of statin therapy in patients with high risk of cardiovascular events (CVE) and NAFLD.
Data of case report forms of 262 patients enrolled in the RAKURS study. NAFLD group – 234 subjects – is formed based on ultrasonic data (hyperechoic appearance of hepatic parenchyma) at the moment of enrollment. It was divided into two subgroups: fatty liver (159 subjects) – patients with normal level of ALT, and nonalcoholic steatohepatitis (NASH, 75 subjects) – patients with elevated level of ALT (the median is 58.9 U/l). The fatty liver subgroup included patients significantly older than in the NASH subgroup: mean age was 61.62 ± 8.19 and 57.86 ± 8.76 years, respectively ($p < 0.05$). The NASH included more men: 65% vs 42% in the fatty liver subgroup ($p < 0.05$).
Results: Statin therapy in combination with UDCA in the fatty liver subgroup was administrated to 92%, in the NASH subgroup – to 97% of patients. The subgroups did not show any difference in terms of initial total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG).
After 6 months of follow-up there was a significant ($p < 0.05$) reduction in TC to 4.1 mmol/l, LDL-C to 1.89 mmol/l and TG to 1.24 mmol/l in the fatty liver subgroup, and TC to 4.0 mmol/l, LDL-C to 1.9 mmol/l and TG to 1.3 mmol/l in the NASH subgroup. Changes of the above listed levels were similar in the subgroups. In the NASH subgroup there was a significant ($p < 0.05$) decrease in ALT to 30 U/l. The dynamics of alkaline phosphatase, gamma glutamine transferase, bilirubin and creatinphosphokinase remained within reference range during the whole period of the treatment.
Among the patients who were taken lipid-lowering therapy for the first time (47 subjects in the fatty liver subgroup and 24 subjects in the NASH subgroup), initial higher TC 6.47 mmol/l and TG 2.03 mmol/l were observed in the NASH subgroup vs TC 6.1 mmol/l and TG 1.19 mmol/l in the fatty liver subgroup. LDL-C was similar in the both subgroups: 3.9 mmol/l. At the end of the first month of statin therapy combined with UDCA in the fatty liver subgroup there was a decrease in TC to 5.1 mmol/l, LDL-C to 3.17 mmol/l, TG to 1.62 mmol/l; in the NASH subgroup there was a decrease in TC to 4.8 mmol/l, LDL-C to 2.72 mmol/l and TG to 1.62 mmol/l. The decrease of the above listed levels was more evident ($p < 0.05$) in the NASH subgroup. A significant positive dynamics of ALT decrease to 53.5 U/l was found in patients with NASH (initially 58.7 U/l).
Conclusion: 6-month statin therapy in combination with UDCA showed significant lipid-lowering effects in patients with high risk of CVE and NAFDL, as well as normalization of ALT in the NASH subgroup. Among the patients who previously had not taken statins in the NASH subgroup, higher levels of TC and TG were observed. The same subgroup showed more evident lipid-lowering effects than the fatty liver subgroup during the first month of the treatment.
Disclosure of Interest: None declared

P0625 METABOLOMIC MARKERS OF LIVER DAMAGE AND THEIR IMPLICATION IN THE ADVANCEMENT OF LIVER INJURY: FROM FATTY LIVER TO HEPATOCELLULAR CARCINOMA

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Introduction: The liver is a key organ in general metabolism and waste handling. Non alcoholic fatty liver disease (NAFLD), can progress to steatohepatitis, fibrosis and cirrhosis, and also to hepatocellular carcinoma (HCC) independently from cirrhosis. Chronic liver disease is associated with alterations in hepatic and whole body lipid metabolism caused by lipotoxicity due to elevated free fatty acid (FFA), oxidative stress and IR. Together these events play a significant role in determining the progression of liver disease.
Aims & Methods: Since circulating metabolites have been proven to be excellent markers of liver function, the aim of this work was to evaluate plasma small-molecule that could mark NAFLD and their differences in subjects with different degrees of liver damage vs. those that already developed HCC.
In 44 patients with NAFLD evaluated with biopsy, 47 patients with HCC and 21 subjects without liver disease (CT), we evaluated, by gas chromatography mass spectrometry, FFAs composition, de novo lipogenesis index (DNL = palmitic/linoleic acid), unsaturated to saturated fat ratio (PUFA/SFA), and a new index (GSG index) of liver damage calculated as glutamate/(serine+glycine). Moreover we evaluated Adipose tissue (Adipo-IR = FFA x Insulin) and peripheral (HOMA = glucose x Insulin/22.5) insulin resistance. Histology was scored according to Kleiner. APRI score (AST/platelet count), that is an index of fibrosis, was calculated in all subjects.
Results: Patients with liver disease had increased IR, especially in HCC that showed higher Adipo-IR (16.4 ± 1.7 vs 8.4 ± 0.8 vs 5.6 ± 0.9) and HOMA (8.38 ± 0.76 vs 3.21 ± 0.28 vs 2.04 ± 0.32) compared to NAFLD and CT (all $p < 0.005$). The worsening of liver disease was associated with the increase of DNL index and a decrease in PUFA/SFA ratio that was more evident in HCC than NAFLD compared to CT ($p < 0.0001$). In NAFLD, DNL index and PUFA/SFA changed proportionally to the severity of fibrosis particularly with Fibrosis score 3-4 (all $p < 0.0001$). GSG-index was increased proportionally to liver enzymes, (all $p < 0.0001$) and was higher in patients with Fibrosis score 3-4 or HCC compared to CT or no fibrosis. In all subjects, GSG, DNL and PUFA/SFA were related to Adipo-IR ($R = 0.23$; $R = 0.34$; $R = -0.38$) and HOMA ($R = 0.25$; $R = 0.43$; $R = -0.20$). Moreover, we found that the increase in APRI score in subjects with FLD and HCC was associated with adipose tissue IR and HOMA DNL index, GSG index and the PUFA/SFA ratio (all $p < 0.0001$).
Conclusion: We found several metabolomic markers of liver damage (GSG, DNL, PUFA/SFA, adipo-IR, HOMA) that mark differences in degree of liver fibrosis in NAFLD or presence of HCC, indicating metabolic dysfunction as one of the major risk factors for liver disease.
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Disclosure of Interest: None declared

P0626 PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA PRO12ALA GENE POLYMORPHISM DETERMINES PERSONALIZED THERAPY FOR FATTY LIVER DISEASE

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Introduction: Multiple studies showed that Peroxisome Proliferator Activated Receptor gamma – NR1C3 (PPARG) plays an important role in various biological processes including lipid and glucose metabolism. PPARG has been implicated in the pathology of numerous diseases including obesity, diabetes, atherosclerosis, and cancer. PPARG agonists have been used in treatment of different metabolic disorders and Nonalcoholic Steatohepatitis (NASH) norm regulating glucose metabolism, decreasing steatosis, inflammation, and fibrosis. However, existing data is confusing, challenging efficacy of therapeutic use of PPARG agonists.

Aims & Methods: The aim of the study was to clarify the perspectives for individualized therapy with thiazolidinediones depending on PPARG Pro12Ala polymorphism. 249 patients with metabolic syndrome, hypertension, and dyslipidemia participated in the study. Among them 50 (20.08%) patients with NASH were selected to form study group. PPARG agonist Pioglitazone administered 30 mg daily during 50-51 weeks. Genetic polymorphism (Pro12, Pro12Ala, Ala12Ala) of PPARG gene determined by PCR. Genotypes distributions were as follows: Pro12 Pro (n = 32, 64.0%); Pro12Ala (n = 14, 28.0%); Ala12Ala (n = 4, 8.0%). Clinical examination and liver biopsies performed prior and after study.

Results: Pioglitazone improved glycemic control and glucose tolerance ($P < 0.001$), normalized liver aminotransferase levels as it decreased AST by $42.1 \pm 1.17\%$ $P = 0.014$; ALT by $57.5 \pm 1.37\%$, $P < 0.001$; decreased hepatic fat by $54.6 \pm 2.09\%$, $P < 0.001$; and increased hepatic insulin sensitivity by $48.5 \pm 1.63\%$ $P = 0.006$. Administration of pioglitazone caused improvement in histologic findings with regard to steatosis, ballooning necrosis, and inflammation. In 4 (8%) Ala12Ala patients no reliable changes were observed, except glycemic control and glucose tolerance. Reduction in fibrosis did not change significantly. Statistically insignificant weight gain and mild lower-extremity edema developed in two subjects with Pro12Ala genotype, no other side effects were observed.

Conclusion: Administration of thiazolidinediones leads to metabolic and histologic improvement in most patients with NASH. However, individual response may be affected by Pro12Ala polymorphism of PPARG gene. This study shows that carriers of Ala genotype whilst comparatively rare among NASH patients are much less sensitive to PPARG agonists' therapy. Our data partially explain the nature of failure of several thiazolidinediones use and their risk of side effects (bladder cancer or hepatitis).

Disclosure of Interest: None declared

P0627 HEPATIC GRANULOMAS: THE EXPERIENCE OF A TERTIARY CENTRE

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Introduction: Hepatic granulomas have been reported in 2-15% of unselected liver biopsies.

Aims & Methods: The aim of our study was to evaluate the prevalence and the aetiology of granulomas in patients who underwent liver biopsy.

A retrospective review of hepatic biopsies performed in our Department between 2010 and 2015. Medical records, biochemistry tests as well as imaging and molecular studies that were relevant for the diagnosis were also reviewed.

Results: Over the study period, 1629 liver biopsies were performed. Hepatic granulomas were identified in 86 (5.3%). Of those, NASH accounted for the majority of cases (26.7%), followed by primary biliary cirrhosis (PBC) (17.4%), autoimmune hepatitis (AIH) (14%) and sarcoidosis (5.8%).

Infectious causes were less common, representing 16.5% of all cases: 4 cases of Hepatits C virus (HCV) infection, 1 case of Hepatits B virus (HBV) infection, 1 case of HBV/HCV coinfection, 1 case of Schistosomiasis, 1 case of Enterobiasis, 2 cases of Tuberculosis, 1 case of Q fever, 1 case of hepatosplenic candidiasis and 1 case of parasitic infection with no agent identified.

Two cases of drug toxicity were found, which were associated with antiretrovirals and etanercept use. Finally, 7 idiopathic cases were also reported.

Conclusion: In accordance with what has been described in previous studies, the prevalence of hepatic granulomas was 5.3%. Our study showed that NASH was the most common cause of granuloma formation, followed by PBC and AIH. Differently to what has been reported in developing countries, infectious causes represented a small fraction of hepatic granulomas in our series.

Disclosure of Interest: None declared

P0628 PREVALENCE AND ETIOLOGY OF ELEVATED AMINOTRANSFERASES IN PORTUGAL

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Introduction: Serum aminotransferases are often used in screening for liver disease. However, the prevalence and causes of elevated aminotransferases have geographic variations and there are no population-based data in Portugal.

Aims & Methods

Aims: determine the prevalence and factors associated with elevated aminotransferases in the general Portuguese population.

Methods: We conducted a nationwide, population-based cross-sectional study of adults resident in mainland Portugal. Serum biochemical liver tests (AST, ALT, GGT), serological markers for hepatitis B and C, as well as metabolic risk factors and alcohol consumption were assessed. Elevated aminotransferases (AST and/or ALT) was defined in women as ≥30 IU/L and in men ≥40 IU/L. The diagnostic criteria of NAFLD included hepatic steatosis (fatty liver index (FLI) > 60), without excessive alcohol consumption (< 20g/day).

Results: From 1688 individuals studied, 50.4% were men, mean age 50.2 ± 18.3 years and mean BMI was 27.0 ± 4.9 Kg/m^2, with 40.4% overweight and 22.8% obese. Insulin resistance (HOMA-IR > = 3), hepatic steatosis (FLI > 60) and metabolic syndrome (MS) were 27%, 14% and 19%, respectively.

Prevalence of elevated aminotransferases was 10.7% (95% CI: 10.0-11.4). The probable cause of this elevation was NAFLD in 45%, excessive alcohol consumption (> 20g/day) in 9.3%, HCV in 1.7%, HBV in 0.6% and unexplained cause in 43.4%.

Patients with elevated aminotransferases were mainly men (70%), overweight/obese (81%), with insulin resistance (47%), hepatic steatosis (42.6%) and MS (38.5 %), $p < 0.05$.

There was a significant positive correlation between aminotransferases and the following variables: FLI ($r = 0.29$), NAFLD ($r = 0.18$), BMI ($r = 0.17$), HOMA-IR ($r = 0.14$), gender ($r = 0.13$), and MS ($r = 0.12$). In multivariate analysis only FLI and BMI were independent risk factors for elevated aminotransferases. No correlation was found among aminotransferases and age, smoking and physical activity.

Conclusion: The prevalence of elevated aminotransferases was 10.7%. Fatty liver and the metabolic risk factors, namely MS and obesity, were the most frequent cause of their increase. These results emphasize the need for considering metabolic risk factors in the presence of elevated aminotransferases.

Disclosure of Interest: None declared

P0629 THE APPLICATION OF FATTY LIVER INDEX AND LIPID ACCUMULATION PRODUCT TO PREDICT METABOLIC SYNDROME IN SUBJECTS WITHOUT FATTY LIVER

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Introduction: Fatty liver has shown strong association with metabolic syndrome in previous cross-sectional studies. Fatty liver index (FLI) is an algorithm to identify fatty liver while lipid accumulation product (LAP) which represents cardiometabolic disorders is used to predict liver steatosis as well. However their predicative value of metabolic syndrome in subjects without fatty liver is still obscure.

Aims & Methods

Aims: To explore the association between LAP and FLI, and metabolic syndrome in subjects without fatty liver.

Method: We enrolled consecutive subjects who received health check-up services at the Taipei Veterans General Hospital from 2002 to 2009. Ultrasonography was applied to diagnose fatty liver. The ability of the FLI and LAP to predict metabolic syndrome was assessed by analyzing the area under the receiver operating characteristic (AUROC) curve.

Results: Among the 29,797 subjects enrolled in this study, fatty liver was diagnosed in 44.5% of the population and it had the highest association with metabolic syndrome by multivariate analysis with an odds ratio of 2.499 (95% confidence interval 2.339-2.670, $p < 0.001$). Moreover, LAP and FLI are better than other serum markers to predict metabolic syndrome (AUROC: 0.884 and 0.875, respectively). Among the 16542 subjects without fatty liver, male gender, larger body mass index, older in age, higher serum alanine aminotransferase, and higher gamma-glutamyl transferase levels were correlated with metabolic syndrome by multivariate analysis. LAP and FLI are still better than other serum markers to predict metabolic syndrome in subjects without fatty liver (AUROC: 0.871 and 0.879, respectively).

Conclusion: FLI and LAP could accurately predict metabolic syndrome among subjects without fatty liver disease in a large-scale population in Taiwan. Accordingly, non-fatty liver patients with a high FLI or LAP may need intensified lifestyle modification and counseling.

Disclosure of Interest: None declared

P0630 PROGNOSTIC SIGNIFICANCE OF SYSTEMIC INFLAMMATORY AND IMMUNE BALANCE IN ALCOHOLIC LIVER DISEASE WITH A FOCUS ON GENDER-RELATED DIFFERENCES

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Abstract number: P0633 Table: Hepatic Lipid Peroxidation and Liver Function Tests in Mice after 24 Hours of CCl_4 Treatment.

Parameter	Saline + Olive oil	6-OHDA + Olive oil	Saline + CCl4	6-OHDA + CCl4	Phentolamine + CCl4	Nadolol + CCl4
4-HNE (μg/μg protein)	0.23 ± 0.02	0.18 ± 0.02**	0.33 ± 0.07*	0.23 ± 0.03$^{\#\#, \dagger\dagger}$	0.25 ± 0.01$^{\#}$	0.28 ± 0.02
ALT (IU/L)	40 ± 11	51 ± 28	15,519 ± 4,678***	7,809 ± 2,527$^{\#\#}$	7,318 ± 3,799$^{\#}$	10,830 ± 4,381

The results are presented as mean ± S.D.; * and ** Denote significant differences compared with the Saline + Olive oil group ($p < 0.05$ and 0.01, respectively); $^{\#}$ and $^{\#\#}$ Denote significant differences compared with the Saline + CCl_4group ($p < 0.05$ and 0.01, respectively)

Introduction: Mechanisms of inflammation in alcoholic liver disease (ALD) are still unclear. Th17 and regulatory T (Treg) cells are critically linked to inflammatory immune response. While Th17 lymphocytes exert pro-inflammatory effects, Treg cells are potent immune suppressors, and they may reciprocally control their function. Human Th17 differentiation is IL-1beta1, IL-6, IL-23 and IL-17A- dependent and suppressed by TGF-beta1. On the other hand TGF-beta1 enhances the differentiation of human Treg cells. To date, the Th17/Treg balance has not been explored in patients with ALD yet. Moreover, women develop more severe alcohol-associated liver injury at lesser ethanol intake and fewer years of exposure. They seem to respond stronger in comparison to males after inflammatory induction. It may result from different hormone patterns (estrogens are immune stimulators, testosterone is rather immunosuppressive).
Aims & Methods: The aim of our study was to determine an impact of the Th17 / regulatory T (Treg) cells balance and its corresponding cytokine profile on the ALD outcome. Possible gender-related differences in the alcohol-induced inflammatory response were also assessed. 147 patients with ALD were prospectively recruited, assigned to subgroups based on their gender, severity of liver dysfunction and presence of ALD complications at admission, and followed for 90 days. Peripheral blood frequencies of Th17 and Treg cells together with IL-1beta, IL-6, IL-17A, IL-23, and TGF-beta1 levels were investigated.
Flow cytometry was used to identify T cell phenotype and immunoenzymatic ELISAs for the corresponding cytokine concentration assessments. Multivariable logistic regression was applied in order to select independent predictors of advanced liver dysfunction and the disease complications.
Results: IL-17A, IL-1beta, IL-6 levels were significantly increased, while TGF-beta1 decreased in ALD patients. The imbalance with significantly higher Th17 and lower Treg frequencies was observed in non-survivors. IL-6 and TGF-beta1 levels differed in relation to the patient gender in ALD group. Concentrations of IL-6 were associated with the severity of liver dysfunction, development of ALD complications, and turned out to be the only independent immune predictor of 90-day survival in the study cohort.
Conclusion: IL-6 revealed the highest diagnostic and prognostic potential among studied immune biomarkers and was related to the fatal ALD course. Gender-related differences in immune regulation might influence the susceptibility to alcohol-associated liver injury.

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Disclosure of Interest: None declared

P0631 A RETROSPECTIVE STUDY COMPARING SURVIVAL, RECIDIVISM AND COMPLICATIONS AFTER LIVER TRANSPLANTATION IN PATIENTS WITH ALCOHOLIC AND HCV-RELATED CIRRHOSIS

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Introduction: Alcohol represents the most common cause of liver cirrhosis in the Western countries. Total alcohol abstinence represents the cornerstone in the management of alcoholic cirrhosis (AC). When liver function fails to improve with abstinence, liver transplantation (LT) is the treatment of choice. However LT in patients with AC remains controversial for the risk of alcohol recidivism after LT, and the perception of AC as a "self-inflicted disease". Actually, HCV-related cirrhosis is the leading indication for LT.
Aims & Methods: The aim of this study was to evaluate the differences in terms of survival, recidivism and complications between patients who underwent LT for AC and HCV-related cirrhosis. A total of 297 patients who underwent LT at the Gemelli Hospital were retrospectively evaluated. In particular 66 (22.2%) patients underwent LT for alcoholic cirrhosis, and 52 (17.5%) patients for HCV-related cirrhosis. The survival rate was evaluated according to the Kaplan-Meier model. Recidivism for patients with AC was defined as any alcohol intake after LT. Recidivism for HCV-related cirrhosis was defined as histological evidence of chronic hepatitis C within 3 years of LT. Moreover post-surgery complications, chronic and acute rejection, onset of cancer, infectious, cardiovascular and metabolic disease was evaluated.
Results: Patients who underwent LT for AC showed a higher, however not significant, rate of survival than patients who underwent LT for HCV-related cirrhosis. Patients with HCV-related cirrhosis showed a significant higher prevalence of recidivism after LT ($p = 0.02$). Patients transplanted for AC presented a significantly higher prevalence of cancer, in particular of upper digestive tract ($p = 0.04$). No differences were found in the prevalence of cardiovascular, metabolic and infectious disease, rejection, and post-surgery complications between the two groups.
Conclusion: This study shows that our patients who underwent LT for AC have a higher survival rate and a lower recidivism rate than patients who underwent LT for HCV-related cirrhosis. No differences in terms of complications after LT were found between two groups, with the except of the higher prevalence of cancer in the AC group. These data are in line with previous literature data
Disclosure of Interest: None declared

P0632 ONE YEAR EFFECTIVENESS OF BACLOFEN TREATMENT IN 100 ALCOHOL-DEPENDENT PATIENTS

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Introduction: Several studies have suggested efficacy of Baclofen (BAC) at low or high dose in reducing alcohol consumption. Since March 2014, Temporary Recommendation for Use of BAC has been allowed by the French drug agency (ANSM) in this indication.
Aims & Methods: The aim of the study was to assess effectiveness and safety of BAC at 12 months in alcohol-dependent patients with or without liver cirrhosis. Between June 2010 and September 2013, 100 consecutive patients from 2 liver and alcohology units were included in this prospective open label study. Patients provided written consent before treatment initiation. BAC was orally administered at a dose of 15mg/day and weekly increased until alcohol indifference was obtained. The treatment was associated to social-psychological support and medical care.
Results: BAC was started in 100 patients (75 males, mean age 53 ± 9 years): 65 were cirrhotic and 16 had a chronic pancreatitis. After 1 year, 86 patients were still involved in the follow up, 83 were treated with BAC, 9 were lost of follow-up, 4 were dead and 1 had been transplanted. At a mean BAC dosage of 40mg/day [30–210], mean daily alcohol consumption (DAC) was reduced from 106 to 18g/day ($p < 0.001$). A decrease of the DAC > 50% was observed in 77 patients. Among them, a « low consumption » group of 64 patients was identified: 44 were completely abstinent and 20 drunk less than 30g/day. No predictive factor of response was identified. In this group, a significant improvement of consumption biomarkers was observed: decrease of mean gGT activity from 4.8N to 2N ($p < 0.001$), mean ASAT activity from 2.6N to 1.1N ($p < 0.001$) and mean erythrocyte globular volume from 100.6 to 92.8m3 and increase of mean platelets count from 171,000 to 193,000/mm3 ($p = 0.032$). In the 39 cirrhotic patients of the « low consumption » group, total bilirubin serum concentration significantly decreased from 34.2 to 19.5mmol/L ($p = 0.026$), prothrombin time increased from 69 to 77% ($p < 0.001$) and albuminemia increased from 34.2 to 37.2g/L ($p = 0.07$). Twenty patients (20%) reported minor side effects leading to a treatment withdrawal in 2 cases. No liver or renal function deterioration occurred in cirrhotic patients.
Conclusion: In our cohort, baclofen treatment associated to a global care led to a dramatic reduction of alcohol consumption. This effective treatment is well tolerated and associated with a significant improvement of consumption biomarkers and of liver function tests in cirrhotic patients.
Disclosure of Interest: None declared

P0633 ABLATION OF THE SYMPATHETIC NERVOUS SYSTEM ATTENUATES CARBON TETRACHLORIDE-INDUCED OXIDATIVE STRESS IN LIVER: KEY ROLES FOR ALPHA-ADRENERGIC SIGNALING, HEPATIC INFLAMMATORY RESPONSE, AND HEME OXYGENASE-1 EXPRESSION

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Introduction: In addition to being the primary organ involved in redox cycling, the liver is also one of the most highly innervated tissues in mammals [1]. Although the sympathetic nervous system (SNS) is known to modulate both liver regeneration [2] and hepatic fibrosis [3], less is known regarding the role of the SNS in modulating the hepatic response to oxidative stress.
Aims & Methods: Our aim was to investigate the role of the SNS in healthy and oxidatively stressed liver parenchyma, theorizing that sympathectomized animals would be protected against oxidative stress. C57Bl/6JNarl male mice were treated with 6-hydroxydopamine hydrobromide to cause chemical sympathectomy or with either the α-adrenergic antagonist phentolamine or the β-adrenergic antagonist nadolol. Thereafter, carbon tetrachloride (CCl_4) injection was used to induce acute oxidative liver injury. Development of liver injury, oxidative stress, hepatocyte ultra-structural damage, and inflammatory responses were investigated.
Results: Sympathectomized animals were protected from acute CCl_4-induced liver injury as measured by an increase in lipid peroxidation as assessed by 4-hydroxy-2-nonenal (4-HNE) levels; elevation of serum alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) levels; DNA oxidative damage; and morphological features of cell damage. In addition, chemical sympathectomy modulated the CCl_4-induced inflammatory response within the liver. Attenuated injury in sympathecomized mice was associated with raised heme oxygenase-1 expression. CCl_4-induced lipid peroxidation and hepatotoxicity were suppressed by administration of an α-adrenergic antagonist.
Conclusion: We conclude that the SNS provides a permissive microenvironment for hepatic oxidative stress and injury indicating the possibility that targeting the hepatic α-adrenergic signaling could be a viable strategy for improving outcomes in patients with acute hepatic injury.

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P0634 MECHANISTIC INSIGHT INTO CHLORPROMAZINE-INDUCED HEPATIC TIGHT JUNCTION DISRUPTION USING A HUMAN HEPARG-BASED LIVERBIOCHIP IMPEDANCE BIOSENSOR

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Introduction: Chlorpromazine (CPZ) is an antipsychotic that can cause severe liver injury including intrahepatic cholestasis (jaundice). Preclinical in vitro models such as rat hepatocyte couplets or primary rat and human hepatocytes sandwich cultures have been the used to analyze hepatic transport processes. Dysregulation of the hepatobiliary transporter, bile salt export pump, is now recognized as a molecular initiating event in cholestasis. However existing models, including animal models, do not accurately predict cholestasis in humans. Therefore, new methods of detecting cholestatic liver injury caused by candidate compounds under development is critical. Cholestatics can also have profound effects on tissue architecture. For example, CPZ and cyclosporine-A have recently been shown to destabilize intercellular tight junctions (TJs) via oxidative stress-mediated effects on TJ-associated cytoskeletal pericanalicular F-actin distribution in a 2D human hepatic HepaRG cell model[1-2]. HepaRG cells correctly localize hepatobiliary transporters to canalicular structures, comparable with primary human hepatocytes, and exhibit functional polarity[3].
Aims & Methods: We aimed to develop a HepaRG-based LiverBioChip, as a preclinical test system for CPZ-mediated cholestatic liver injury, using impedance-based biosensing. Differentiated HepaRGs were cultured to confluence on 8-well (8W10E+) gold micro-electrode arrays. On day 8, CPZ time-/dose-response [0-100 μM] was monitored with quantitative impedance, |Z|, measurements (180s intervals; multiple frequencies: 4-64kHz) for 24h; to detect the TJ parameter (Rb), using |Z|-spectra modeling. Correlative hepatotoxicity/ phenotypic assays were performed: i) ATP-depletion; Prestoblue (PB: live-cell viability); and i) F-actin/phalloidin fluorescent staining.
Results: Real-time |Z| monitoring showed highly-sensitive/ temporal dose-response to CPZ; with a decrease of impedance at all frequencies, indicating a global decline in cellular health. Subsequent |Z|-spectra modelling reflected significant early (1h) disruption of TJ, and the cell-substrate adhesion parameter (z-alpha), at all CPZ doses [25, 50, 100 μM]. Endpoint ATP-depletion and PB assays (24h) correlated with |Z| changes only at the lethal [100 μM] dose. Fluorescent F-actin/phalloidin staining confirmed disruption to bile canalicular- [50-100 μM CPZ] and TJ-associated hepatic structures (ZO-1 TJ protein).
Conclusion: LiverBioChip provides a continuous/ quantitative real-time indicator of hepatic TJ integrity; revealing early, dose-dependent disruption of TJs even at sub-toxic CPZ levels (25 μM). This non-invasive platform may provide mechanistic insight into effects of putative cholestatic compounds for pre-clinical drug discovery.

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P0635 DOPAMINE TRANSPORTER AVAILABILITY IN ALCOHOL-DEPENDENT PATIENTS BEFORE AND AFTER DEEP REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION: A 123I-FP-CIT STUDY

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Introduction: Experimental and neuroimaging studies suggest a striatal dopaminergic dysfunction in alcohol dependence. Repetitive transcranial magnetic stimulation (rTMS) is a new promising treatment for substance addiction. Preliminary data in alcohol-dependent patients showed that rTMS of the dorsolateral prefrontal cortex increases dopamine release in the striatum, reducing craving.
Aims & Methods: The aim of this study is to assess DAT availability in actively drinking alcoholics before and after deep rTMS by 123I-FP-CIT SPECT, exploring changes in DAT levels and clinical parameters. We enrolled 14 untreated patients (12 M, mean age: 49 ± 10 years) with a DSM-IV diagnosis of alcohol dependence and a current alcohol drinking phase and without a major psychiatric disorder. After baseline SPECT scan, 11/14 patients were randomised to a real rTMS ($n = 5$) or a sham stimulation ($n = 6$). Each patient underwent 12 rTMS sessions for one month and a second SPECT scan was carried out at the end of treatment. Severity of alcohol dependence and craving were assessed before and after rTMS through the Alcohol Dependence Scale, Penn Alcohol Craving Scale and Obsessive Compulsive Drinking Scale. Anxiety and depression were evaluated by the State-Trait Anxiety Inventory and Zung Depression Self-Rating Scale. The alcohol Timeline Follow-back (TLFB) was used to estimate daily drinking. A ^{123}I-FP-CIT template was created with images of 20 healthy subjects (HS, 12 M, mean age: 47 ± 16 years). Patient scans were spatially normalised to the ^{123}I-FP-CIT template by SPM8. Analysis was performed using VOIs selected from a digital atlas; VOI mean activity concentration was obtained through Marsbar toolbox and Specific Binding Ratios (SBR) were calculated in the caudate nuclei and putamina.
Results: At baseline, alcoholics showed higher SBR in caudate nuclei and putamina ($p < 0.05$) in comparison with HS. An inverse correlation was found between SBR in the left caudate and anxiety levels ($p < 0.05$). After treatment, patients submitted to real rTMS had a reduction in SBR and no differences were any longer detected in comparison with HS. Conversely, patients submitted to sham stimulation showed higher SBR as compared with HS ($p < 0.05$) also at SPECT examination after treatment. When considering TLFB data, a significant reduction in alcohol intake ($p < 0.05$) was detected only in patients submitted to real rTMS.
Conclusion: Our preliminary data show that striatal DAT availability is increased in alcohol-dependent patients, supporting the assumption of a dysfunctional dopaminergic system. The finding of a SBR ''normalization'' as well as a reduction in alcohol intake after real rTMS, although obtained in a small sample, could suggest a clinical usefulness of deep rTMS.
Disclosure of Interest: None declared

P0636 INCIDENCE OF DRUG INDUCED LIVER INJURY AMONG GOVERNMENT TERTIARY HOSPITAL PATIENTS ON ANTI-KOCH'S TREATMENT

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Introduction: Tuberculosis (TB) remains a major global health problem. Anti-TB drugs have proven efficacy against TB, however, they can induce various adverse events of which hepatoxicity is the most serious. Anti-tuberculosis drug induced liver injury (ATLI) is emerging as a significant threat to TB control, though limited data is available at present. This study aims to estimate the incidence of ATLI and understand its clinical features.
Aims & Methods: This was a single-center, prospective study which consisted of cohort of TB patients who received DOTS treatment at EAMC from December 2013 to May 2014. Only 285 patients who were at least 18 years of age were included. Clinical and laboratory features of ATLI were monitored for the treatment duration.
Results: We monitored 240 TB patients, 52 were dropped from the study while 188 continued. Nine patients developed ATLI with cumulative incidence of 4.8 % (95% CI, 2.4 – 7.19%). Nausea, abdominal pain were the most frequently observed signs and symptoms. Three (33.33%) ATLI patients had severe

hepatotoxicity, 7 (77.77 %) recovered, 1 (11.11%) failed to respond to treatment with continued elevation of aminotransferases and 1 (11.11%) died as a result of ATLI.
Conclusion: For this cohort, ATLI incidence was higher compared to data from China and Canada, comparable with Hongkong, and Singapore but lower than Taiwan. Presence of comorbidities showed trend to increase ATLI, however, further analysis only showed those with liver and biliary diseases to be statistically significant. Larger cohort of patients is suggested.

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P0638 BOVINE COLOSTRUM PLUS CORTICOSTEROIDS IN THE TREATMENT OF SEVERE ALCOHOLIC HEPATITIS: A PROSPECTIVE, PROOF OF CONCEPT, PHASE I TRIAL

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Introduction: Severe Alcoholic Hepatitis (SAH) is defined by modified Maddrey's Discriminant Function (mDF) $\geq$32 and is associated with very high short-term mortality. Corticosteroids reduce mortality in SAH patients but not to the desired extent. Bovine Colostrum is a biologic, food supplement and has immunomodulatory functions (1). Its effector constituents are immunoglobulins, growth factors (Insulin Like Growth Factor 1, 2; Transforming Growth Factor Beta), Lactoferrin and Lactoperoxidase. Lactoferrin is converted to Lactoferricin B in the stomach by pepsin which is bactericidal. Immunoglobulin G (IgG) interacts with mucosa associated lymphoid tissue, to maintain a healthy mucosal barrier and prevents gram negative bacteria and endotoxins from entering the porto-systemic circulation. Decreased endotoxemia dampens the pro-inflammatory cytokine cascade (IL 1β, IL 6, α TNF). Thus hepatocyte death and development of multisystem organ failure is averted. We aimed to study the efficacy of combination therapy of Corticosteroids and Bovine colostrum in improving mDF and reducing short-termmortality in patients with SAH.
Aims & Methods: Seventeen patients with SAH were prospectively evaluated, and 10 out of these were included. Bovine Colostrum (20 grams thrice in a day for eight weeks) and Prednisolone (40 mg once a day for four weeks, tapered over next four weeks) were administered to these patients. Serum Cytokines IL6, IL8, IL10 and TNFα were measured at 0 and 8 weeks. Paired t Test was used for analyzing the data. Data are expressed as mean $\pm$ SD. Trial was registered at Clinical Trial.gov -NCT02265328.
Results: The mean age was 41.6 $\pm$ 7.9 years and 100% were males. There was a significant improvement in mDF level from 78.1 $\pm$ 14.2 at baseline to 43.6 $\pm$ 23.8 at 8 weeks; p = 0.001]. Also there was a significant change in IL6 and IL8 levels at 8 weeks (table). The survival at one month and three months was 90% and 70% respectively.

Table: Test of difference: baseline versus 8 weeks in patients with severe alcoholic hepatitis after treatment with bovine colostrum and corticosteroids.

	Paired Differences						
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference	T		p value
IL 8	0.09443	0.06111	0.02310	0.03791	0.01509	4.088	0.0064
IL 6	0.05014	0.02284	0.008634	0.1620	0.1119	5.808	0.0011
α –TNF	-0.0064	0.02964	0.01326	-0.04320	0.03040	0.4827	0.6545
mDF	34.714	14.829	5.605	21.000	48.429	6.194	0.001

Conclusion: In patients with SAH, treatment with combination therapy of Bovine Colostrum plus Prednisolone lead to significant improvement in the liver biological functions. The 3 month survival of 70% in this study was much better than 30% survival reported prevoiusly with the use of corticosteroids alone in SAH patients (2). Therefore, this combination could be a better option for treatment of patients with SAH. Larger randomized controlled trials are required to confirm these findings.

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P0639 CLIF-ORGAN FAILURE SCORE IS A PREDICTOR OF MORTALITY IN PATIENTS WITH ACUTE ALCOHOLIC HEPATITIS

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Introduction: Acute alcoholic hepatitis (AAH) is a distinct clinical entity in the spectrum of alcoholic liver disease and is associated to high short-term mortality. Different score systems have been used to assess the severity and predict the prognosis of patients with AAH.
Aims & Methods: Evaluate the ability of seven different score systems to predict 90-day mortality and analyse other potential predictors of mortality.
Retrospective analysis of patients admitted to our department due to AAH, between November 2009 and October 2014. The following score systems were analysed: Child-Pugh (CP), Maddrey discriminant function (MDF), model for end-stage liver disease (MELD), Glasgow alcoholic hepatitis score (GAHS), Age-Bilirubin-INR-Creatinine (ABIC), Lille score (LS) and CLIF consortium-organ failure score (CLIF-OF).
Results: We included 59 cases of AAH (78% men, mean age 47 $\pm$ 8 years). The mortality rate at 90 days was 22% (n = 13). Forty-nine percent of patients (n = 29) initiated therapy with corticosteroids. Only 28% (n = 8) of patients were complete responders (LS $<$ 0.16) while 38% (n = 11) were non-responders (LS $>$ 0.56). Encephalopathy (p = 0.038), ascites (p = 0.013), CP score $>$ B (p = 0.034), LS $>$ 0.56 (p = 0.002), and a higher GAHS (p = 0.009) and CLIF-OF (p $<$ 0.001) score were significantly associated with higher 90-day mortality. In multivariate analysis, CLIF-OF score was the only one independently associated with higher mortality at 90 days (OR 2.99, 95% CI: 1.63-5.50, p $<$ 0.001).
Conclusion: AAH was associated with a 90-day mortality of 22%. The CLIF-OF score was the only score significantly associated with higher mortality at 90 days, with an OR of 2.99.
Disclosure of Interest: None declared

P0640 LIVER INJURY IN TREATED INFLAMMATORY BOWEL DISEASE PATIENTS: PREVALENCE, SEVERITY, EVOLUTION AND IMPLICATIONS FOR FURTHER TREATMENT

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Introduction: Drug-induced liver injury (DILI) is the most common cause of acute liver injury. IBD patients might have an increased risk of DILI due to long-term treatment, multiple therapies and altered nutritional status. Any liver injury during IBD treatment might further compromise treatment choices, efficacy and overall health.
Aims & Methods: First, prospectively evaluate on-treatment prevalence, severity and evolution of liver injury in IBD patients for 6 months. Second, evaluate the impact of IBD treatment with azathioprine and/or anti- TNF on the prevalence of liver injury. Third, evaluate liver injury implications for further IBD therapy. From 1/1/2014 to 1/6/2014 all IBD cases visiting a single center were included. Demographics, IBD status, IBD therapy and possible PSC were recorded. Liver blood tests were measured at three time points 3 months apart. Liver injury was defined as elevated ALT, GGT and ALP above 1.5 times the upper limit of normal (ULN). Two types of liver injury were predefined: transient elevation (once or twice) and persisting elevation (at all three time points). Severe liver injury was defined as ALT $>$ 5xULN at any time. The prevalence of hepatotoxicity was compared among 4 treatment groups (no azathioprine, no anti-TNF (1), azathioprine (AZA) solo (2), anti-TNF solo (3), and combination therapy (4). Finally, we evaluated the need for change of IBD therapy caused by liver injury.
Results: 205 IBD patients were included, with median age of 40, male/female ratio 102/103, Crohn's/UC ratio 127/78, 27% with prior GI resection, 2 cases with PSC. IBD was treated with no AZA and no anti-TNF in 40 cases, azathioprine solo in 40 cases, anti-TNF solo in 63 cases and combination therapy in 62 cases. For 6 months, transient ALT elevation was observed in 18 cases (8.78%), GGT in 21 cases (10.24%) and ALP in 5 cases (2.44%). Persisting ALT elevation was observed in 3 cases (1.46%), GGT in 3 cases (1.46%) and none of ALP. Severe liver injury was observed in 1 case (0.49%) with bilirubin $<$ ULN. The prevalence of transient liver injury among the 4 treatment groups was 5 vs. 10 vs. 12.7 vs. 9,6% for ALT and 12.5 vs. 17.5 vs. 15.9 vs. 3.2% for GGT and was not statistically different. Liver injury did not result in any change of IBD therapy.
Conclusion: Liver injury in treated IBD patients was relatively common (~10%). However, it was mostly transient, non-severe and rarely (~1.5%) persisted for 6 month. IBD therapy with azatioprine and/or anti-TNF did not increase the risk of liver injury. No changes of IBD treatment resulting from liver injury were needed.
Disclosure of Interest: None declared

P0641 LIPOCALIN 2 DRIVES NEUTROPHILIC INFLAMMATION IN ALCOHOLIC LIVER DISEASE

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Introduction: Alcoholic steatohepatitis (ASH) is a severe condition in the spectrum of alcoholic liver disease (ALD) that is histologically characterised by

neutrophil infiltration which correlates with mortality.[1] The underlying mechanisms of neutrophilic inflammation in the development of ALD are poorly understood and treatment options are rare.[2] Lipocalin-2 (LCN2) was originally found in granules of neutrophil granulocytes and termed neutrophil gelatinase-associated lipocalin (NGAL). Recently, it was shown that the liver is the predominant source of LCN2 during infections and that LCN2 is essential in liver homeostasis and experimental hepatic injury.[3,4]

Aims & Methods: Our aim was to investigate the role of LCN2 in the pathogenesis of ASH. Hepatic and systemic LCN2 elevation was measured in patients with histologically ensured ASH. Furthermore, 6- to 8-week-old female C57BL/6 WT and Lcn2-deficient (*Lcn2*$^{-/-}$) mice were fed a Lieber-DeCarli diet containing 5% (vol/vol) ethanol or a control diet for 2 weeks ad libitum. ASH was determined by liver-to-body-ratio, GPT-elevation, steatosis and hepatic inflammation. Adoptive transfer experiments of wild-type and *Lcn2*$^{-/-}$ neutrophils were performed to dissect the role of hepatic and neutrophil-derived LCN2 in ASH.

Results: We found a systemic and hepatic upregulation of LCN2 in patients with ASH compared to NAFLD controls, which we similarly observed in wild-type mice on a Lieber-deCarli diet. Immunocytes in hepatic tissue were the predominant source of *Lcn2* expression. *Lcn2*$^{-/-}$ mice were protected from ASH as demonstrated by diminished GPT elevation, steatosis and neutrophil infiltration. Mechanistically, we found in adoptive transfer experiments of WT and *Lcn2*$^{-/-}$ neutrophils that cell-intrinsic (rather than hepatic) LCN2 is required for neutrophilic inflammation in ASH.

Conclusion: LCN2 drives neutrophilic inflammation in ASH in a neutrophil-intrinsic manner. Our study suggests that pharmacologic neutralisation of Lcn2 blocks neutrophil migration and protects from ASH.

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P0642 SODIUM BENZOATE AND RIFAXIMIN ARE ABLE TO RESTORE BLOOD-BRAIN BARRIER INTEGRITY IN HE CIRRHOTIC RATS

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Introduction: Hepatic encephalopathy (HE) is a severe complication of cirrhosis which independently influences prognosis. We previously showed an increase in blood-brain barrier (BBB) permeability in cirrhotic rats with HE. The aim of the present work was to assess the effects of sodium benzoate (Bna), a drug removing ammonia through non-urea cycle pathway, and Rifaximin (RFX), a non adsorbable antibiotic, on BBB permeability in cirrhotic rats with HE.

Aims & Methods: Three groups of rats were considered: SHAM, Bile Duct Ligation (BDL), BDL + hyperammonic dietary (BDL-NH3). In each group, rats were treated by BNa or RFX. HE was assessed using neurocomportemental testing (6 minutes tail suspension test assessing the time of immobility). NH3 levels were assessed before sacrifice. BBB permeability was assessed by IV injection of a fluorochrome (Texas Red 10kDa) before transcardial washing. Brain fluorescence was estimated by fluorimetry after right hemisphere squeezing.

Results: Mean time of immobility was longer in BDL-NH3 and BDL rats than in SHAM ($p = 0.0004$). Ammonemia was significantly higher in the BDL-NH3 than in BDL rats, and higher in the BDL than in SHAM rats ($p < 0.0001$). Intra-cerebral fluorescence was significantly higher in BDL-NH3 than in BDL group, and higher in BDL than in SHAM group ($p = 0.029$) confirming the passage of the fluorochrome through the BBB. BNa treatment significantly decreased ammonemia levels and intra-cerebral fluorescence in the BDL and BDL-NH3 rats ($p < 0.04$ for all) but did not modify the mean time of immobility. On the contrary, RFX treatment did not modify ammonemia levels but significantly decreased intra-cerebral fluorescence ($p < 0.05$) and the mean time of immobility ($p = 0.0004$).

Conclusion: In cirrhotic rats displaying HE, BBB permeability is increased, through different mechanisms dependent and independent of hyperammonemia. BNa and RFX are effective in restoring BBB integrity in HE cirrhotic rats but only RFX is able to decrease HE in this model.

Disclosure of Interest: None declared

P0643 EVALUATION OF 13C-AMINOPYRINE BREATH TEST IN LIVER CIRRHOSIS AND HEPATOCELLULAR CARCINOMA

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Introduction: ^{13}C- aminopyrine breath test (^{13}C-ABT) is a simple, sensitive tool to evaluate liver function, and its results may discriminate between patients with or without cirrhosis. Also, it was previously reported that, in patients suffering from chronic liver disease of various etiologies, ^{13}C-ABT can discriminate between those with chronic hepatitis and those with cirrhosis. It was reported that breath test can be used as a prognostic index in liver metastases even if concurrent biochemical liver tests are normal or only slightly disturbed.

Aims & Methods

The aim of this study: The aim of this study was to compare ^{13}C-ABT results between normal subjects, patients with liver cirrhosis with and without hepatocellular carcinoma in order to identify function differences between various chronic liver diseases and to evaluate different methods of expressing ^{13}C-ABT results and to maximize the information obtained from the test.

Patients and Methods: This study was carried out on 60 patients with cirrhosis and 15 normal subjects divided into three groups: group I (30 patients with liver cirrhosis), group II (30 patients with liver cirrhosis and hepatocellular carcinoma) and group III (15 healthy volunteers of matched age and sex to patient groups as a control group). ^{13}C-ABT was done to all subjects of this study.

Results: The mean aminopyrine % dose/hour after 60 minutes was significantly lower in cirrhosis group and HCC group compared to control group, and it was significantly lower in HCC group compared to cirrhosis group.

The mean aminopyrine % cumulative dose after 120 minutes was significantly lower in cirrhosis group and HCC group compared to control group, and it was significantly lower in HCC group compared to cirrhosis group.

Conclusion: ^{13}C-ABT is non-invasive test and easy to perform in identifying quantitatively different degrees of liver cirrhosis. ^{13}C-ABT correlates well to Child classification and degree of chronic liver diseases. Liver biopsy remains the gold standard technique for the evaluation of patients with cirrhosis, its causes, and presence of hepatocellular carcinoma. ^{13}C-ABT will not replace liver biopsy in diagnosing causes of cirrhosis or diagnosing of HCC. However, in patients in whom biopsy is not safe or in whom an etiologic diagnosis has been established, the aminopyrine breath test may replace serial biopsies.

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Disclosure of Interest: None declared

P0644 ASSOCIATION OF GENETIC VARIANTS IN PNPLA3, MERTK, PCSK7 AND RNF7 WITH LIVER CIRRHOSIS

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Introduction: Liver cirrhosis(LC) is a progressing disease commonly caused by alcohol consumption, infections of chronic hepatitis B and C and many other causes. Time period of fibrosis progression to cirrhosis varies in individual patients despite of etiology of liver cirrhosis. The search for genetic factors that could help to select patients at higher risk of developing LC is necessary. Current data indicate role of *PNPLA3* gene product in lipid homeostasis and genome-wide association studies (GWAS) revealed *PNPLA3* (rs738409) single-nucleotide polymorphism (SNP) association with liver diseases and fibrosis risk. A recent GWAS suggest a possible relationship between the clearance of apoptotic cells and liver fibrosis, revealing impact of *MERTK* (rs4374383) and *RNF7* (rs16851720) SNPs. Other GWAS demonstrated that *PSCK7* (rs236918) is a risk factor of cirrhosis in hereditary hemochromatosis (HH) patients. The role of these SNPs for the risk of developing LC needs to be evaluated in independent replication studies.

Aims & Methods: The aim of this study was to determine the association between the presence of *PNPLA3*, *MERTK*, *PCSK7* and *RNF7* SNPs and the risk of developing LC. We included 244 individuals with LC of different etiology and 498 healthy controls. The diagnosis of cirrhosis was confirmed by clinical features, liver biopsy and radiological imaging tests. *PNPLA3*, *MERTK*, *PCSK7* and *RNF7* SNPs in cirrhotic patients and control group were detected using real-time PCR TaqMan® method. Statistical analysis was performed using statistical software PLINK for genetic association studies. Odds ratio was adjusted for age and sex.

Results: *MERTK* and *PCSK7* SNPs were not associated with the risk of developing liver cirrhosis (adjusted odds ratio (OD_a)-1.2, 95% confidence interval (CI_{95}) 0.96-1.52, $p = 0.109$; OD_a-0.79, CI_{95} (0.56-1.11), $p = 0.169$, respectively). *RNF7* SNP showed no significant association in allelic association analysis (OD_a-0.75, CI_{95} (0.56-1.28), $p = 0.074$), but showed lower risk of developing

LC in recessive model when comparing CC *vs.* AA + CA genotype (OD_a-0.18, CI_{95} (0.04-0.79), p = 0.023). *PNPLA3* SNP showed allelic association with higher risk of developing LC (OD_a -1.91, CI_{95} (1.47-2.50), $p = 1.812*10^{-8}$), genotypic association analysis in a recessive model GG *vs.* GC + CC revealed higher risk of developing LC when compared to GG genotype (OR_a-5.01, CI_{95} (2.52-9.94), $p = 4.158*10^{-6}$) and dominant model GG + GC *vs.* CC genotype (OR_a-1.61, CI_{95} 1.13-2.29, p = 0.09).

Conclusion: *PNPLA3* and *RNF7* SNPs were associated with the risk of developing LC and these genetic alterations might contribute to progression to end stage liver disease. *MERTK*, *PCSK7* SNPs were not linked with the risk of LC.

Disclosure of Interest: None declared

P0645 EFFECT OF THE AT1 RECEPTOR ANTAGONISTS: LOSARTAN AND TELMISARTAN ON THIOACETAMIDE-INDUCED LIVER FIBROSIS IN RATS

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Introduction: Antifibrotic effects on the drugs used in the study were assessed by determining activity of biochemical parameters: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP) and concentration of proinflammatory cytokines: interleukin 6(Il-6), interleukin beta 1(Il-beta1), tumour necrosis factor alpha (TNF-alfa), transforming growth factor beta (TGF-beta1) and platetet-derived growth factor (PDGF-AB). Oxidative stress was evaluated by oxidised (GSSG) and reduced glutathione (GSH) levels. Moreover, activity of paraoxonase1 (PON-1), an antioxidative enzyme as well as histological inflammatory changes and fibrosis extent in the liver were evaluated.

Aims & Methods: The aim of the present study was to determine the effects of the selected AT_1 receptor antagonists (losartan, telmisartan) on liver fibrosis induced by chronic administration of thioacetamide (TAA) in rats.

Results: The experiments were performed on Wistar rats. Animals were divided into 6 groups, 8 individuals each: Control (received water, ad libitum'' for 12 weeks), TAA (thioacetamide-treated rats in a dose of 300 mg/L, ad libitum'' for 12 weeks), losartan (30 mg/kg bw) or telmisartan (10 mg/kg bw, intraperitoneally (ip.) once a day for 4 weeks), TAA + L (thioacetamide- treated rats, 300 mg/L, ad libitum ' for 12 weeks followed losartan in a dose 30 mg/kg/bw ip. for 4 weeks), TAA + T (thioacetamide-treated rats, 300 mg/L, ad libitum'' for 12 weeks followed telmisartan in a dose 10 mg/kg bw ip. for 4 weeks).

The immunoenzymatic findings revealed a significant decrease in concentrations of the following cytokines: TNF-alpha in groups: TAA + L ($P < 0.01$), TAA+ T ($P < 0.01$), TGF-beta1 in the groups: TAA+ T ($P < 0.01$), TAA + L ($P < 0.05$) and Il-6 in group: TAA+ T ($P < 0.05$), as compared to the TAA group. Analysis of oxidative stress indices (GSH and GSSG) in the liver homogenates revealed statistically significant improvement: concentration of GSH in groups: TAA+ L and TAA+ T increases ($P < 0.001$) and concentration of GSSG in groups: TAA+ L ($P < 0.05$) and TAA + T ($P < 0.001$) decreases compared to the TAA group.

Conclusion: The present study suggest that both used drugs: losartan and telmisartan significantly inhibited the progression of hepatic fibrosis induced by TAA. Inhibitory effect of losartan and telmisartan might be associated with ability to inhibit the production of profibrotic cytokines such as TNF-alfa, TGF-beta1, IL-6 and improvement concentration parameters of oxidative stress.

Disclosure of Interest: None declared

P0646 FECAL CALPROTECTIN, SEVERITY OF LIVER CIRRHOSIS AND HEPATIC ENCEPHALOPATHY - A PROSPECTIVE SINGLE-CENTER ROMANIAN STUDY

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Introduction: Bacterial translocation from the gut and inflammation play an important role in the pathogenesis and complications of liver cirrhosis, including hepatic encephalopathy (HE). Calprotectin is a protein derived from neutrophilic granulocytes and it is used as an indirect marker of intestinal inflammation.

Aims & Methods: We aimed to study the correlations between fecal calprotectin (FC) concentration, the severity of liver cirrhosis and hepatic encephalopathy. We performed a prospective study which included 92 patients with liver cirrhosis between April 2014 – September 2014. Cantitative FC (by fluorescent-enzyme imuno-assay) was measured in all subjects. Patients with gastrointestinal bleeding or diarrhea, who were given proton pump inhibitors, antiplatelet therapy or antibiotics, were excluded. HE grading was measured by West Heaven criteria and the degree of liver insufficiency was assessed according to the Child-Pugh classification and Model for End Stage Liver Disease (MELD).

Results: 64.5% of patients were female and the mean age was 54.34 ± 8.72 years. The major cause for liver cirrhosis was virus C infection (65%) and the most common precipitating factors for HE were infections (51%) and constipation (42%). There were no significant differences in values of FC between the patients with different stages of liver cirrhosis according to Child-Pugh classification and MELD score ($p < 0.05$). The mean concentrations of FC significantly increased with aggravating hepatic encephalopathy as it follows: 84 ± 32μg/g (without HE), 144 ± 43μg/g (Grade I HE), 196 ± 56μg/g (Grade II HE), 238 ± 48μg/g (Grade III HE) and 291 ± 45μg/g (Grade IV HE), $p < 0.05$.

Conclusion: FC was not associated with the severity of liver disease. FC concentrations increased with aggravating HE grade. FC could be used as a simple, non-invasive and rapid test for the diagnosis and evaluation of HE severity in patients with liver cirrhosis.

Disclosure of Interest: None declared

P0647 L-CARNITINE PREVENTS LIVER FIBROSIS AND PRENEOPLASTIC LESIONS IN RAT LIVER CIRRHOSIS MODEL INDUCED BY A CHOLINE-DEFICIENT L-AMINO ACID-DEFINED DIET (CDAA) AND DIETHYLNITROSAMINE (DEN)

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Introduction: Non-alcoholic steatohepatitis (NASH) can progress to advanced liver fibrosis and ultimately make hepatocellular carcinoma. L-carnitine is synthesized in the body from the amino acids and was proposed as the antioxidant for kidney disease and many body conditions.

Aims & Methods: The aim of this study is to investigate whether L-carnitine has any effects on the enlargement of liver fibrosis as well as preneoplastic lesions.

Methods: The effects of L-carnitine were examined using the choline-deficient L-amino acid-defined (CDAA) diet-induced NASH model. Diethylnitrosamine (DEN) 10 mg/kg was injected intraperitoneally once a week. The total study periods were 16 and 20 weeks. One group received a CDAA diet containing L-carnitine (200mg/kg/day) and DEN injection, the other group received a CDAA diet and DEN injection without L-carnitine as controls. Liver fibrosis was analyzed by Azan, Sirius–red, a-SMA, ED-1 expression. Development of preneoplastic lesions was assessed by glutathione S-transferase placental form (GST-P) expression. The change of laboratory data was analyzed. Type I procollagen, TIMP-2, aSMA,TGF-b, AFP, TNF-a, MCP-1,IL-6,EpCAM mRNA expression were analyzed using real-time RT-PCR system.

Results: After 16, 20 weeks, L-carnitine prevented liver fibrosis in a dose-dependent manner by Azan, Sirius-red expression ($p < 0.05$). Furthermore, L-carnitine reduced the area of GST-P positive lesions known as preneoplastic lesions ($p < 0.05$). Administration of L-carnitine significantly reduced levels of serum alanine aminotransferase (AST) (mean value: L-carnitine 239.3 vs Control 391.3 IU/l, $p < 0.05$), serum albumin (mean value: L-carnitine 4.2 vs Control 3.9 g/dl, $p < 0.05$). L-carnitine significantly inhibited Type 1 procollagen, TNF-a, IL-6, AFP mRNA expression (all of $p < 0.05$).

Conclusion: Our results indicated that L-carnitine prevented liver fibrosis and inflammation. We suggested that L-carnitine will be the new drug for NASH.

Disclosure of Interest: None declared

P0648 HEPATIC ENCEPHALOPATHY IN ICU: CEREBROSPINAL FLUID METABOLOMICS HIGHLIGHTS ALTERATION OF MULTIPLE METABOLIC PATHWAYS REPRESENTING NEW POTENTIAL THERAPEUTIC TARGETS

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Introduction: Hepatic encephalopathy (HE) is a neurological complication of cirrhosis, impairing survival and quality of life. Its incidence is growing because of the improved prognosis of other complications of cirrhosis, and of the widespread use of TIPS. However, besides hyperammonemia which is often pointed out as a cause of HE, the pathophysiological mechanisms of HE remains poorly understood, which prevents the development of therapeutic strategies. To address this issue, metabolomics was used to identify dysfunction of metabolic pathways in cerebrospinal fluid (CSF) samples of cirrhotic patients suffering from HE.

Aims & Methods: The aim of this study was to detect new therapeutic targets for HE associated with cirrhosis.

Cerebrospinal Fluid (CSF) samples were collected on 14 cirrhotic patients admitted in ICU for HE, in whom infection of central nervous system has to be ruled out, and were compared to CSF of 27 control patients without any proven neurological disease. Metabolomic analysis was performed using 3 liquid chromatographies coupled to high resolution mass spectrometry methods (LC-HRMS). Informatic data processing tools were used.

Results: LC-HRMS methods led to the characterization of 150 metabolites in CSF samples of HE patients, which were mainly amino acids and organic acids. Interestingly, according to human metabolome database, 40% of those metabolites had never been retrieved were not reported as present in CSF before. HE patients could be easily discriminated from controls on the basis of

metabolomicic information. Concentrations of 102 metabolites were found to be significantly altered in HE patients: metabolotypes displayed alterations in several major metabolite classes such as ammoniac, bile acids, but also amino-acids, acylcarnitines, and nucleosides. Accumulations of acetylated compounds, which could be due to a defect of the Krebs cycle, were reported for the first time in HE patients, and could constitute interesting therapeutic targets.
Conclusion: By enabling the simultaneous monitoring of a large set of metabolites in cirrhotic patients with HE, CSF metabolomics highlighted several altered metabolite pathways linked to ammonia metabolism, neurotransmission and energy metabolism. The pharmacological relevance of our findings has to be explored on animal models, as they could constitute interesting new therapeutic targets.
Disclosure of Interest: None declared

P0649 FREQUENCY OF HEPATIC HYDROTHORAX AND ITS RELATIONSHIP WITH SERUM ALBUMIN IN LIVER CIRRHOSIS PATIENTS

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Introduction: Cirrhosis is defined as the development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, which leads to portal hypertension and end-stage liver disease[1]. Patients with cirrhosis can develop several pulmonary conditions related to portal hypertension, including hepatopulmonary syndrome, porto pulmonary hypertension, spontaneous bacterial empyema and hepatic hydrothorax[2]. Hepatic hydrothorax (HH) is defined as the accumulation of significant pleural effusion (>500ml) in patients with cirrhosis without primary pulmonary or cardiac disease[3].
Aims & Methods: All patients with established diagnosis of decompensated chronic liver disease were included in study after getting a written informed consent.
After detailed history, thorough physical examination and routine laboratory investigations, chest X-ray chest and abdominal ultrasound were carried out in all patients to find out the presence of pleural effusion and ascites respectively. Fifty milliliters of pleural fluid was aspirated in all patients with pleural effusion using the transthoracic approach, taking ultrasound guidance wherever required. Fluid was sent for microscopic, biochemical, microbial analysis. SBEM defined when if pleural fluid with polymorphonuclear (PMN) cell count >500 cells/mm3 or positive culture with PMN cell count >250 cells/mm3 with exclusion of a parapneumonic effusion.
Results: Two hundred and six patients who met the inclusion criteria were included in the study with mean age of 41.25 ± 13.593 years. Among those 149 (72.3%) were males and 57 (27.7%) were females. Twenty three (11.2%) had hydrothorax; with right sided involvement was in 18 (78.3%) subjects, 3 (13%) had left sided while bilateral pleural effusion was found in 2 (8.7%) cases. SBEM was found in 07 (30.43%) cases. Mean serum albumin 3.125 ± 0.718 gram/dl. There was lack of correlation between serum albumin levels and hydrothorax but significant association with Child Pugh scoring system.
Conclusion: Our study highlighted the high frequency of hepatic hydrothorax having a significant association with hepatic function as assessed by Child Pugh scoring system but lack of correlation with serum albumin.

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P0650 COMPARATIVE EVALUATION OF MELD AND CHILD-PUGH SCORES IN PROGNOSIS OF CIRRHOSIS

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Introduction: The existence of reliable prognostic indices is of paramount importance in the management of cirrhosis. The MELD score and its modifications are widely used. However there have been reports that the older Child-Pugh scores are equally effective and due to their simplicity they should be used instead.
Aims & Methods: The aim therefore was to compare the prognostic accuracy of MELD,MELDNa, Child-Pugh and the corrected for Creatinine Child-Pugh score in a genetically homogeneous Cretan cirrhotic population. 195 cirrhotics (127 males, Median age 66 years) hospitalized in the past 2 years were studied and MELD, MELDNa, Child-Pugh (CP-I) and Child-Pugh adding 0-4 points according to Creatinine value (CP-II) was calculated. 142 were presented with decompensated cirrhosis.
Results: Median values were: MELD 14 (range 6-30), MELDNa 17 (range 6-33), CP-I 7 (range 5-13) and CP-II 8 (range 5-17). ROC curves for 6 and 12 months mortality showed that MELD and MELDNa were significantly better ($p < 0.001$) for prognosis. Areas under the curve for 6 and 12 month mortality were 0.776 and 0.766 for MELD and 0.798 and 0.786 for MELDNa. There was no difference between the two. MELD and MELDNa were also superior to CP-I and CP-II when only decompesated cirrhosis was evaluated.
Conclusion: MELD and MELDNa are better prognostic indicators of mortality in cirrhosis and should be preferred to the Child-Pugh scores.
Disclosure of Interest: None declared

P0651 KIDNEY DISFUNCTION: MAIN MARKER OF INTRA-HOSPITAL MORTALITY ASSOCIATED WITH SPONTANEOUS BACTERIAL PERITONITIS

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Introduction: Liver cirrhosis is often complicated by spontaneous bacterial peritonitis (SBP), being the kidney dysfunction common and associated with elevated mortality. Risk stratification improves prognosis. Some studies assessed predictors of severity in SBP, with controversial results.
Objective: To evaluate the predictive factors and prognosis scores in SBP.
Aims & Methods: A retrospective study of 143 consecutive episodes of SBP, between 2009 and 2014. It was evaluated the association between intra-hospital mortality and clinical and analytical variables (serum and ascitic fluid) in the diagnosis of SBP and prognostic scores: the modern acute kidney injury network (Akin) criteria, Akin progression in the first 48 hours, the simplified model of prognosis (PCR >6, age >6years and Platelet <100000) and the Model 11/22 (White blood cell >11000 and MELD >22).
Results: At admission, kidney dysfunction (Cr > 1.5 and/or urea > 30) was presented in 55.9% of patients (oligoanuric in 38.8%). The progression of kidney dysfunction in first 48 hours occurred in 50.0% of patients. The intra-hospital fatal outcome occurred in 35.0% of the cases and 80.0% in the first 30 days. The mortality associated with Akin 0, 1, 2, and 3 was respectively 10.1%, 33.3%, 57.1% and 66.7%. Oligoanuria at admission (OR 4.950; $p = 0.008$), lower serum sodium (OR 1.094; $p = 0.031$), higher total bilirubin (OR 1.166; $p = 0.002$), higher serum urea (OR 1.042; $p = 0.001$), higher Akin at admission (OR 3.144; $p = 0.009$) and Akin progression (OR 3.607; $p = 0.010$) were independent predictors of poor prognosis. Of prognostic scores, the progression of Akin (AUROC 0.779; $p < 0.001$) and Akin at admission (AUROC 0.672; $p = 0.001$) had more accuracy to prognosis assessment of SBP, followed by the Model 11/22 (AUROC 0.641; $p = 0.006$).
Conclusion: Kidney dysfunction is common in liver cirrhosis complicated by SBP, being the main predictor of intra-hospital mortality. The Akin has good applicability in the selection of patients with severe SBP. Therapy with albumin, vasopressors and admission in the intensive care unit should be early started in cases of kidney dysfunction at admission and progression of that within the first 48 hours.
Disclosure of Interest: None declared

P0652 SECONDARY BACTERIAL PERITONITIS IN CIRRHOSIS LIVER: A RARE OR UNDERDIAGNOSED CONDITION?

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Introduction: Secondary bacterial peritonitis (SeBP) in liver cirrhosis represents an often underdiagnosed entity with high morbidity and mortality. It early recognition improves the prognosis. Studies about this clinical condition are scarce.
Objective: To determine the frequency, clinic and prognosis of SeBP in liver cirrhosis.
Aims & Methods: A retrospective study of 250 cirrhotic patients admitted for bacterial peritonitis, between 2006 and 2014. These were selected all patients with SeBP (G1: 19patients) and compared with patients with spontaneous bacterial peritonitis (SBP) (G2: 143patients).
Results: The secondary etiology of bacterial peritonitis occurred in 7.6% of patients (male: 63.2%, mean age 60.58 ± 12.06 years). This condition was not recognized in 26.3% of cases. At admission, 47.4% showed signs of peritoneal irritation. Relatively to Runyon's criteria, 73.3% had ≥2 criteria and 40.0% all criteria, with a sensitivity of 73.3% and specificity of 86.9%. The culture of ascitic fluid was polymicrobial in 69.2%(vs 14.3%; $p < 0.001$). The factors associated to SeBP were an increased LDH and Glucose < 50 in ascitic fluid (1219.79 ± 185.47 and 1632.02 vs 168.05 ± 46.7% vs 8.04%; $p < 0.001$). For patients with SeBP undergoing surgery (42.1%) appears to be a tendency to lower mortality (62.5% vs 72.7%; $p = 0.275$), with a surgical timing higher in patients who did not survive (18.00 ± 23.43 vs 3.83 ± 13.91; $p = 0.047$). The intra-hospital mortality associated with SeBP was 68.4%(vs 34.96%; $p = 0.005$). The corticosteroids (30.0% vs 0.0%; $p = 0.035$), higher serum LDH (292.70 ± 297.38 vs 165.33 ± 48.24; $p = 0.048$), ascitic glucose < 50 (77.8% vs 0.0%; $p = 0.012$), higher INR (2.33 ± 1.28 vs 1.48 ± 0.33; $p = 0.022$), higher MELD-Na (27.31 ± 8.46 vs 20.50 ± 4.23; $p = 0.037$) and higher CLIF-SOFA (11.15 ± 4.52 vs 6.17 ± 1.60; $p = 0.012$) were associated

with higher risk of mortality. The CLIF-SOFA and MELD-Na scores were good predictors of intra-hospital mortality by SeBP (AUROC 0.859[0.000;1.000]; p = 0.014 and 0.750[0.531;0.969]; p = 0.047).
Conclusion: Although infrequent, the SeBP have the double mortality of SBP. The Runyon's criteria and polymicrobial culture are good indicators of presence of intra-abdominal infection. Corticosteroid therapy, elevated INR, MELD-Na > 22.5 and CLIF-SOFA > 6.5 allows identify the patients at higher risk of mortality, that will benefit from more timely combined approach (medical and surgical).
Disclosure of Interest: None declared

P0653 EFFECT'S EVALUATION OF THE TREATMENT WITH CARVEDILOL VERSUS PROPRANOLOL PLUS LOSARTAN ADMINISTRATION ON HEPATIC HAEMODYNAMIC PARAMETERS IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Primary prevention of variceal bleeding is an important and long-debated topic in the management of patients with cirrhosis and portal hypertension. Non-selective β-blockers are recommended for primary prophylaxis of variceal bleeding in patients with oesophageal varices. Carvedilol appears to be more effective than propranolol in the treatment of portal hypertension in cirrhotic patients [1,2]. Losartan, a specific angiotensin II receptor antagonist, has beneficial effects on splanchnic hemodynamics and liver fibrosis [3].
Aims & Methods: We have examined the efficacy of the treatment with Carvedilol versus combination therapy with Propranolol plus low dose Losartan on hepatic haemodynamic parameters in patients with liver cirrhosis. The study included 64 patients with liver cirrhosis of viral HBV or HCV etiology with different cirrhotic stage. We evaluated the portal system and hepatic artery before and after 6 months of treatment using duplex Doppler ultrasonography. 34 patients (gr. 1) received Carvedilol (6.25 - 25 mg/day) and 30 patients (gr. 2) received Propranolol (30 - 120 mg/day) plus Losartan (12.5 - 25 mg/day).
Results: Administration of Carvedilol, such as administration of Propranolol and Losartan improves hepatic haemodynamics parameters in cirrhotic patients. The diameter of portal vein the same decreased in gr. 1 and gr. 2 (15.1 ± 0.6% vs 15.8 ± 0.7%, p > 0.05). Portal blood flow velocity significantly increased in gr. 2 versus gr. 1 (15.3 ± 0.8% vs 11,2 ± 0.6%, p < 0.05) and hepatic artery resistance index significantly decreased in gr. 2 versus gr. 1 (16.1 ± 0.9% vs 10.7 ± 0.8%, p < 0.05). The mean arterial pressure insignificantly decreased in both groups (p > 0.05).
Conclusion: Our study indicates that the combination treatment with Propranolol and Losartan in patients with liver cirrhosis significantly improve portal blood flow velocity and hepatic artery resistance index, probably, because Losartan contributes to decrease the intrahepatic vascular resistance in cirrhotic patients more than Carvedilol.

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P0654 HOW TO PREDICT NONINVASIVELY THE PRESENCE OF OESOPHAGEAL VARICES?

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Introduction: Upper gastrointestinal endoscopy, despite being an invasive diagnostic procedure, is yet the gold-standard to evaluate the presence oesophageal varices in cirrhotic patients. Non-invasive methods are currently being developed in order to obviate the need for endoscopy.
Aims & Methods: The aim of our study was to assess the diagnostic accuracy of non-invasive methods that quantify hepatic fibrosis in predicting the presence of oesophageal varices.
Retrospective study including 150 patients with compensated cirrhosis of various aetiologies who performed upper endoscopy to assess the presence of oesophageal varices. Clinical, laboratorial, ultrasonography and endoscopic features were analyzed. The non-invasive methods evaluated were APRI score (AST/ platelet ratio index), SPRI score (spleen size/ platelets ratio), Fib-4 score (based on patients' age, platelet count, AST and ALT) and FibroQ (based on patients' age, platelet count, AST, ALT and INR).
The ability of the scores to predict oesophageal varices was assessed by the area under the ROC curve (AUROC).
Results: 150 patients included, 75% male with mean age 59 ± 10 years. On upper endoscopy, 120 patients (80%) had oesophageal varices. The APRI score better predicted oesophageal varices (AUROC 0.737; CI 95% 0.628-0.847), followed by Fib-4 (AUROC 0.709; CI 95% 0.606-0.813), SPRI (AUROC 0.706; CI 95% 0.596-0.816) and finally FibroQ (AUROC 0.678; CI 95% 0.572-0.785). For APRI score the best *cut-off* values were 0.87 with a sensitivity of 71%, specificity of 80%, positive predictive value of 93% and negative predictive value of 41%.
Conclusion: Among the studied scores, the APRI score proved to be a non-invasive method with good ability to predict the presence of oesophageal varices - an APRI value greater than 0.87 predicts the identification of oesophageal varices on endoscopy in 93% of the cases. This score, easy to use and readily accessible in clinical practice, may be valuable in a careful selection of patients with cirrhosis for early referral to upper gastrointestinal endoscopy.
Disclosure of Interest: None declared

P0655 DEVIATIONS IN PERIPHERAL BLOOD CELL POPULATIONS ARE ASSOCIATED WITH THE STAGE OF PRIMARY BILIARY CIRRHOSIS

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Introduction: Primary biliary cirrhosis (PBC) is a chronic cholestatic liver disease characterized by progressive destruction of small size intrahepatic bile ducts leading to cirrhosis. Among genetic, environmental, also immunological factors have conclusively been shown to contribute to the pathogenesis of PBC. The role of peripheral blood cell subpopulations, particularly Treg and Th17 in PBC pathogenesis remains still uncertain.
The aim of this research was to describe the percentages and absolute counts of Th17, Treg in patients with newly diagnosed PBC and the relationships between analyzed cell subsets and selected clinical parameters (itching and the degree of PBC severity).
Aims & Methods: The frequencies of Treg and Th17 were measured by flow cytometry in 40 previously untreated female patients with PBC. The control group consisted of 20 healthy age- and sex-matched volunteers.
The diagnosis of PBC was based on the common known criteria. The degree of severity of PBC was evaluated in each patient by histologic examination.
Results: Significantly lower frequencies and absolute counts of CD4(+)CD25(+)FoxP3(+) Treg cells were found in the study group in comparison with controls (p < 0.0001).
Higher percentages and absolute counts of IL-17A(+)CD3(+)CD4(+) Th17 lymphocytes were found in the PB of PBC patients than in the control group (p < 0.0001).
Among 40 patients with PBC, 7 showed the I stage of severity- portal stage, 16 patients the II stage- periportal stage, 11 the III - septal stage, and 6 patients the IV stage – cirrhosis. Itching of the skin was observed in 18 patients with PBC.
The frequencies and absolute counts of CD4(+)CD25(+)FoxP3(+) Treg cells correlated with the degree of severity of PBC however not with itching. The correlation between frequencies and absolute counts of IL-17A(+)CD3(+)CD4(+) Th17 lymphocytes and histological stage of PBC and/ or presence of itching was not observed.
Conclusion: The study demonstrates that both Treg and Th17 cells might play an important role in the pathogenesis of PBC. The reduced number of Treg cells and higher levels of Th17 cells in PBC could be responsible for the loss of immune tolerance and development of inflammatory and autoimmune process in PBC. The counts of Treg cells correlates with the degree of severity of PBC but no with presence of itching. Th17 cells did not show association between histologic stage of PBC and presence of itching.

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P0656 RELIABILITY OF SERUM VONWILLBRAND FACTOR ANTIGEN IN PREDICTION OF ESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Bleeding esophageal varices (OV) due to portal hypertension is one of the major complications with high mortality in liver cirrhosis. So, early detection and management is mandatory.

Aims & Methods

Aim: To evaluate the role of Vonwillbrand factor in predicting the presence of OV.

Patients and methods: 62 patients with liver cirrhosis representing different Child-Pugh classes were included. The diagnosis of liver cirrhosis was based on the combination of clinical, laboratory and US examinations. All included patients were underwent the following investigations: complete blood count, liver function tests (ALT, AST, serum bilirubin, albumin and total protein, prothrombin time (PT) and concentration (PC), INR and serum alkaline phosphatase), serum creatinine, Vonwillbrand factor antigen measurement and abdominal US. Upper endoscopic evaluation was done to detect presence or absence of varices (oesophageal or gastric) and/or PHG.

Results: 38 males and 24 females with their main age 46± 12 years old were included. Absence of OV (NO) was found in 22(35.5%) patients and presence of OV were found in 40(64.5%) patients; whom were as follow: 12(19.3%) patients were G1, 14(22.6%) were G2 and 14(22.6%) were G3. Gastric varices were found in 5(8%) patients and portal hypertensive gastropathy in 40(64.5%) patients. Serum Vonwillbrand factor-Ag level was significantly higher in patients with O.V than those without varices (p value = 0.000). Also, its level was significantly higher in patients with higher grade of OV; G3 than those with G1 or G2 (p value = 0.000). Patients with large OV including those with G2 and G3 showed statistically significant higher values of Vonwillbrand factor than those with small OV (NO and G1) (p value = 0.000). Vonwillbrand factor was independent predictor for detecting the presence of OV with good sensitivity (90), specificity (77.3) and accuracy (85.5) when its cutoff value was at 1.74. Also it was independent predictor for detecting the presence of large OV with good sensitivity (91.2), specificity (85.7) and accuracy (88.7 when its cutoff value was at 2.16.

Conclusion: Vonwillbrand factor antigen could be used as non invasive laboratory independent predictor for the presence of esophageal varices.

Disclosure of Interest: None declared

P0657 THE EFFECT OF NON-SELECTIVE BETA-BLOCKERS ON SURVIVAL IN DECOMPENSATED LIVER CIRRHOSIS PATIENTS

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Introduction: Recent studies evaluating outcomes associated with nonselective beta-blockers (NSBB) in cirrhosis have yielded mixed results (1). Due to their effect on cardiac output and on intestinal permeability, NSBB have been hypothesized to increase the risk of mortality especially in advanced liver disease (2). The aim of this study was to assess the effect of NSBBs on survival in decompensateted liver cirrhosis patients.

Aims & Methods: Liver cirrhosis patients who were admitted to our tertiary center from January 2005 to December 2005 were enrolled, and survival data until December 2014 was measured. Stratified randomization according to the Child–Pugh class and age was done and a total of 702 patients were divided into beta-blocker group (Propranolol, 40 mg/day) and non beta-blocker group. Overall survival and predictors of mortality were evaluated.

Results: There were 702 cirrhotic patients included in the study, mean age 55.82 ± 11.52 years, 392 (55.8%) males. Out of these 340 patients (48.8%) received NSBB treatment. There was no significant difference of survival (P = 0.321) and infection free survival (P = 0.910) between two groups. Two subgroups analyses according to the Model of End Life Disease (MELD) (MELD < 15, and MELD ≥ 15) also showed no significant difference of survival and infection free survival. Significant univariate predictors of death were age, Child–Pugh score, MELD score, prothrombin time, total bilirubin, albumin, and aspartate aminotransferase. The independent predictors of mortality were Child–Pugh score, and MELD score. Presence of esophageal varices was not predictor of mortality.

Conclusion: Non-selective beta-blockers have no effect on survival and infection free survival in cirrhotic patients. That means that NSBBs may not be used for the purpose of improving survival in decompensated liver cirrhosis patients.

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P0658 TERLIPRESSIN-INDUCED HYPONATREMIA IN CIRRHOTIC PATIENTS WITH VARICEAL BLEEDING

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Introduction: Terlipressin is frequently used in acute variceal bleeding due to its important effect on vasopressin V1 receptors. Terlipressin has agonistic effects on the V1 receptor and partial agonistic effects on renal vasopressin V2 receptors. However, its effects on serum sodium concentration are controversial. The aim of this study was to examine the effects of terlipressin on serum sodium concentration in cirrhotic patients with variceal bleeding.

Aims & Methods: All consecutive cirrhotic diagnosed with variceal bleeding treated with terlipressin were investigated Terlipressin induced hyponatremia was defined as a decrease in serum sodium (Na) level of >5 mEq/L from the baseline level. Main outcome measure was fall in Na level during and up to 5 days post therapy.

Results: The study included 214 patients (mean age, 54.3 ± 10.7 y) with male predominance (60.7%). Median Na pretreatment was 130.0 ± 6.5 mmol/L and 126/214 (58.87%) had existing hyponatraemia. Serum sodium level was at the baseline 130.0 ± 6.5 mmol/L and 131.4 ± 6.2 mmol/L after 5 days of terlipressin treatment (P = 0.758) in all patients. Changes in serum Na levels from baseline were 0.2 ± 1.2 whereas the frequencies of terlipressin-indiced hyponatremia was 6.07% (13 patients). Occurrence of hyponatremia was related neither to duration or dosage of terlipressin treatment but with the severity of the underlying chronic liver disease. No complications of hyponatremia were observed.

Conclusion: Terlipressin-induced hyponatremia was uncommon in cirrhotic patients with variceal bleeding. Hyponatremia was related with the severity of the underlying liver cirrhosis.

Disclosure of Interest: None declared

P0659 ANTIVIRAL THERAPY IMPROVES POST-TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT SURVIVAL IN PATIENTS WITH HEPATITIS B VIRUS-RELATED LIVER CIRRHOSIS

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Introduction: Antiviral treatment has been shown to be effective in patients with hepatitis B virus (HBV)-related decompensated cirrhosis. However, the effect of antiviral therapy in the subset of post-transjugular intrahepatic portosystemic shunt (TIPS) patients with HBV-related decompensated cirrhosis is uncertain.

Aims & Methods: From January 2007 to December 2012, a total of 211 patients who underwent TIPS for variceal bleeding or refractory cirrhosis due to HBV-related cirrhosis were included in this prospective cohort study. Of these, 124 (58.7%) patients started antiviral therapy before or after TIPS foremed the antiviral group, and the remaining 87 (41.3%) patient formed untreated group. The primary endpoint was transplant-free survival. The secondary endpoints included recurrent variceal bleeding, occurrence of complications and shunt dysfunction.

Results: The baseline characteristics were comparable in the two groups. Antiviral used included adefovir (n = 49), entecavir (n = 36), lamivudine (n = 29), telbivudine (n = 2), combination of lamivudine and adefovir (n = 7), and combination of lamivudine and telbivudine (n = 1). Among the patients in antiviral group, 20 died during the study period, as compared with 33 patients in the untreated group. Patients in antiviral group had a significantly better transplant-free survival ($P = 0.004$, by the log-rank test). The cumulative survival rates at 1, 2, and 3 year were 93.742%, 89.466% and 85.671% in the antiviral group, and 86.207%, 71.034% and 64.284% in the untreated group, respectively. Patients who started antiviral therapy before TIPS had better survival than post-TIPS antiviral patients. The use of antiviral therapy, age and MELD score were the independent predictors for survival. The incidence of HCC tend to be lower in the antiviral group, and the difference was borderline significant ($P = 0.053$). The cumulative incidence of HCC at 1, 2, and 3 year were 2.639%, 6.291% and 9.836% in the antiviral group, and 3.949%, 14.970% and 19.118% in the untreated group, respectively. The incidence of variceal rebleeding and primary shunt patency were not significantly different between the two groups (P = 0.126, P = 0.330 respectively).

Conclusion: Antiviral interventions improves survival in post-TIPS patients with HBV-related decompensated cirrhosis, especially in those with early treatment. This result underscore the use of antivirals as a mandatory etiology treatment in patients who underwent TIPS.

Disclosure of Interest: None declared

P0660 HIGH INCIDENCE OF RESISTANCE TO THIRD-GENERATION CEPHALOSPORINS IN CIRRHOTIC PATIENTS IN A PORTUGUESE GASTROENTEROLOGY DEPARTMENT

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Introduction: Bacterial infections are one of the main causes of decompensation in cirrhosis and contribute significantly for morbidity and mortality in cirrhotic patients.

Aims & Methods

Aims: Characterize the infections and microbiological agents in patients admitted for decompensated cirrhosis in a Gastroenterology Department in Portugal. Analyze the antibiotic therapy used in these patients and its effectiveness.

Methods: Retrospective analysis of incoming patients admitted for decompensated cirrhosis in 2013 in a Portuguese Gastroenterology Department. Clinical/demographic (cirrhosis' etiology, Child-Pugh score, previous hospitalizations,

antibiotic therapy, inpatient outcome) and microbiologic (infections' focus, agents and its sensibility profile) data were analysed.
Results: 95 patients were admitted for decompensated cirrhosis. Bacterial infections were the cause of decompensation in 54% (n = 51). Average age: 67 years; > 50% with advanced (Child-Pugh C, 71%) and alcoholic cirrhosis; average time of hospitalization: 11 days. We diagnosed 30 cases of health care-associated infections, 16 community-acquired infections and 5 nosocomial infections. The most frequent infection was urinary tract infection (47%, n = 24), followed by spontaneous bacterial peritonitis and respiratory tract infections, with the same incidence (22%, n = 11). The most commonly used empirical antibiotic therapy was third-generation cephalosporins (35%, n = 18), amoxicillin/clavulanic acid (22%, n = 11) and quinolones (17%, n = 9). In 45% of the patients, no agent was isolated. In the remaining patients, 36 agents were isolated. Two thirds were Gram negatives and *E. coli* was the most frequent. 40% of the agents were resistant to third-generation cephalosporins. Ten agents were multiresistant bacteria (four *extended-spectrum β-lactamase-producing enterobacteriaceae* and one *vancomycin-resistant enterococcus*). Hospitalization in the previous 90 days was related with infection by multiresistant agents ($p < 0.05$).
Conclusion: The difficulty in obtaining a microbiological isolate, makes antibiotic choice more challenging. Although third-generation cephalosporins continue to be a first-line antibiotic in patients admitted for decompensated cirrhosis, we found a significant resistance rate to these antibiotics. In the choice of antibiotic therapy, hospitalization in the last 90 days should also be considered because multiresistant bacteria involvement is more probable.

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Disclosure of Interest: None declared

P0661 LIVER CIRRHOSIS DOES NOT IMPAIR THE SHORT-TERM OUTCOME IN PEPTIC ULCER BLEEDING

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Introduction: Variceal bleeding in patients with liver cirrhosis is associated with a considerable mortality around 10-20%. The outcome of peptic ulcer bleeding (PUB) in patients with liver cirrhosis compared to patients without cirrhosis has not been studied in detail.
Aims & Methods: Data were prospectively collected from consecutive patients admitted with PUB at our department through an 11-year period. We compared patient characteristics, bleeding episode, and outcome between patients with liver cirrhosis and patients without cirrhosis.
Results: A total of 1002 patients were admitted with PUB during the period of inclusion. Thirty-five (3.5%) patients had cirrhosis. Compared to patients without liver cirrhosis patients with cirrhosis were younger (mean age: 58 vs 73 years; $p < .001$), were more often males (74% vs 54%; $p = .02$), more frequently had hemodynamic shock at time of admission to hospital (46% vs 29%; $p = .039$), a higher ASA-score ($p = .005$), high intake of alcohol (79% vs 12%; $p < .0001$), high frequency of daily smokers (78% vs 32%), and a longer duration of admission to hospital (mean: 7.5 vs 5.6 days; $p = .018$). However, patients with cirrhosis was only rarely diagnosed with cardiac disease (5.7% vs 42%; $p < .0001$) and only few had intake of aspirin (14% vs 50%; $p = .001$). There were no differences in B-hemoglobin (5.1 vs 5.4mmol/L), duodenal ulcer location (71% vs 57%), high-risk stigmata of bleeding (37% vs 39%), rate of rebleeding (20% vs 16%), or in-hospital mortality (8.6% vs 5.3%).
Conclusion: Patients with PUB and cirrhosis are younger and only rarely diagnosed with cardiac comorbidity compared with PUB-patients without cirrhosis. Nevertheless, patients with cirrhosis and PUB have a high level of non-cardiac comorbidity and negative lifestyle factors that may explain the lack of difference in short-term mortality. Beside a difference in rate of hemodynamic shock, that may be explained by impaired cardiac response in cirrhotics, the character and severity of PUB seem similar in both groups of patients.
Disclosure of Interest: None declared

P0662 THE PREVALENCE, PROGNOSIS AND OUTCOME OF SIRS, SEPSIS AND SEVERE SEPSIS IN PATIENTS WITH CIRRHOSIS OF THE LIVER

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Introduction: Cirrhotic patients are particularly susceptible to bacterial infections. Once an overt infection occurs, it may lead to systemic inflammatory response syndrome (SIRS)/sepsis which can precipitate hypotension (severe sepsis), renal dysfunction, encephalopathy, and coagulopathy, that is, multi organ failure. We studied sepsis and severe sepsis in a tertiary hospital in S India.
Aims & Methods
Aims: To estimate the prevalence of SIRS, sepsis and severe sepsis in patients with cirrhosis of liver and to study the pattern of clinical presentation; to assess the correlation between CRP and clinical outcomes in these patients and to elucidate the prognostic factors related to progression of disease and/ or death.
Methods: 70 patients with cirrhosis were prospectively evaluated at baseline, 3, 6, 9 and 12 months of follow up for sepsis, severe sepsis and septic shock and complications related to cirrhosis such as SBP, hepatorenal syndrome and mortality. Sepsis was diagnosed by CRP levels and culture of blood and urine. Data were analysed for study variables and survival.
Results: 70 patients (64 males and 6 females)in the age group of 30 -80 years were studied. 32.9% belonged to the 40-50 year age group. The mean age was 55.6 ± 10.1 years.The clinical presentation of patients with cirrhosis were as follows: melena in 57.1%; hematemesis and abdominal distension in 39 patients (55.7%). Alcohol consumption accounted for cirrhosis in 72.9%, Hepatitis B infection and concomitant alcohol intake in 11.4%, isolated Hepatitis B infection in 2.9% and Hepatitis C infection in 1.4%. No cause could be identified 10%.2 patients (2.9%) had SIRS, 12 patients had sepsis (17.1%), 6 had severe sepsis (8.6%), and 7 had septic shock (10%). Spontaneous bacterial peritonitis accounted for 48% of infections, followed by equal percentage of urinary tract infection, pneumonia and cellulitis (16% each), bacteremia was seen in 4%. CRP was positive in 25 patients (35.7%) and negative in 45 (64.3%). 29 patients (41.4%) hepatic encephalopathy; 18 had hepato renal syndrome (25.7%) and a total of 24 patients expired (34.3%). A statistically significant correlation was noted between CRP positivity and sepsis (p value- 0.000), severe sepsis (p value -0.001) and septic shock (p value -0.007), SBP (p value 0.000), UTI (p value -0.014) pneumonia (p value -0.014), hepatic encephalopathy (p value 0.000), hepatorenal syndrome (p value 0.000) and death (p value 0.000). A statistically significant correlation with mortality was established for severe sepsis (p 0.016), septic shock (p-0.000), SBP (P value 0.000), UTI (p 0.012), hepatic encephalopathy and hepatorenal syndrome. (p value- 0.000). 12 patients had SBP during their initial presentation. The prevalence of SBP at 3, 6,9,12 months was 7(10%), 8(11.4%), 3(4.3%), 5(7.1%). 24 patients had expired at the end of 1 year and 4 were lost to follow up.malaena was the presenting feature in 40 patients.
Conclusion: There was high prevalence of sepsis and severe sepsis with a high mortality at 1 year of follow up.
Disclosure of Interest: None declared

P0663 THE EFFECT OF LACTULOSE, RIFAXIMIN, L-ORNITHINE L-ASPARTATE, THEIR COMBINATION ON MINIMAL HEPATIC ENCEPHALOPATHY TREATMENT

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Introduction: Minimal hepatic encephalopathy (MHE) is observed in 84% of patients with liver cirrhosis without the presence of overt HE. It adversely affects health-related quality of life (HRQOL).
Aims & Methods
Aim: to compare lactulose, rifaximin, L-Ornithine L-Aspartate (LoLa), their combination on MHE treatment and HRQOL.
Methods: After screening for MHE, 126 patients with MHE were assigned for the following treatment regimens; 30-60 ml lactulose twice daily (n = 31), 200 mg rifaximin thrice daily (n = 32), 6 g LoLa thrice daily (n = 32), and combined therapy (n = 31). All patients were assessed by critical flicker frequency (CFF), number connection test (NCT), serial dotting test (SDT), ammonia and sickness impact profile (SIP) questionnaire at baseline and two consecutive months.
Results: By repeated measure ANOVA test, there was favorable treatment induced changes in all groups concerning the three consecutive values of CFF (36.6 vs. 31.33 vs. 38.09 Hz; $p = 0.001$ except LoLa; $p = 0.167$), NCT (-2.5 vs. -1.15 vs. -0.9 SD; $p = 0.001$), SDT (-2.6 vs -1.27 vs. -1.07 SD; $p = 0.001$), ammonia (85.75 vs. 76.93 vs. 69.65 mmol/l; $p = 0.001$ except rifaximin; $p = 0.50$) and SIP questionnaire score (24.75 vs. 16.1 vs. 16.31; $p = 0.001$). The overall comparison of all groups was insignificant ($p > 0.05$). The predictors of MHE were age (odds = 1.069), bilirubin (odds = 5.254), albumin (odds = 0.163), INR (odds = 73.816) and Child-Pugh score (odds = 2.459).
Conclusion: Lactulose, rifaximin, LoLa, their combination are the same on MHE treatment and HRQOL.
Disclosure of Interest: None declared

P0664 NUTRITIONAL STATUS OF CIRRHOTIC PATIENTS IN A REFERRAL CENTRE FOR LIVER DISEASE IN CRETE GREECE

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Introduction: Prognosis of cirrhotic patients is related to their nutritional status even in the compensated stages. Protein-energy malnutrition is not always recognized by attending physicians.
Aims & Methods: We aimed to assess the nutritional status of Greek cirrhotic patients, followed at the Department of Gastroenterology and Hepatology of the University Hospital of Heraklion (Crete, Greece).

We studied 101 cirrhotic patients (48 compensated, 52 females), median age 67.07 (31-88) years and 71 healthy controls (35 females), median age 66.04 (37-94) years. Cirrhosis etiology was viral hepatitis 43 pts. (23 HCV, 20 HBV), 20 non alcoholic steatohepatitis (NASH), 14 primary biliary cirrhosis (PBC), 5 autoimmune hepatitis (AIH), 14 alcoholic and 3 cryptogenic. Patients with hepatic encephalopathy or active alcohol drinking were not included in the study. MELD score was calculated to assess the severity of liver disease. Nutritional assessment included Body mass index (BMI), anthropometry, handgrip strength, bio-impedance analysis (BIA), the mini nutritional assessment (MNA) questionnaire, the Subjective Global Assessment (SGA) and the Malnutrition Universal Screening Tool (MUST) evaluation.
Comparisons were made by Student's T-test for continuous variables. Fisher's exact probability test and the $\chi 2$ test for the analysis of categorical variables. Spearman's rank coefficient was used for correlations. All tests were made at a 0.05 level of significance.
Results: Median MELD score was 14.6 (SD 2.43),
Parameters with significant differences between groups are shown in the table. MUST score and SGA score also differ significantly between groups ($p < 0.001$). A strongly positive correlation between MELD & MNA (rho = 0.87, p = 0.01) and strongly negative correlations between MELD and phase angle (ϕ) (rho = -0.80, p = 0.01) and MELD & handgrip (rho = -0.79, $p < 0.001$) were found.

Parameters	PatientsMean (SD)	ControlsMean (SD)	p value
BMI	29.85 (5.93)	28.08 (5.68)	**0.04**
MAMC	21.68 (3.29)	23.11 (3.44)	**0.007**
Handgrip (kg)	27.26 (11.61)	42.90 (10.34)	**0.002**
Handgrip <85%	70%	30%	**<0.001**
(BIA) ICW%	45.41 (10.58)	48.93 (9.81)	**0.04**
(BIA) BCM%	46.21 (11.74)	51.61 (11.55)	**0.01**
(BIA)Muscle mass%	37.13 (8.71)	42.90 (10.34)	**0.02**
(BIA) Phase angle (ϕ)	4.9 (1.15)	5.67 (1.22)	**<0.001**
MNA	21.78 (3.94)	23.39 (3.91)	**0.01**

Conclusion: BMI and most anthropometric measurements, except MAMC, did not detect the protein malnutrition of Greek cirrhotic patients. MUST, SGA, MNA, BIA, and handgrip were found all sensitive tools for its detection, the last three also correlating with the severity of liver disease.
Disclosure of Interest: None declared

P0665 TERLIPRESSIN AND ALBUMIN IS AN EFFECTIVE TREATMENT IN PATIENTS WITH CIRRHOSIS AND HEPATORENAL SYNDROME TYPE 2

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Introduction: Untreated hepatorenal syndrome (HRS) is associated with a very bad prognosis in patients with advanced liver cirrhosis. Hepatorenal syndrome is subdivided into a HRS type 1 with a rapid-progressive loss of renal function and a HRS type 2, characterized by chronic ascites and persistently but moderately elevated renal parameters. While treatment with terlipressin and albumin improves renal function in patients with type 1 HRS, it is less clear if this treatment is effective in type 2 HRS.
Aims & Methods: Aim of this study was to examine the effect of treatment with terlipressin and albumin on renal function and survival in patients with HRS type 2.
All patients who presented to our center between April 2013 and February 2015 with a first episode of HRS type 1 or type 2 and who were treated with terlipressin and albumine were included in this observational study. Relevant clinical and laboratory parameters were prospectively examined – e.g. HRS type, baseline liver function, patient characteristics, side effects, renal function and overall survival as well as survival free of renal replacement therapy or liver transplantation.
Results: Overall 80 patients with liver cirrhosis and a first episode of HRS were prospectively followed over a median of 76 days. Most patients had advanced liver disease (Child-Pugh C: 67; 84%). 29 patients had HRS type 1, while 51 patients were diagnosed with a type 2 HRS (36%; 64%). Baseline patient characteristics such as etiology of cirrhosis, Child-Pugh stage, degree of ascites or hepatic encephalopathy grade were similar in both subgroups. As expected, median serum creatinine concentration was significantly higher in patients with HRS type 1 (3.1 vs. 2.4 mg/dl; p = 0.0003). Complete or partial response to terlipressin treatment was observed in 38 and 4 of 80 patients (CR: 48%; PR: 5%). Overall response rates were not significantly different between patients with HRS type 2 and type 1 (52% vs. 53%; p = 0.92). Overall survival and survival free of renal replacement therapy or liver transplantation was comparable too. Response to terlipressin treatment in HRS type 2 was associated with a significantly improved median survival ($p < 0.0001$).
Conclusion: Terlipressin in combination with albumine is effective in HRS type 2 – a response to treatment can be expected in approximately 50% of patients. Response to treatment is an important prognostic indicator as it is associated with improved survival.
Disclosure of Interest: None declared

P0666 SCREENING FOR HEPATOPULMONARY SYNDROME IN CIRRHOTIC PATIENTS: DIAGNOSTIC APPROACH AND CLINICAL CORRELATIONS

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Introduction: Hepatopulmonary syndrome (HPS) affects 10-30% of patients with cirrhosis and/or portal hypertension, but is frequently underdiagnosed. It is characterized by the triad of advanced liver disease, arterial hypoxemia and intrapulmonary arteriovenous shunting in absence of primary cardiopulmonary disease. The aim of the study was to screen cirrhotics with arterial blood gases and albumin perfusion scan, identify those fulfilling the classic HPS criteria and correlate with clinical parameters.
Aims & Methods: Data on 102 patients presenting to the Liver Clinic or hospitalized in the Gastroenterology wards within one year and were analyzed. Clinical, metabolic and biochemical variables were measured, as well as MELD MELDNa, and Child-Pugh score, arterial blood gases, alveolar-arterial oxygen gradient [P(A-a)O2] were recorded. All patients underwent Technetium 99m-macroggregated albumin perfusion lung scan (Tc-MAA) and a subset of those had contrast-enhanced transthoracic echocardiography with saline (microbubbles >10μm in diameter). Diagnosis of HPS was based on the presence of the quantitative index Tc-MAA ≥ 6% and a $[P(A\text{-}a)O_2] \geq 15$mmHg ($\geq$20 mmHg for patients over > 64 years).
Results: 61 were male (59.8%) .Median age 66.5 years (range, 31-84). Mean BMI was 27.5 (SD 4.7) and median MELD was 12 (range, 6-22). 66 patients presented with decompensated cirrhosis, 10 with HCC. The mean P(A-a)O2 and P02 were 24 (SD14.1) and 81.3 (SD13.6) mmHg respectively. Patients with concomitant respiratory disease had all P(A-a)O2 > 20mmHg and were not evaluated further for HPS. Average P(A-a)O2 did not differ according to decompensation status (P = 0.6).
Quantitative median index in the Tc-MAA was 6% (range, 1-17). Diagnosis of HPS was made on 24/94 patients. In 8 patients the Tc-MAA scintigraphy could not be interpreted. In the multivariate analysis only the quantitative index was significant for the diagnosis of HPS. (p = 0.001, OR; 95% CI: 7,05; 2,27-21,87) Three patients with positive bubble echo had all quantitative index > 9% in Tc-MAA. The latter index was not statistically correlated with P(A-a)O2, PO2, or MELD score (p = n.s). Five patients died over the short follow-up period with no significant differences in survival time according to P(A-a)O2 or the results of Tc-MAA.
Conclusion: Tc-MAA is a useful screening tool in patients with arterial hypoxemia for complications as HPS which is a frequent complication of cirrhosis. Qualitative analysis is not reliable with false negative and positive results. Quantitative analysis should always be performed.

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P0667 SOLUBLE CD163 (SCD163) IS A MARKER OF INFECTION IN PATIENTS WITH CIRRHOSIS AND ACUTE DECOMPENSATION AND AN INDEPENDENT PREDICTOR OF THE SHORT-TERM MORTALITY

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Introduction: sCD163 is shed from macrophages in response to inflammatory stimuli and suggested to modulate the inflammatory response. We aimed to determine the predictive potential of sCD163 levels in the determination of disease phenotype and disease course in a prospective referral cirrhotic cohort.
Aims & Methods: 378 consecutive patients with cirrhosis(LC) of different etiology (54.0% males, 70.6% alcoholic) and severity (ChildA/B/C: 39.2/38.1/22.7%, acute decompensation[AD]: 48.9%) were enrolled and followed until death or last attendance. Serum levels obtained at enrollment were assayed for

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SVR12 by baseline factors, n/N (%)	GT1a with no cirrhosis 3D + RBV for 12 weeks	GT1a with cirrhosis 3D + RBV for 24 weeks	Overall
Overall	569/593 (96)	115/121 (95)	684/714 (96)
Sex			
Male	353/370 (95)	84/89 (94)	437/459 (95)
Female	216/223 (97)	31/32 (97)	247/255 (97)
Treatment-naïve	403/420 (96)	53/56 (95)	456/476 (96)
Prior PegIFN/RBV non-response	47/50 (94)	13/13 (100)	60/63 (95)
Relapse	36/36 (100)	10/10 (100)	46/46 (100)
Partial response	83/87 (95)	39/42 (93)	122/129 (95)
Null response			
IL28B genotype	157/163 (96)	24/25 (96)	181/188 (96)
CCCTTT	323/338 (96)	72/75 (96)	395/413 (96)
	89/92 (97)	19/21 (90)	108/113 (96)

sCD163 by ELISA. Detailed clinical phenotypes regarding first decompensation event (ascites formation, variceal bleeding[VB], hepatic encephalopathy or systemic bacterial infection[INF]), development of hepatocellular carcinoma[HCC] and mortality were determined prospectively during the follow-up (median[IQR], 778[182-1720] days). Control group comprised 150 healthy subjects (HC).
Results: Serum levels of sCD163 were significantly higher in patients with LC compared to HC (median, 3724 vs. 1104 ng/ml,$p < 0.001$). In LC, sCD163 levels were associated to disease severity, as rated by the Child-Pugh stage ($p < 0.001$) but not to the presence of varices or prior VB. In non-AD patients, sCD163 levels were not able to predict the advent of the first decompensation events, development of HCC and also not the long-term mortality. In patients with AD episodes, sCD163 levels were significantly higher compared to non-AD patients but only in the presence of INF (AD-INF: 4969, AD-NON-INF: 3497 and NON-AD: 3471 ng/ml, $p < 0.001$ for both). Furthermore, during INF episodes ($n = 119$), sCD163 levels were significantly higher in those complicated with organ failure (31%) and increased gradually according to ACLF grade (No-ACLF: 4121, ACLF gr1: 7335, gr2: 7490, gr3: 12610 ng/ml, $p = 0.001$). Rate of 28-day mortality was higher among patients with sCD163 level > 7110 ng/ml compared to those with ≤ 7110 ng/ml (46.5% vs. 15.8%, $p < 0.001$). This cut-off level of sCD163 was associated with a shorter time to death (pLogRank < 0.001) in Kaplan-Meier analysis and was identified as an independent predictor in multivariate Cox- regression model (HR:2.91, 95%CI:1.34–6.32,$p = 0.007$) comprising age, gender, etiology, co-morbidity and MELD score as covariates.
Conclusion: Admission sCD163 levels may be an additional help in rapid identification of patients with high-risk for death during AD epsiodes complicated with INF in LC.
Disclosure of Interest: None declared

P0668 SUSTAINED VIROLOGIC RESPONSE RATE OF 96% IN HCV GENOTYPE 1A-INFECTED PATIENTS TREATED WITH OMBITASVIR/PARITAPREVIR/R AND DASABUVIR WITH RIBAVIRIN

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Introduction: The interferon-free 3 direct-acting antiviral (3D) regimen of ombitasvir (an NS5A inhibitor), paritaprevir (an HCV NS3/4A protease inhibitor identified by AbbVie and Enanta, boosted with ritonavir [r]) and dasabuvir (a non-nucleoside NS5B RNA polymerase inhibitor) is approved to treat patients infected with HCV genotype (GT) 1. Using pooled data from four phase 3 studies in treatment-naïve and prior pegIFN/RBV-experienced patients with GT1a infection, with or without cirrhosis, we report the safety and efficacy in patients who received the label-recommended 3D regimen plus ribavirin (RBV).
Aims & Methods: Genotype 1a-infected patients from the PEARL-IV, SAPPHIRE-I, SAPPHIRE-II, and TURQUOISE-II studies were included in this post-hoc analysis. Efficacy was assessed by the proportion of patients achieving sustained virologic response (HCV RNA <25 IU/mL) 12 weeks after completion of treatment (SVR12). Per the US Prescribing Information and European SmPC, the label-recommended regimen for GT1a infection is 3D + RBV for 12 weeks in non-cirrhotic patients, and 3D + RBV for 24 weeks in patients with cirrhosis. Adverse events (AEs) and laboratory measures are reported for all patients receiving the label-recommended regimen.
Results: Among 714 HCV GT1a-infected patients treated with the label-recommended 3D + RBV regimen, 64% were male, 33% were treatment-experienced, 17% had cirrhosis, and 85% had baseline viral loads ≥800,000 IU/mL. Sustained virologic response was achieved in 96% (95% CI, 94-97%) of patients (**Table**). Response rates were similar regardless of the presence or absence of cirrhosis (95 versus 96%, respectively). Virologic failure was observed in 18 (2.5%) patients, 5 (0.7%) with on-treatment breakthrough and 13 (1.8%) with post-treatment relapse. Seven patients (1.0%) discontinued treatment due to AEs, 4 of whom subsequently achieved SVR12. The most common AEs were fatigue (41%), headache (33%), nausea (23%), and insomnia (17%). Grade 3+ laboratory abnormalities were infrequent for ALT (0.9%), AST (0.6%), haemoglobin (0.3%), and total bilirubin (2.8%).
Conclusion: In HCV GT1a-infected patients, the label-recommended 3D regimen with RBV achieved high SVR12 rates, including historically difficult-to-cure subgroups of patients with prior PR null response and/or cirrhosis.
Disclosure of Interest: H. Wedemeyer Financial support for research: Abbott, Bristol-Myers Squibb, MSD, Novartis, Roche, Consultancy: Abbott, AbbVie, Achillion, BMS, Boehringer Ingelheim, Gilead, GSK, ITS, Janssen, Merck, Novartis, Roche, Roche Diagnostics, Siemens, Transgene, P. Pockros Financial support for research: Gilead, AbbVie, Janssen, Bristol-Myers Squibb, Merck, Conatus, Roche Molecular, Consultancy: Gilead, AbbVie, Janssen, Bristol-Myers Squibb, S. Lee Financial support for research: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead, Idenix, Janssen, Merck, Roche, Vertex, Lecture fee(s): Bristol-Myers Squibb, Gilead, Merck, Roche, Vertex, Consultancy: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead, Idenix, Janssen, Merck, Roche, Vertex, E. Gane Consultancy: AbbVie, Gilead, Achillion, Idenix, Novartis, Roche, Merck, Janssen, C. Moreno Financial support for research: Merck, Janssen, Gilead, Novartis, Roche, Lecture fee(s): MSD, Janssen, Gilead, AbbVie, Bristol-Myers Squibb, Consultancy: MSD, Janssen, Gilead, AbbVie, Bristol-Myers Squibb, S. Strasser Lecture fee(s): AbbVie, Janssen, MSD, Bristol-Myers Squibb, Gilead, Roche, Consultancy: AbbVie, Janssen, MSD, Bristol-Myers Squibb, Gilead, Roche, V. De Ledinghen Consultancy: AbbVie, Bristol-Myers Squibb, Gilead, Merck, Janssen, Echosens, A. Maieron Financial support for research: Roche, MSD, Consultancy: MSD, Janssen Therapeutics, AbbVie, Boehringer Ingelheim, Gilead, Bristol-Myers Squibb, Rottapharm-Madaus, W. Xie Shareholder: AbbVie, Conflict with: AbbVie, R. Trinh Shareholder: AbbVie, Conflict with: AbbVie, Y. Luo Shareholder: AbbVie, Conflict with: AbbVie, F. Tatsch Shareholder: AbbVie, Conflict with: AbbVie, V. Rustgi Financial support for research: AbbVie, Gilead, Hyperion, Inovio, Consultancy: AbbVie, Bristol-Myers Squibb, Gilead, Merck

P0669 99.7% SUSTAINED VIROLOGIC RESPONSE RATE IN 369 HCV GENOTYPE 1B-INFECTED PATIENTS TREATED WITH LABEL-RECOMMENDED REGIMEN OF OMBITASVIR/PARITAPREVIR/R AND DASABUVIR WITH OR WITHOUT RIBAVIRIN

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Introduction: The 3 direct-acting antiviral (3D) regimen of ombitasvir (an NS5A inhibitor), paritaprevir (an HCV NS3/4A protease inhibitor identified by AbbVie and Enanta, boosted with ritonavir) and dasabuvir (a non-nucleoside NS5B RNA polymerase inhibitor) is approved to treat patients infected with HCV genotype (GT) 1. We report the safety and efficacy of the label-recommended 3D regimen with or without ribavirin (RBV) in treatment-naïve and prior pegIFN/RBV-experienced patients with GT1b infection, with or without cirrhosis, using pooled data from three phase 3 studies.
Aims & Methods: Genotype 1b-infected patients from the PEARL-II, PEARL-III, and TURQUOISE-II studies were included in this post-hoc analysis. Efficacy was assessed by the proportion of patients achieving sustained virologic response (HCV RNA <25 IU/mL) 12 weeks after completion of treatment (SVR12). Per the US Prescribing Information and European SmPC, the label-recommended regimen for GT1b infection is 3D for 12 weeks in non-cirrhotic patients, and 3D + RBV for 12 weeks in patients with cirrhosis. Adverse events (AEs) and

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SVR12 by baseline factors, n/N (%)	GT1b without cirrhosis 3D for 12 weeks	GT1b with cirrhosis 3D + RBV for 12 weeks	Overall
Overall	301/301 (100)	67/68 (98.5)	368/369 (99.7)
Sex			
Male	141/141 (100)	44/45 (97.8)	185/186 (99.5)
Female	160/160 (100)	23/23 (100)	183/183 (100)
Treatment-naïve	210/210 (100)	22/22 (100)	232/232 (100)
Prior PegIFN/RBV non-response			
Relapse	33/33 (100)	14/14 (100)	47/47 (100)
Partial response	26/26 (100)	6/7 (85.7)	32/33 (97.0)
Null response	32/32 (100)	25/25 (100)	57/57 (100)
IL28B Genotype			
CC	51/51 (100)	9/10 (90.0)	60/61 (98.4)
CT	197/197 (100)	45/45 (100)	242/242 (100)
TT	53/53 (100)	13/13 (100)	66/66 (100)

laboratory measures are reported for all patients receiving the label-recommended regimen.
Results: Among 369 HCV GT1b-infected patients treated with the label-recommended 3D ± RBV regimen, 50% were male, 37% were treatment-experienced, 18% had cirrhosis, 83% had an IL28B non-CC genotype, and 78% had baseline viral loads ≥800,000 IU/mL. Sustained virologic response was achieved in 368/369 (99.7%; 95% CI, 98.2-99.9%). One patient experienced post-treatment relapse, a 56 year-old white male with cirrhosis who received 3D + RBV. The majority of AEs were mild to moderate in severity, and most common AEs were headache (24%), fatigue (22%), and asthenia (9%). Grade 3 laboratory abnormalities were infrequent for ALT (0.3%), AST (0.3%), and total bilirubin (2.2%). No patient experienced a grade 3 haemoglobin decline and no patient discontinued treatment prematurely due to an AE.

Conclusion: Patients with HCV GT1b infection treated with the label-recommended 3D regimen, with or without RBV, achieve very high SVR12 rates, including those with historically difficult-to-cure disease characteristics such as prior pegIFN/RBV null response and cirrhosis.
Disclosure of Interest: J.-F. Dufour Lecture fee(s): Bayer, Boehringer-Ingelheim, Novartis, and Roche, Consultancy: Bayer, Bristol-Myers Squibb, Gilead, Janssen Cilag, Jennerex, Merck, Novartis, Roche, H. Wedemeyer Financial support for research: Abbott, Bristol-Myers Squibb, MSD, Novartis, Roche, Lecture fee(s): Abbott, AbbVie, Achillion, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead, GSK, ITS, Janssen, Merck, Novartis, Roche, Roche Diagnostics, Siemens, Transgene, Consultancy: Abbott, AbbVie, Achillion, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead, GSK, ITS, Janssen, Merck, Novartis, Roche, Roche Diagnostics, Siemens, Transgene, D. Bernstein Financial support for research: AbbVie, Bristol-Myers Squibb, Gilead, Janssen, Vertex, Merck, Genentech, Lecture fee(s): AbbVie, Gilead, Janssen, Vertex, Merck, Consultancy: AbbVie, Gilead, Janssen, Vertex, Merck, M. Colombo Financial support for research: Merck, Roche, Bristol-Myers Squibb, Gilead, Lecture fee(s): Tibotec, Roche, Novartis, Bayer, Bristol-Myers Squibb, Gilead, Vertex, Consultancy: AbbVie, Merck, Roche, Novartis, Bayer, Bristol-Myers Squibb, Gilead Sciences, Tibotec, Vertex, Janssen Cilag, Achillion, Lundbeck, Abbott, Boehringer Ingelheim, GSK, GenSpera, M. Romero-Gomez Lecture fee(s): AbbVie, Roche, Gilead, MSD, Janssen, Merz, Bristol-Myers Squibb, Boehringer Ingelheim, GSK, Consultancy: AbbVie, Roche, Gilead, MSD, Janssen, Merz, Bristol-Myers Squibb, Boehringer Ingelheim, GSK, N. Reau Financial support for research: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Merck, Consultancy: AbbVie, Bristol-Myers Squibb, Gilead, Merck, R. Trinh Shareholder: AbbVie, Conflict with: AbbVie, W. Xie Shareholder: AbbVie, Conflict with: AbbVie, J. Enejosa Shareholder: AbbVie, Conflict with: AbbVie, D. Cohen Shareholder: AbbVie, Conflict with: AbbVie, M. Martinez Shareholder: AbbVie, Conflict with: AbbVie, I. Jacobson Financial support for research: AbbVie, Achillion, Bristol-Myers Squibb, Gilead, Janssen, Merck, Lecture fee(s): AbbVie, Bristol-Myers Squibb, Gilead, Janssen, Consultancy: AbbVie, Achillion, Bristol-Myers Squibb, Enanta, Gilead, Janssen, Merck, Roche

P0670 HEPATITIS C VIRUS–ASSOCIATED B-CELL NON-HODGKIN LYMPHOMAS – AN ALTERNATIVE THERAPEUTIC APPROACH?

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Introduction: The most compelling argument for a causal relationship between hepatitis C virus (HCV) infection with B-cell non-Hodgkin Lymphoma (B-NHL) results from the demonstration of regression of some indolent B-NHL with the eradication of HCV. The role of HCV treatment as a first line therapy remains to be defined, particularly with the availability of new antivirals.
Aims & Methods: Clinical and demographic characterization of population with B-NHL and hepatitis C. Evaluation of eligibility for HCV therapy as the first line treatment for B-NHL.
Retrospective study of patients with B-NHL anti-HCV+, followed in a clinical center for 11 years. The clinical and demographic characteristics were analysed. Eligibility criteria for HCV therapy: indolent lymphomas, unless bulky or symptomatic disease.
Results: Of 2826 patients with B-NHL 37 were anti-HCV+, 17 men, mean age 60 ± 16 years. Viral load determined in 21 patients, detected in 16 (HCV-RNA +).
Fifteen patients had indolent lymphomas (non-classifiable-5, extranodal marginal-2, chronic lymphocytic leukemia-4, lymphoplasmacytic lymphoma-2, follicular lymphoma-2). Eleven were HCV-RNA+. According to the eligibility criteria, one would be excluded for being bulky and the remaining 10 would be candidates for primary therapy of HCV (only 7 eligible for INFpeg and ribavirin: 2 non responders to prior treatment and 1 anemia). No patient was treated for HCV as first-line therapy for lymphoma. 10/15 patients received chemotherapy (CT). Two patients had elevated transaminases during chemotherapy that did not require dose reduction.
Conclusion: Given the low prevalence of HCV infection, the number of patients who could benefit from anti-HCV therapy as primary treatment for B-NHL is reduced. However, given the possibility of regression of indolent lymphomas and the availability of new drugs for HCV with fewer side effects and greater efficiency, this therapy should be offered to eligible patients before chemotherapy.
Disclosure of Interest: None declared

P0671 "EARLY" SUBCLINICAL LEFT VENTRICULAR DISFUNCTION IN HEPATITIS C VIRUS INFECTION

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Introduction: Hepatitis C virus (HCV) infection has been associated with several extrahepatic manifestations in a variety of tissues and organs, including the myocardium. Reduced myocardial perfusion or increased pro-B-type natriuretic peptide (NT-proBNP) have been described in HCV-infected individuals but, until now, no study clearly demonstrated the occurrence of myocardial dysfunction in the early stages of HCV-related liver diseases
Aims & Methods: Aim was to evaluate the impact of HCV infection on ventricular geometry and function by a standard 2D and 3D echocardiography.
50 out of 125 consecutive genotipe 1 HCV infected patients with histologically proved HCV-related chronic hepatitis and 30 Healthy Controls (HCs), comparable for age and gender prevalence were enrolled in the study. Laboratory tests, abdominal utrasonography, liver biopsy or FibroScan and ecocardiography were performed in all the patients. The echocardiography protocol consisted of: standard echo Doppler plus LV volumetric and systolic function analysis through 3D echocardiography. Left ventricular systolic function thorough 3D echo was evaluated by Speackle tracking echocardiography (STE) derived global longitudinal strain (GLS), global circumferential strain (GCS), global area strain (GAS) and global radial strain (GRS).
Results: Overall we enrolled 28 males and 22 females with HCV (genotype 1) related chronic liver disease. Mean age was 59.8 ± 6.9yrs. Age, gender distribution, body mass index, heart rate and blood pressure did not significantly differ between patients and controls. In HCV infected subjects standard 2D echocardiography point out a transmitral E/A ratio marginally lower (0.84 ± 0.2) compared to HC (1.01 ± 0.3) (p = 0.04). Moreover, more detail 3D STE showed in 38 (76%) of the cases a subclinical alteration of LV function, documented by lower GCS (HCV = -15.3 ± 2.2%, HC = -17.6 ± 3.9%, p = 0.02), GAS (-25.2 ± 2.6%, HC -29.9 ± 5.2%, p = 0.03), and GRS (37.6 ± 4.6% vs 44.9 ± 12%, p = 0.04) whereas HCV-releated changes of GLS were not significant. Interestingly, myocardial impairment was independent of viral load and staging of liver biopsy.
Conclusion: HCV infected patients show a subclinical myocardial dysfunction independently of viral load and liver fibrosis; circumferential fibers of the left ventricular mid wall are primarily involved in LV subclinical dysfunction.

Abstract number: P0674 Table 1: Week zero and week 72 values of different biomarker panels among group 1 (SVR) and groups 5 (control) patients.

Biomarker panels	Week zero(95 % CI)	Week 72(95 % CI)	P-value
APRI (mean ±SD)- SVR- Control	1.14±1.160.9 ±0.92	0.44± 0.41.14±1.27	<0.0010.004
FIB-4 (mean ±SD)- SVR- Control	2.13±1.462.52±2.25	1.52±0.892.86± 2.5	<0.0010.058*
PLASA(mean ±SD)- SVR- Control	0.53±1.180.53±1.04	-0.29±0.630.71±1.19	<0.0010.008
FRT(mean ±SD)- SVR- Control	10.0± 3.511.8± 6.5	8.4 ±1.913.6±10.1	<0.0010.034
Fibro-alpha(mean ±SD) - SVR- Control	1.33±0.131.38±0.25	1.36±0.131.42± 0.3	<0.0010.057*
BRC(mean ±SD)- SVR- Control	7.5 ±3.110.0± 6.8	6.9 ±2.511.7± 9.9	0.0160.038

*Non -significant difference. SVR: Sustained virologic response

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Disclosure of Interest: None declared

P0672 USEFULNESS OF LIVER FIBROSIS ASSESSMENT IN PATIENTS WITH CHRONIC HEPATITIS C (CHC) USING GLYCO-ISOMER OF SERUM MAC-2-BINDING PROTEIN

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Introduction: The degree of liver fibrosis is a major issue for making decision of therapeutic strategies on chronic liver diseases. Recently glyco-isomer of serum Mac-2-binding protein (M2BPGi) could be supposed to be a novel and useful biomarker to assess liver fibrosis. However little is known about its usefulness for diagnosis of CHC patients.

Aims & Methods: In this study, we were trying to reveal the significance of serum M2BPGi for assessment of liver fibrosis. One hundred twenty seven CHC patients (male/female = 67/60, mean age 58 y.o.) scheduled for the anti-viral therapy were enrolled. Liver biopsies were undertaken in all of the patients. We evaluated the relation between liver fibrotic degrees and the serum levels of M2BPGi, and the correlation between the serum levels of M2BPGi and examined liver function tests, i.e. T-Bil, AST, ALT, GGT, platelet, AFP, γ-globulin and hyaluronic acid (HA). Additionally we evaluated the ability of M2BPGi by Receiver Operating Characteristic (ROC) analysis compared with the serum levels of HA and Fib4 index.

Results: The patients were classified into two groups according to liver fibrosis stage, F0 (n = 34) and F1/2 (n = 93). The serum levels of M2BPGi were significantly higher in F1/2 group (median = 1.73C.O.I.) than in F0 group (median = 0.85C.O.I.), ($p < .0001$). Among the other serum liver tests, the levels of serum HA were strongly related with liver fibrosis stage (F0 = 23.0ng/ml vs F1/2 = 93.5ng/ml, $p < .0001$), and the serum levels of AST (F0 = 32IU/L vs F1/2 = 50IU/L, $p < .0005$), ALT (F0 = 36IU/L vs F1/2 = 59IU/L, $p < .01$), platelet (F0 = 21.0×10^4/μl vs F1/2 = 16.9×10^4/μl, $p < .001$) and γ-globulin (F0 = 18.6% vs F1/2 = 21.1%, $p < .001$) also indicated significant difference between the two groups. The serum levels of M2PBGi showed the positive correlation with the serum levels of AST (R = 0.32), ALT (R = 0.26), GGT (R = 0.29), γ-globulin (R = 0.38) and HA (R = 0.70), and the negative correlation with the serum levels of platelet (R = -0.28), respectively. ROC analysis showed that both serum HA (AUC = 0.830) and the Fib4 index (AUC = 0.809) were the most useful determinants of liver fibrosis comparing between the two groups. The serum levels of M2BPGi (AUC = 0.759) showed the possible indicator for liver fibrosis staging as well.

Conclusion: In this study, we could demonstrate that the serum M2BPGi was a potentially significant biomarker for liver fibrosis, even in minimal or mild liver fibrosis. The serum M2BPGi could be one of the most useful tools for assessment of liver fibrosis in CHC patients.

Disclosure of Interest: None declared

P0673 RESPONSE TO HEPATITIS B VACCINE IN CHRONIC HEPATITIS C EGYPTIAN PATIENTS

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Introduction: Egypt is cursed with the highest worldwide prevalence of chronic hepatitis C (CHC). Patients with CHC are advised to be vaccinated against hepatitis B virus (HBV) infection. Response to vaccination and risk factors for weak response are not clearly identified.

Aims & Methods

Aim: To assess response to hepatitis B vaccination in CHC patients and identify predictors of weak response.

Patients and methods: This prospective study included 112 consecutive adult, treatment- naive patients with CHC (cases group) and 54 non HCV subjects (control group). Demographic and laboratory variables including HCV-viral load and antischistosomal antibody beside histopathological examination were all collected. Three doses (0, 1 & 6 months) of HBV-vaccine (Euvax B, LG Life Sciences, Korea) were given and hepatitis B surface antibody (HBs-Ab) titre was evaluated 1.5 - 2 months after the 3rd dose.

Results: Out of 112 patients with CHC, 5 (4.5%) had HBs Ab titre less than 10 IU, 20 (17.9%) had less than 100 IU, and 50 (44.6%) had more than 1000 IU. In comparison, out of 54 controls, one (1.9%) had less than 10 IU, 2 (3.8%) had less than 100 IU, and 41 (75.9%) had more than 1000 (P = 0.001). CHC patients had highly significant lower mean antibody titre than controls ($P < 0.001$). In univariate regression analysis, HBs Ab titre was negatively associated with age ($P < 0.001$), ALT (P = 0.03), AST (P = 0.03), FIB4 score (P = 0.008), and antischistosomal antibody titre (P = 0.007) and positively associated with platelet count (P = 0.01). There was no association with gender, body mass index, viral load or other variables (including METAVIR grade or stage). Multivariate regression analysis in CHC patients showed that age (P = 0.02) and antischistosomal antibody titre (P = 0.04) were the independent predictors for HBs Ab titre response.

Conclusion: CHC patients have a significantly weak response to HBV-vaccine, particularly those with older age and schistosomiasis.

Disclosure of Interest: None declared

P0674 DIFFERENT SERUM FIBROSIS BIOMARKERS AS MONITORING TOOLS FOR DETECTING FIBROSIS REGRESSION IN TREATED HCV PATIENTS

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Introduction: Treating chronic hepatitis C (CHC) is associated with improving long-term outcomes and health-related quality of life. Monitoring fibrosis regression in response to treatment is important to identify patients with residual cirrhosis after CHC cure as they need long-term surveillance for hepatocellular carcinoma (HCC). Due to limitations of repeating liver biopsy after treatment; surrogate biomarkers can be an alternative to monitor fibrosis regression and to identifying patients with residual cirrhosis.

Aims & Methods: We aimed at monitoring regression of fibrosis in a group of CHC patients in response to treatment by calculating six different panels (APRI, FIB-4, PLASA, FRT, Fibro-alpha and BRC) used as non-invasive markers of hepatic fibrosis. Data of 363 CHC patients (140 males) were retrospectively analyzed. Data included pretreatment and post treatment laboratory parameters according to the national guidelines for treating CHC in Egypt (2007-2014). Patients were classified into 4 groups according to treatment response; patients who had sustained virologic response (group 1; n = 90), relapsers after treatment (group 2; n = 65), patients who had breakthrough during treatment (group 3; n = 12) and null responders (group 4; n = 71) in addition to a control groups (group 5; n = 125) of CHC patients whom were in eligible or refusing to receive standard of care treatment. All treated patients received pegylated interferon and ribavirn combination. APRI, FIB-4, PLASA, FRT, Fibro-alpha and BRC were calculated at weeks 0 and 72 for all groups and correlated to fibrosis stage by METAVIR and to treatment outcome in different groups.

Results: APRI, FIB-4, PLASA, FRT, Fibro-alpha and BRC could predict significant hepatic fibrosis (≥F2 METAVIR), advanced hepatic fibrosis (≥F3 METAVIR) and cirrhosis (F4 METAVIR) accurately. All panels showed significant decrease of their values in group 1 (sustained virologic response) in response to treatment. On the contrary; APRI, PLASA, FRT and BRC showed significant increase of their values in the control group (table 1). FIB-4 and Fibro-alpha had increase in their values in the control group but this was not significant. There were no other significant changes in the values of the studied panels in other treatment groups.

Conclusion: All of the studied biomarker panels for liver fibrosis assessment were useful in monitoring regression of fibrosis in treated CHC patients and most of them were useful in monitoring progression of fibrosis in untreated patients.

Disclosure of Interest: None declared

P0675 31PHOSPHORUS MAGNETIC RESONANCE SPECTROSCOPY OF THE LIVER IDENTIFIES INFLAMMATION IN AUTOIMMUNE HEPATITIS

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Introduction: Remission in autoimmune hepatitis (AIH) is defined as normal aminotransferases and normal IgG levels and no or only slight inflammation in liver biopsy. Transient elastography (TE) has become a useful method in measuring fibrosis, but biopsy has remained the gold standard in revealing both fibrosis and inflammation of the liver. Liver biopsy is invasive, costly, and subject to complications and sampling variability. The information about inflammation in addition to fibrosis is important in clinical decision of continuing or stopping the treatment. Thus, a non-invasive and accurate test for diagnosis of inflammation would be of great value and we have tested ^{31}phosphorus magnetic resonance spectroscopy (^{31}P MRS) in this setting.

Aims & Methods: Twelve consecutive AIH patients (mean age 42.8 years, eleven women) who underwent liver biopsy for disease staging, were evaluated with TE and ^{31}P MRS. Inflammation and fibrosis in liver biopsy were categorized according to Metavir score. ^{31}P-MRS of liver was performed on a 3 Tesla clinical imager (Philips, Achieva). A 125-216 cm3 voxel was placed in the center of right liver lobe and proton decoupled 31P-MR spectra were obtained using image selective in vivo spectroscopy (ISIS) with TR of 6000 ms and 128 acquisitions. 31P-MRS data was collected with a circular 31P transmit receive loop coil. Body coil was used for obtaining localizer images and for proton decoupling.
Phosphoenolpuryvate (PEP)/phosphatidylcholine (PtdC), phosphoethanolamine (PE), glyserophosphoethanolamine (GPE), total phosphomonoester level (PME), total phosphodiester level (PDE), and PE/PC, PE/GPE, and PC/(PME + PDE) ratios were compared to Metavir grade and stage, stiffness in TE and alanine aminotransferase (ALT), aspartate aminotransferase (AST), immunoglobulin-G (IgG), alkaline phosphatase (ALP), thrombolastin time (TT), and albumin (Alb). Spearman's and Pearson correlations were used to assess statistical relationships. $p < .05$ was considered statistically significant.

Results: PEP/PtdC correlated with inflammation grade ($r = .663$, $p = .019$) and ALP ($r = .598$, $p = .040$). PE/PC ($r = .764$, $p = .006$), PE/GPE ($r = .618$, $p = .043$), and PC/(PME + PDE) ($r = -.636$, $p = .035$) correlated with inflammation, as measured with IgG ($r = .764$, $p = .006$; $r = .618$, $p = .043$; and $r = -.636$, $p = .035$), respectively. There was no correlation between phosphorus metabolites and TE, histological fibrosis and aminotransferase levels.
The histological inflammation correlated with ALT and AST ($r = .800$, $p = .002$ and $r = .673$, $p = .023$ respectively) and IgG ($r = .604$, $p = .049$). TE did not correlate with phosphorus metabolites, liver histology, or laboratory parameters.

Conclusion: ^{31}P MRS measures inflammatory activity in AIH patients. TE and MRS were not effective in fibrosis quantification.

Disclosure of Interest: None declared

P0676 THE ROLE OF POINT SHEAR WAVE ELASTOGRAPHY TECHNIQUE (ELASTPQ) IN THE NON-INVASIVE ASSESSEMENT OF LIVER FIBROSIS IN VARIOUS LIVER DISEASES

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Introduction: Point shear wave elastography (PSWE) is a novel non-invasive technique that assesses liver fibrosis by measuring liver stiffness (in kPa) with few studies published so far. The aim of this study was to determine the accuracy and the feasibility for the assessment of liver stiffness in comparison to the fibrosis stage in patients undergoing liver biopsy (LB) for various etiologies.

Aims & Methods: Consecutive patients scheduled for LB were studied by using the iU22 Philips ultrasound system with ElastPQ technique. The correlations between laboratory findings, liver stiffness and the Metavir score were analyzed using Spearman correlation and ROC curve analyses were performed to calculate AUC for $F \geq 2$, $F \geq 3$ and $F = 4$.

Results: We enrolled 217 patients (140/77 males/females) who underwent LB for viral or non-viral chronic hepatitis (HCV 44%; NASH 21%; AIH/PBC 18%; other 17%). Liver stiffness measurements performed on the right lobe were reliable in all cases but two (due to morbid obesity and narrow intercostal spaces). After univariate and multiple regression analysis PSWE showed a strong correlation with the fibrosis stage; no significant correlation was found with the degree of necroinflammation or steatosis. Mean kPa values in the whole cohort were 4.01 (range 2.30–5.69) for F0, 4.89 (range 2.62-9.68) for F1, 8.00 (2.81-20.79) for F2, 10.98 (3.88-21.44) for F3 and 18.61 (9.51-31.34) for F4 in the right lobe. AUROCs were 0.90 (±0.02), 0.91 (±0.02) and 0.97 (±0.01), when comparing F0-F1 vs F2-F4, F0-F2 vs F3-F4 and F0-3 vs F4, respectively. The optimal cut-off values for different levels of fibrosis were 6.03, 7,63 and 9.47 kPa for $F \geq 2$, $F \geq 3$ and F4, respectively. When analyzing PSWE values according to different etiologies, AUROCs were 0.85 (±0.04), 0.97 (±0.29) and 0.94 (±0.03) for $F \geq 2$; 0.88 (±0.04), 0.95 (±0.03) and 0.95 (±0.03) for $F \geq 3$; 0.98 (±0.01), 0.99 (±0.01) and 0.99 (±0.01) for F4 in HCV, NASH and AIH/PBC patients, respectively.

Conclusion: PSWE with ElastPQ appears to be a useful tool for non-invasive evaluation of fibrosis not only in patients with viral chronic hepatitis, but also for patients with different liver diseases. In order to validate such a non-invasive technique these findings need to be confirmed in larger studies.

Disclosure of Interest: None declared

P0677 PHARMACOKINETICS, RADIATION DOSIMETRY AND TOXICOLOGY STUDIES OF 111IN-DTPA HEXA-LACTOSIDE IN NORMAL MICE

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Introduction: Asialoglycoprotein receoptors residing on hepatocyte membrane has been known to specifically bind with GalNAc or Gal terminal glycoligands. ^{111} In-DTPA hexa-lactoside with Gal termini were developed as a biomarker for liver reserve measurement. In previous study, 111In-DTPA hexa-lactoside has been validated as a specific imaging biomarker for asialoglycoprotein receptors on hepatocyte membrane.

Aims & Methods: To advance ^{111} In-DTPA hexa-lactoside to first-in-human trial, pharmacokinetics, radiation dosimetry and toxicology studies of ^{111}In-DTPA hexa-lactoside in normal mice were performed to meet the requirements of regulatory approval for Investigational new drug (IND). The pharmacokinetic parameters were calculated according to the radioactivity elimination curve with the assistance of PK-Solver 2.0 software. The radiation exposure dose was measured by the OLINDA/EXM program on the basis of residence time of radioactivity in each organ, radiation energy of radionuclide, radionuclide type and tissue-weighting factor of International Commission on Radiological Protection (ICRP). A 14-day GLP extended acute toxicity was evaluated in male Sprague-Dawley (SD) rats via single intravenous injection administration of DTPA-hexa-lactoside.

Results: ^{111}In-DTPA hexa-lactoside exhibited biexponential elimination from the blood in normal mice following tail vein i. v. administration. The distribution half-life (α-phase) was 0.42 min. The elimination phase half-life (β-phase) was 11.46 min. The highest concentration of radioactivity was mostly found in liver (up to 55.48 ± 8.19 %ID/g) within 30min p. i. The mean residence time in blood and liver were 8.22 min and 22.44 h, respectively. The estimated total body dose was 2.86E-05 mSv/MBq which corresponds to a whole body dose of 1.0582 mSv per 1 mCi administered dose, i.e. 1/10 exposure dose of Chest X ray. No significant differences were observed for hematology and serum biochemistry parameters. The physiological functions of all animals were remaining normal during the study period. All parameters of clinical pathology were within the range of historical data.

Conclusion: Our data indicates ^{111}In-DTPA hexa-lactoside is suitable for advancement to a first-in-humans clinical trial.

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Disclosure of Interest: None declared

P0678 NEAR INFRARED FLUORESCENCE DYE LABELED MULTIVALENT DEOXYGLUCOSE AS AN IMAGING AGENT FOR DETECTION OF LIVER CANCER

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Introduction: According to the statistics of American Cancer Society, one-fourth quarter of deaths are due to cancer in US. There is still a lot of unmet need in medical technology, especially in early diagnosis and therapeutic monitoring of liver cancer. Although F-18 FLT is very good as cell proliferation agent, we did not see good image in the orthotopic SK-HEP-1 bearing hepatoma mice in our preliminary experiment because the high unwanted interference in the abdomen.

Aims & Methods: In this study, we develop a fluorescent imaging biomarker with multivalent deoxyglucoside to see its feasibility for hepatoma targeting. Trivalent deoxyglucoside was made by a nitrile-triacetic acid linking three aminohexanoyl-deoxyglucoside. Hexa-deoxyglucoside was synthesized by dimerization of trivalent deoxyglucoside via amide bond formation with cy dye. The fluorescence imaging was performed in the Xtreme system. Biodistribution study was studied by imaging individual organ in vitro after sacrifice mice by cervical dislocation.

Results: Both Cy dye and cy dye-hexa-deoxyglucose performed accumulation in the tumor site bearing SK-HEP-1; however, cy dye-hexa-deoxyglucoside showed more specific for hepatoma targeting than cy dye only. The biodistribution imaging indicated there is highest absorption in the hepatoma region than normal region. Kidney was the next high accumulation organ, which revealed its water solubility property. There is low absorption in the other major organs such as heart, normal liver region, spleen and lung etc.

Conclusion: Our preliminary data indicated the cy dye-hexa-deoxyglucoside has hepatoma targeting property and was possible a good predictor for surgery-guided therapy.

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Disclosure of Interest: None declared

P0679 PERCUTANEOUS SCLEROTHERAPY USING COMBINED ETHANOL AND TETRACYCLINE FOR TREATING SYMPTOMATIC SIMPLE HEPATIC CYSTS

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Introduction: Simple hepatic cysts are benign congenital cysts with a prevalence of 2.5-4.25%. very few cases of simple hepatic cysts need treatment. Ethanol is the most commonly used agent for percutaneous sclerotherapy. Pain is a common complication with ethanol sclerotherapy and is related to the injected amount.
Aims & Methods: our aim is to evaluate the safety and efficacy of the combination of tetracycline and ethanol for percutaneous sclerotherapy of simple hepatic cysts. A total of 34 adult patients with symptomatic simple hepatic cyst underwent clinical evaluation, laboratory evaluation, radiological evaluation and diagnostic cyst aspiration. They were divided into 2 groups. The first group was treated by percutaneous ethanol sclerotherapy and the second was treated by combined ethanol and tetracycline sclerotherapy.
Results: Combined ethanol and tetracycline sclerotherapy was associated with fewer sessions than ethanol sclerotherapy($P = \leq 0.001$) and higher rate of sustained cyst size reduction on follow up ($P = \leq 0.001$). There was no significant difference between the two procedures regarding the complications. Hepatitis C virus infected patients and those with hepatic steatosis had non-significant changes in the serum transaminases with the two procedures.
Conclusion: percutaneous sclerotherapy of simple hepatic cysts using tetracycline and ethanol is more effective than ethanol sclerotherapy.

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Disclosure of Interest: None declared

P0680 FACTORS THAT INFLUENCE THE CONTROLLED ATTENUATION PARAMETER (CAP) VALUE IN CHRONIC LIVER DISEASE PATIENTS

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Introduction: Controlled Attenuation Parameter (CAP) measured by transient elastography has been suggested as a non-invasive method for detection and quantification of hepatic steatosis. Factors that influence the assessment of steatosis by CAP are not well established.
Aims & Methods: To evaluate the factors influencing the CAP value in a group of patients with chronic liver disease (CLD). This study included CLD patients who underwent CAP measurement using the M probe of Fibroscan (Echosens, Paris, France).
Results: We included 159 patients (61% men, mean age 47.9 ± 12.9 years). CLD aetiology was non-alcoholic fatty liver disease (34.8%), viruses (28.3%), autoimmune hepatitis (10.7%), alcohol (8.7%) and others (17.5%). CAP value was related to the degree of steatosis in liver histology ($p < 0.001$) and ultrasound ($p < 0.001$). The value of CAP was significantly higher in patients with hypertension (267.5 vs. 234.8 dB/m, $p = 0.007$), dyslipidaemia (273.5 vs. 212.1 dB/m, $p < 0.001$), type 2 diabetes mellitus (280.9 vs. 234.8 dB/m, $p = 0.001$), body mass index (BMI) > 25 Kg/m^2 (277.8 vs 213.0 dB/m, $p < 0.001$) and non-alcoholic fatty liver (290.8 vs 212.6 dB/m, $p < 0.001$). In the multivariate analysis, BMI > 25 Kg/m^2 (OR 48.4, 95% CI: 23.78 - 72.95, $p < 0.001$), serum cholesterol [OR 3.803, 95% CI: 2203-13889, $p < 0.008$) and non-alcoholic fatty liver aetiology (OR 40.8, 95% CI: 15.01 - 66.66, $p = 0.002$) were independently associated with higher CAP values; CAP was not influenced by the degree of fibrosis ($p = 0.794$) or inflammatory activity ($p = 0.893$) in histology, triglycerides ($p = 0.104$), glucose ($p = 0.871$), ALT ($p = 0.817$) or AST ($p = 0.372$).
Conclusion: CAP mean value increases according to the degree of steatosis in histology and ultrassonography. NAFLD, BMI > 25 kg/m^2 and serum cholesterol were independently associated with higher values of CAP. The degree of fibrosis and inflammatory activity in histology, triglycerides, blood glucose and transaminases did not influence the value of CAP.
Disclosure of Interest: None declared

P0681 ALTERATIONS IN THE PORTAL VENOUS SYSTEM IN IDIOPATHIC NON-CIRRHOTIC PORTAL HYPERTENSION: A PROSPECTIVE LONG-TERM FOLLOW-UP STUDY

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Introduction: Idiopathic Non-Cirrhotic Portal Hypertension (INCPH) is a group of diseases that are characterized by an increase in portal pressure, due to intrahepatic or prehepatic lesions, in the absence of cirrhosis of the liver. INCPH includes Extra Hepatic Portal Vein Obstruction (EHPVO) and Non-Cirrhotic Portal Fibrosis (NCPF). The natural history of INCPH is still not clear.
Aims & Methods: Aim of the present was to determine prospectively the changes in the portal venous system in patients with NCPH. Patients with a diagnosis of NCPF and EHPVO registered since 2001 were serially followed at an yearly interval for changes in liver size, its echotexture, and in the intra and extrahepatic portal venous system. Baseline demographic details, LFT, and co-morbid illness including virological profile were noted. Patients with co-morbid illness and those with known etiology of cirrhosis were excluded from the study.
Results: There were 34 patients with NCPF (M: F 1:1.8) and 30 patients with EHPVO (M: F ratio 1.6:1). The mean age was 24.9 yrs and 41.2 yrs respectively. During follow up, 20 out of 34 and 16 out of 30 patients with NCPF and EHPVO respectively had no progression of disease. 14 patients with NCPF progressed to cirrhosis over a mean period of 5.21 years. Eight patients developed ascites and required diuretics. 14 patients with EHPVO progressed to NCPF over the mean period of 8.6 years, 12 patients further progressed to cirrhosis over a mean period of 5.1 years. Overall 40% of patients with EHPVO progressed to cirrhosis over a mean period of 13.7 years.
Conclusion: INCPH is a spectrum wherein EHPVO progresses to NCPF and further to cirrhosis over a period of 13.7 years at least in a proportion of patients. So our report clearly emphasizes that INCPH is a spectrum of disease, so this patients should monitored periodically to observer the changes in the portal venous system.
Disclosure of Interest: None declared

P0682 NON-ALCOHOLIC FATTY LIVER DISEASE RISK FACTORS ASSESSMENT AMONG THE GENERAL PRACTITIONER'S AND GASTROENTEROLOGIST'S PATIENTS FLOW

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Introduction: Prevalence of suspected Non-alcoholic fatty liver disease (NAFLD) has more than doubled over the past 20 years and currently affects nearly 11% of adolescents and one-half of obese males. In Russia prevalence of NAFLD is increasing from 26,1 to 37,3% during last 7 years. The rapid increase among those obese, independent of body mass index, suggests that other modifiable risk factors have influenced this trend. For a better understanding of the disease etiology and its correlations with risk factors it is necessary to conduct epidemiological studies in Russia. This study was funded and managed by Sanofi Russia.
Aims & Methods
Objective: To evaluate the hierarchy of risk factors of NAFLD in general and within the every age subgroups in GP's and gastroenterologist's patient flow.
Materials and methods: A total of 50145 patients meeting the inclusion/exclusion criteria in 16 Russian cities were enrolled in the Program. The investigators were 1031 qualified doctors (GPs \ therapists \ gastroenterologists \ pediatricians), providing outpatient care for the population. The epidemiological data were obtained, recorded during two routine patient visits to investigating centers.
Results: The patients with Non-cirrhotic non-alcoholic fatty liver disease (NANCFLD) had significant elevated weight, BMI and WC in both gender groups and in total. Among the adult population with NANCFLD, it is important to note a higher and significant value of glucose, insulin, total cholesterol, TG, and HDL cholesterol when compared with participants who had normal liver data. Additionally, patients with NANCFLD resulted in major and significant value of AST, ALT and GGT compared with patients without liver

diseases.The more frequent risk factors for females with NANCFLD were: abdominal obesity, BMI ≥ 27kg/m2, menopause, hypertension and metabolic syndrome. The prevalence of reduced High Density Lipoprotein within NANCFLD female patients was 58,0%. The more frequent risk factors for males with NANCFLD were: BMI ≥ 27kg/m2, abdominal obesity, hypertension, hypertriglyceridemia and metabolic syndrome. The prevalence of reduced High Density Lipoprotein within NANCFLD male patients was 40,2%. The main 4 risk factors for NAFLD in males and females were the same and were ranged by odds ratio values as the following: hypertriglyceridemia, metabolic syndrome, BMI ≥ 27kg/m2, abdominal obesity.
Conclusion: NAFLD is closely associated with hypertriglyceridemia, metabolic syndrome, BMI ≥ 27kg/m2, abdominal obesity. It has been confirmed the hypothesis that for each studied risk factor the proportion of patients with NANCFLD is higher than the proportion of patients with the same risk factor in the population without liver diseases.
Disclosure of Interest: None declared

P0683 XRCC1RS1799782, RS25487, RS25489 AND HOGGR1052133 POLYMORPHISM ARE SUSCEPTIBILITY TO EXTRAHEPATIC CHOLANGIOCARCINOMA: A POPULATION-BASED CASE–CONTROL STUDY IN A MEXICAN POPULATION

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Introduction: Up to 90% of patients with extrahepatic cholangiocarcinoma (ECC) have no identifiable risk factors; genetic background (genes programmed to halt proliferation in damaged cells, involved in DNA repair), geographical and environmental factors are considered to play a role in carcinogenesis.
Aims & Methods: The aim was to establish if XRCC1rs1799782, rs25487, rs25489 and hOGG1rs1052133 SNP are susceptibility to ECC. Multicenter, case-control study performed in Mexico between May 2011- December 2013, included adults diagnosed with ECC (cases), benign pathology of the bile duct and asymptomatic patients (controls) matched by sex, age (± 5 years) and place of residence. Genomic DNA was extracted from peripheral blood using QIAamp DNA, quantified using the PicoGreen kit, and stored at -20º C. All SNPs were done with 10 ng genomic DNA in 384-well plates, using TaqMan technologie. The order of DNAs from cases and controls was randomized, for quality control duplicates 10% of the samples were done, PCR reactions were performed using a Hydrocycler instrument and the GeneAmpVR PCR System, PCR plates were read on a ViiA7 real time instrument, the ViiA7 RUO Software, version 1.2.2 was used to determine the genotypes. Hardy-Weinberg equilibrium was tested; logistic regression analyses were used for association between genetic polymorphisms and ECC. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated for each genotype under a codominant, dominant, recessive and additive inheritance model.
Results: Included 391 Mexican patients, 98 EEC: 63 common bile duct, 9 gallbladder and 26 of Vateŕs papilla. Mean age of cases (62.2 ± 14.36), 40 men, 58 women. Controls; 92 benign biliary pathology (C1) and 201 asymptomatic blood donors (C2). XRCC1rs1799782_AG, rs25489_CT and hOGG1rs1052133_CG SNP no showed significant differences among groups. rs25487_CT was present in 18.36% of cases (18/98), 38.89 % of C1 (35/90), p = 0.0031, OR = 0.35 (0.17-0.72) and 34% of C2 (69/199), p = 0.056, OR = 0.42 (0.23-0.79). XRCC1rs1799782 genotype A/A was observed in 7.94% of choledochal cancer (5/63) vs 1.54% of C2 (2/130) p = 0.0385 OR = 5.52 (0.91-42.4), genotype A/G was present in 88.89% of gallbladder cancer (8/9) vs 27.77% (5/18) of C2, p = 0.0039 OR = 20.80 (1.70-587.88) In choledochal cancer, rs25487_CT was observed in 15.87% (10/63) vs 40% of C1 (24/60), p = 0.0052, OR = 0.28 (0.11-0.71) and 36.92% of C2 (48/130), p = 0.0047, OR = 0.32 (0.14-0.73), while C/C genotype, 74.60% of (47/63) vs 57.69% of C2 (75/130), p = 0.0335, OR = 2.15 (1.06-4.43).
Conclusion: In Mexican population, our results suggest that XRCC1rs1799782 genotype A/A is risk factor in choledochal cancer, and SNP rs25487 is protective factor while in gallbladder cancer, SNP rs1799782 is a risk factor.
Disclosure of Interest: None declared

P0684 FREQUENCY OF MUTATIONS IN KRAS, MET AND PIK3CA IN EXTRAHEPATIC CHOLANCHIOCARCINOMA IN MEXICAN PATIENTS

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Introduction: Extrahepatic cholangiocarcinoma (ECC) is a rare but a highly lethal malignancy due to difficulties of early diagnosis and lack of effective therapies. In Mexico endoscopic retrograde cholangiopancreatography (ERCP) still is considered a valuable tool for assessing biliary tract strictures because it allows obtain radiological images biliary tract, therapeutic interventions, and collection of brushing cytology specimens although highly specific, has low/moderate sensitivity (15% > 68%). The progress in molecular biology of human cancers along with increased understanding of oncogenic mutations and cell signaling pathways, led to the successful application of mutation analysis as a part of diagnostic techniques as well as new targeted therapies in many solid tumors. The mass spectrometry technique, matrix-assisted laser desorption/ionization–time of flight, has been used to assess tumors for point mutations and small deletions in commonly altered oncogenes.
Aims & Methods: The goal was determine the frequency of somatic mutations in common oncogenes in ECC in epithelial cells obtained by scraping the biliary ducts. Multicenter study performed in Mexico between May 2012 December 2013, included adults with diagnosis of ECC by ERCP, plus endoscopic ultrasound, intraductal biliary ultrasound and direct cholangioscopy. All cases were confirmed by brush cytology, histopathology and clinical course. Epithelial cells were obtained by scraping the biliary ducts during ERCP and the brushes were suspended in buffer solution at -80°C until tested. DNA was extracted from brushed cells using the QIAamp DNA easy kit and quantified using the PicoGreen kit, and evaluated using the Sequenom MassARRAY and OncoCarta v1.0 Mutation Profiler Panel.
Results: Included 28 cases: 17 woman and 11 men, mean age 64.41 ± 14.74, the ECC was distributed; 14 (50%) choledocho, 4 (14.29%) gallbladder and 10 (35.71%) in ampulla of Vater. Mutations were identified in 39.29% (11/28) of ECC in follow genes KRAS 28.57% (8/28); G12D, MET 7.14% (2/28); T992I, M1250T and PIK3CA 3.57% (1/28); P539R. The highest mutation rate was observed in cancer of choledocho 42.86% (6/14), followed by ampulla of Vater 40% (4/10) and gallbladder 25% (1/4). Follow-up was 30 months. Survival in patients without mutations was 9.25 ± 6.56 months and 9.78 ± 3.73 months in patients with mutations without significance.
Conclusion: Mutations in oncogenes as KRAS, MET and PIK3CA decrese efficacy of specific chemotherapies and in our study this frequency was 39.29% of ECC. MassARRAY technology can be used to detect mutations in a wide variety of oncogenes using epithelial cells obtained by scraping biliary ducts during ERCP and could be used for molecular profile in ECC protocol as diagnosis tool and individualized therapy.
Disclosure of Interest: None declared

P0685 CHITOSAN NANOPARTICLES FOR THE DELIVERY OF A PHOTOSENSITIZER TO HUMAN CHOLANGIOCARCINOMA CELLS

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Introduction: Chitosan is known as a natural and biocompatible polymer which has immune adjuvants and anticancer activities. Therefore, chitosan can be used in drug such as Ce6 that is adaptable to incorporate anionic drug because of the cationic properties of chitosan.
This study was produced using the water-soluble chitosan incorporated nanoparticles containing Ce6. Photodynamic potentials and physicochemical properties of Ce6-incorporated chitosan nanoparticles were studied against human cholangiocarcinoma cells in vitro and in vivo.
Aims & Methods: We purchased chitosan from Kittolife Co. Korea and Ce6 from Frontier Sci. Co. Ltd. USA.
We fabricated Ce6-incorporated nanoparticles using chitosan by dissolving 100mg of chitosan in 10ml of deionized water. Then 5-20 mg of Ce6 in 0.5ml DMSO was added to chitosan solution following sonication using bar-type ultrasonicator. To remove organic solvent and free drug, this solution was dialyzed against water.
Results: Ce6-incorporated nanoparticles was fabricated through ion-complexation formation between amine group of chitosan and carboxyl group of Ce6 using water-soluble chitosan. By simple mixing of Ce6 and chitosan, photosensitizer-incorporated were prepared following sonication and dialysis which has spherical shapes with less than 500nm. When Ce6-incorporated nanoparticles were treated to human cholangiocarcinoma cells with irradiation, they enhanced delivery of Ce6 to human cholangiocarcinoma cells and then enhanced ROS level in tumor cells rather than free Ce6. Futhermore, nanoparticles enhanced treatment efficiency. Photo-induced toxicity against human cholangiocarcinoma cells were increased compared to Ce6 only treatment. Nanoparticles enhanced delivery of Ce6 through bile duct in ex vivo study using porcine bile duct slice. Also, nanoparticles significantly enhanced delivery of Ce6 to tumor at in vivo animal study.
Conclusion: Ce6-incorporated nanoparticles using water-soluble chitosan were prepared. ChitoCe6 nanoparticles enhanced cellular uptake, phototoxicity, and ROS generation compared to Ce6i only. Also, Ce6-incorporated nanoparticles

enhanced delivery to human cholangiocarcinoma cells in vivo animal study and ex vivo porcine bile duct slice experiment.
Disclosure of Interest: None declared

P0686 PROMISING CANDIDATE FOR VORINOSTAT-INCORPORATED NANOPARTICLES AGAINST HUMAN CHOLANGIOCARCINOMA CELLS

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Introduction: This study evaluates the anticancer activity of vorinostat-incoporated nanoparticles (vorinostat-NPs) against cholangiocarcinoma cells.
Aims & Methods: By using a nanoprecipitation method, Vorinostat-NPs were fabricated and presented its spherical shapes with small particles size less than 100 nm. Also, Vorinostat-NPs were coated onto covered-stent. We observe the anticancer activity of Vorinostat-NPs and their coated stent in vitro and in vivo.
Results: Vorinostat and vorinostat-NPs have similar anticancer efficacy in terms of cytotoxicity, cell growth inhibition, and apoptosis of HuCC-T1 cholangiocarcinoma cells in vitro. Also, they have equal potency in inhibition of histone deacetylase (HDAC) expression, mutant type p53 suppression, increased p21expression, and PARP/cleaved caspase-3 expression. However, vorinostat-NPs and their coated stent showed improved antitumor activity against HuCC-T1 cancer cell-bearing mice compared to vorinostat itself, whereas empty nanoparticles had no effect on tumor growth. Vorinostat-NPs increased the expression of acetylated histone H3 in tumor tissue and suppressed HDAC expression in vivo. The improved anticancer efficacy of vorinostat-NPs was confirmed by molecular imaging studies using NIR-dye-incorporated nanoparticles.
Conclusion: This study shows the anticancer activity of vorinostat and vorinostat-NPs against HuCC-T1 cholangiocarcinoma cells by specific inhibition of HDAC expression. Therefore, vorinostat-NPs can be used in anticancer chemotherapy in cholangiocarcinoma.
Disclosure of Interest: None declared

P0687 PRE-EXPOSURE WITH SIMVASTATIN INHIBITS LIPOPOLYSACCHARIDE-INDUCED EPITHELIAL-MESENCHYMAL TRANSITION VIA DOWNREGULATION OF TLR4 AND NF-KB IN HUMAN BILIARY EPITHELIAL CELLS

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Introduction: Epithelial-mesenchymal transition (EMT) of biliary epithelial cells (BECs) plays a role in biliary fibrosis. Lipopolysaccharide (LPS) promotes EMT in BECs.
Aims & Methods: The present study investigated the effects of simvastatin on the EMT of BECs induced by LPS. Transformed human BECs (H69) were exposed with LPS (1μg/mL) or transforming growth factor-β1 (TGF-β1, 5 ng/ml) for 5 days. The expression of E-cadherin, vimentin, N-cadherin, and toll-like receptor 4 (TLR4) was determined by quantitative real-time PCR, western blotting, and confocal microscopy. The effect of simvastatin on the EMT induced by LPS or TGF- β1 was determined by the expression of E-cadherin, vimentin, and TLR4.
Results: After exposure to 1μg/mL of LPS for 5 days, E-cadherin decreased and vimentin increased in mRNA and protein levels. The mRNA expression of TRL4 was increased by the exposures of LPS and TGF-β1 (5ng/ml) for 5 days. As compared with BECs treated with LPS alone, co-treatment with simvastatin plus LPS showed a remarkable increase of E-cadherin and a slight decrease of vimentin. LPS-induced TLR4 slightly decreased by co-treatment with simvastatin and LPS. In the proliferation analysis, LPS-induced BECs growth was remarkably inhibited by the application of simvastatin (1μM). In BECs morphology analysis, as compared with BECs pre-treatment with simvastatin before LPS exposure (preSL), BECs pre-exposure with LPS (postSL) or co-exposure with LPS plus simvastatin (LS) were more potentiated EMT effects (cell morphology changes round shape to spindle like morphology). Furthermore, BECs pretreated with simvastatin (preSL) inhibited LPS-induced EMT by downregulation of NF-kB phsophorylation. These findings indicate that, while LPS or TGF-β1 promoted EMT, the BECs pre-treated with simvastatin (preSL) inhibited LPS-induced EMT by downregulation of TLR4 and NF-kB.
Conclusion: Our results demonstrate that pre-exposure with simvastatin (preSL) inhibits the LPS-induced EMT of human BECs. This finding suggests that simvastatin can be considered as a new agent to prevent biliary fibrosis associated with EMT of BECs.
Disclosure of Interest: None declared

P0688 ANALYSIS OF DISCREPANCY IN RADIOLOGIC AND PATHOLOGIC DIAGNOSIS OF GALLBLADDER ADENOMYOMATOSIS

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Introduction: Adenomyomatosis of gallbladder (GB) is considered as benign condition, but several reports suggest association with malignancies, especially for segmental subtype. Because of this chance, patients suspected to have segmental or diffuse type adenomyomatosis on the imaging study may undergo cholecystectomy. But, in some cases, histopathology reveals only chronic inflammation. In this study, we aimed to analyze radiologic and pathologic features of chronic cholecystitis and adenomyomatosis for more accurate diagnosis.
Aims & Methods: Patients who performed cholecystectomy during recent four years in one medical center were reviewed retrospectively. Among those, patients who were suspected to have adenomyomatosis on their abdominal imaging but with no adenomyoma detected on the histopathologic examination were analyzed for their radiologic, pathologic and clinical features compared to patients who had consistent results between abdominal imaging and histopathologic examination.
Results: Among 3144 patients who underwent cholecystectomy, 358 patients were suspected to have GB adenomyomatosis on the abdominal imaging study. Among them (358 patients), only 92 patients had histopathologic findings compatible with adenomyomatosis. Remaining 266 patients (74.3%) did not have adenomyomatosis. Instead, many GB specimens showed chronic cholecystitis. In this group, diffuse subtype of adenomyomatosis was significantly frequent compared to 92 patients who had coherent adenomyoma finding for both imaging study and pathology. The frequency of accompanying GB stones was significantly higher in mismatching group. Radiologically, contour of GB wall thickening, intralesional cystic area and inner layer enhancement pattern was helpful in differentiating adenomyomatosis from chronic cholecystitis.
Conclusion: Chronic cholecystitis mimicking adenomyomatosis is difficult to diagnose solely based on the abdominal imaging, and this can lead to unnecessary cholecystectomy. Existence of gallstones and several radiologic features can help differentiate these challenging entities.

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P0689 THE EFFICACY OF VARIOUS ENDOSCOPIC TRANSPAPILLARY SAMPLING METHODS FOR MALIGNANT BILIARY LESIONS

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Introduction: Various methods for endoscopic transpapillary sampling have been developed. However, the accuracy rate of these methods for bile duct cancer are controversial. The aim of the present study was to determine the factors affecting the accuracy of endoscopic transpapillary sampling methods.
Aims & Methods: We reviewed the results from 92 patients with bile duct cancer who underwent transpapillary sampling by aspiration bile cytology, brushing cytology, and fluoroscopic forceps biopsy. The final diagnosis of bile duct cancer was made on the basis of pathological evaluation of specimens obtained at surgery or the clinical course over at least 1 year in patients not operated. We carried out subgroup analyses for the factors affecting the accuracy of each transpapillary sampling method.
Results: Transpapillary biopsy (71.2%) had a significantly higher level of sensitivity for cholangiocarcinoma than brush cytology (58.8%) and bile cytology (62.5%). Bile cytology (85.7%) showed higer diagnostic yield for pancreatic cancer with bile duct invasion than transpapillary biopsy (60%) and brush cytology (66.7%). In patients with negative biopsy results, bile cytology had higher diagnostic yield than brush cytology.
Conclusion: Transpapillary bile duct biopsy is a simple, safe, and effective technique for diagnosing biliary malignant lesion. It showed more sensitive for cholangiocarcinoma than for pancreatic cancer with bile duct invasion. After negative biopsy result, bile cytology presented higher diagnostic yield.

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P0690 MULTIPLE METAL STENTS FOR COMPLEX MALIGNANT HILAR STRICTURES: PATIENTS SURVIVAL, STENTS PATENCY AND OUTCOMES OF RE-INTERVENTIONS FOR OCCLUDED STENTS

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Introduction: Endoscopic biliary drainage of malignant hilar biliary strictures (MHS) with self-expandable metal stents (SEMS) is a well-established palliative

treatment for unresectable hilar tumors. Efficacy of SEMS has been well described in distal biliary strictures, but data in complex MHS are lacking.
Aims & Methods: Retrospective review of a prospective database of all patients with MHS that underwent ERCP for symptoms palliation. Of these, only patients with multiple SEMS placement were included. Survival-associated factors and stents patency were analyzed by Cox multivariate analysis. Patients survival, stents patency and outcomes of re-interventions for occluded stents were evaluated.
Results: Between January 1998 and June 2014, 740 patients with complex MHS that underwent ERCP for palliation were identified. Among these, 134 (18.2%) patients were treated with two or more multiple SEMS. Of the 134 patients, 76 (56.7%) previously had plastic stents, 34 (25.4%) had one or more percutaneous biliary drainages and 24 patients (17.9%) received SEMS as first treatment. Mean age at time of diagnosis was 67.2 (SD26.8) years, female patients were 53.7%. Histologically, cholangiocarcinoma was the cause of stricture in 59% of patients, while 28.3% had gallbladder carcinoma. Hilar compression by lymphnodes and hilar hepatocellular carcinoma had 9.7% and 3% respectively. Regarding the Bismuth type of hilar stricture, 25.3% had type II, type III had 50.7% and type IV had 24% of the patients. Chemotherapy was done in 38.3% of patients, external-beam radiotherapy in 12.7% and high-dose-rate brachytherapy in 10%. Multiple SEMS were placed "side-by-side" after 2 to 4 guidewires were left in place into the ducts to be drained. Post-procedure complications (5.2%: 4 sphincterotomy bleedings, 3 pancreatitis) were managed conservatively. No procedure-related mortality was observed. Histological and follow-up data were available for all of the 134 patients. Seventy-nine (59%) patients died without clinical signs of SEMS occlusion, while 55 (41%) patients had SEMS occlusions and underwent ERCP. Overall mean survival of the 134 patients was 380 days (28-1455). Survival was not influenced by tumor or Bismuth type, palliative chemotherapy, sex or age ($P = 0.5$). Longer survival was found in patients that underwent high-dose rate brachytherapy with Iridium 192 ($P = 0.02$), but not in those that underwent external beam radiotherapy ($P = 0.8$). The 55 patients that had SEMS occlusion underwent 93 endoscopic re-interventions (1-6/patient) after mean 201.3 days (32-867) from the first multiple SEMS insertion and mean 140 days (30-330) between further re-interventions. Main causes for SEMS occlusion were due to sludge, overgrowth and ingrowth. Sludge was removed with balloon and flushing with saline, while plastic stents or SEMS were placed into the previous SEMS in cases of ingrowth and overgrowth. Overall mean survival after re-interventions was 432 days (91-1425) and was prolonged compared to patients that died without signs of stents occlusion ($P = 0.001$).
Conclusion: Endoscopic insertion of multiple SEMS is safe and effective in patients with complex MHS. Survival is satisfactory independently from age, sex and type of tumor. High-dose rate brachytherapy and prompt recognition of signs of SEMS occlusion are associated with prolonged survival.
Disclosure of Interest: None declared

P0691 RISK FACTORS OF GALLBLADDER NEOPLASMS IN SUSPICIOUS ADENOMYOMATOSIS ON COMPUTED TOMOGRAPHY

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Introduction: Gallbladder (GB) adenomyomatosis is not uncommon findings on computed tomography (CT). Sometimes, the lesions are confirmed as GB neoplasms (adenoma or carcinoma). However, it is quite difficult to diagnose adenomyomatosis when showing GB wall thickness on CT.
Aims & Methods: The aim of this study is to find out predictors which may indicate GB neoplasms in suspicious GB adenomyomatosis on CT before cholecystectomy.
Patients with suspicious GB adenomyomatosis on CT (the presence of one or more of the following CT findings; mucosal epithelium with intramural diverticula, multiple intramural cysts, discrete hypoattenuating lesions) and underwent cholecystectomy between January 2010 and February 2015 were reviewed retrospectively. They were divided into three groups based on the pathologic findings: chronic cholecystitis group ($n = 144$), adenomyomatosis group ($n = 92$) and GB neoplasms group ($n = 13$). The clinical data and CT findings were compared between the three groups.
Results: A total of 249 patients were enrolled. There was no differences between chronic cholecystitis, adenomyomatosis and neoplasms groups in terms of clinical characteristics except age (50.4y vs. 50.6y vs. 64.3y, respectively, $p < 0.001$). Moreover, morphologic types (diffuse, fundal and segmental) on CT did not predict GB neoplasms. When further analyzing between adenomyomatosis group and GB neoplasms group, older age, combined GB polyp, and GB wall enhancement were independent risk factors on GB neoplasms with statistical significance.
Conclusion: We suggest that older age, combined GB polyp, and GB wall enhancement are independent risk factors on GB neoplasms in suspicious GB adenomyomatosis on CT. Therefore, the older with suspicious adenomyomatosis would be needed further evaluations, when combined GB polyps or GB wall enhancement.

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P0692 PREDICTABLE FACTORS FOR PANCREATICOBILIARY MALIGNANCY IN PATIENTS WITH ANOMALOUS UNION OF PANCREATICOBILIARY DUCT

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Introduction: Anomalous union of the pancreaticobiliary duct (AUPBD) is a rare congenital anomaly in which the pancreatic and biliary ducts join anatomically outside of the duodenal wall, usually forming a markedly long common channel. The most clinically important feature of AUPBD is frequently associated with carcinomas of the biliary tract, i.e., bile duct and gallbladder. Evaluation of AUPBD-related pancreaticobiliary malignancies is essential to determining appropriate treatment of anomalous union of pancreaticobiliary duct (AUPBD).
Aims & Methods: The aim of this study is to determine the incidence of AUPBD-related pancreaticobiliary malignancies and to propose their predictable factors. We retrospectively reviewed data from 229 patients with AUPBD between January 1999 and December 2013. The incidence of AUPBD-related pancreaticobiliary diseases, particullary according to the presence of bile duct dilatation and the predictable factors for pancreaticobiliary malignancies were evaluated.
Results: Among 229 patients with AUPBD, 152 patients had common bile duct dilatation (≥ 10 mm) (dilated group) and 77 patients did not have bile duct dilatation (< 10 mm) (non-dilated group). Intrahepatic cholangiocarcinoma (ICC) occurred more frequently in the non-dilated group than in the dilated group (non-dilated group vs. dilated group; 3.9% vs. 0%, $P < 0.05$). On the other hand, although extrahepatic cholangiocarcinoma (ECC) tended to occur more frequently in the dilated group (1.3% vs. 3.9%, P *value* $= 0.271$), there were no significant differences in most pancreaticobiliary diseases between the two groups. In univariate analysis to determine predictable factors for AUPBD-related biliary tract cancer, age, type of AUPBD, and refluxed pancreatic enzyme level in bile duct showed significant differences. In multivariate analysis, age ≥ 45 years (OR, 1.042; 95% CI, 1.011-1.073; $P < 0.05$), P-C type (OR, 3.327; 95% CI, 1.031-10.740; $P < 0.05$), and a high level of biliary lipase (OR, 4.132, 95% CI, 1.420-12.021; $P < 0.05$) showed a significant association with AUPBD-related biliary tract cancer.
Conclusion: ICC may occur more frequently in AUPBD patients without bile duct dilatation. Age ≥ 45 years, P-C type, and biliary lipase level $\geq 45{,}000$ IU/L are significantly related to AUPBD-related biliary tract cancer.
Disclosure of Interest: None declared

P0693 LONG-TERM FOLOW-UP OF ENDOSCOPIC PAPILLECTOMY (PE) IN PATIENTS WITH MALIGNANCY OF THE MAJOR DUODENAL PAPILLA

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Introduction: The Endoscopic Papillectomy (EP) still is a controversial procedure used to treat malignancy of the major duodenal papilla. Nowadays, the treatment chosen is duodenopancreatectomy. The aims of of this transversal and multicentric study was to establish the endoscopic treatment parameters of malignancy of the major duodenl papilla in a controlled group of patients.
Aims & Methods: From January of 2008 to June of 2014, 54 patients were referred to undergo EP after staging by endosonography. We analyzed the occurrence of adverse events, relapses and the median follow-up results of 21.3 (3-96) months. We included those whose final diagnosis was adenocarcinoma, adenoma with high-grade dysplasia or neuroendocrine tumor of the major papilla.
Results: The endoscopic biopsy shown the diagnostic of malignancy in 45% (20/54) of cases. The majority (13/20 - 65%) had jaundice at the time of the exam. The total number of patients who met the inclusion criteria was 20: 15 with the histologic diagnosis of adenocarcinoma, three with neuroendocrine carcinoma and two with adenoma with high-grade dysplasia. The resection was complete in 18/20 (90%). Adverse events occurred in 7/20 (35%): the most frequent was bleeding (3/20 - 15%), followed by acute pancreatitis (2/20 - 10%). 14 (70%) of the selected patients keep monitoring and have no sign of the disease. Six patients were submitted to surgical treatment, and three of them had residual lesion (1 with pT1 and 2 with pT3) and metastatic lymph nodes in the surgical specimen (1 with pTxN1 and 2 with pT3N1). The main indication for surgery was the final diagnosis of EP product and the involvement of the lateral and deep margin of the lesion.
Conclusion: The EP is a safe and effective procedure for the treatment of the malignnacy of the papilla. The involvement of deep and lateral resection margins was determinant to the surgical indication. To optimize the approach of the carcinomas of major duodenal papilla endoscopically, we should expect a diligent patient selection, reference centers and specialized team.
Disclosure of Interest: None declared

Abstract number: P0696

		Sensitivity (%)	Specificity (%)	LR-positive	LR-negative
	CRP(> 0.6 mg/dL)	86.8	73.8	3.31 (1.8-4.86)	0.17 (0.11-0.41)
	PCT(>0.5 ng/ml)	86.8	91.7	10.4 (3.5-23.28)	0.15 (0.07-0.29)
	TLC	43.4	71.4	1.52 (0.86-2.67)	0.79 (0.58-1.07)
Decompensated chronic liver disease					
PCT + CRP	79.2	91.7	9.54 (3.2-21.3)	0.23 (0.13-0.39)	
PCT + CRP + TLC	43.4	92.8	6.08 (1.9 – 18.6)	0.61 (0.47 – 0.78)	
Acute liver failure	CRP(> 0.49 mg/dl)	75	67	2.27 (1.12-3.14)	0. 37 (0.22-0.98)
	PCT(> 0.5 ng/ml)	83.3	57.8	1.97 (1.34-2.9)	0.29 (0.11-0.73)
	TLC	41.6	73.3	1.56 (0.79-3.08)	0.79 (0.34-0.94)
	PCT + CRP	62.5	75.5	2.56 (1.4-4.6)	0.5 (0.29-0.85)
PCT + CRP + TLC	37.5	88.9	3.37(1.27 – 8.94)	0.7(0.5 – 0.97)	

P0694 LONG-TERM FOLLOW-UP OF ENDOSCOPIC PAPPILLECTOMY (EP) IN PATIENTS WITH MALIGNANCY OF THE MAJOR DUODENAL PAPILLA

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Introduction: The EP is still controversial procedure used to treat malignancies of the major duodenal papilla. Nowadays, the best treatment for this disease is duodenopancreatectomy.

Aims & Methods: The aim of this transversal and multicentric study was to establish the best parameters of the endoscopic treatment in patients with a malignant tumor of the major duodenal papilla tumor. From January of 2008 to June of 2014, 54 patients were referred to undergo EP after endosonography staging. We analyzed the occurrence of adverse events, relapses and the median follow-up results of 21.3 (3-96) months. We included those whose final diagnosis was adenocarcinoma, adenoma with high-grade dysplasia or neuroendocrine carcinoma.

Results: The endoscopic biopsy shown the diagnostics of malignancy in 45% (20/54) of cases. The majority (13/20 - 65%) had jaundice at the time of the exam. The total number of patients who met the inclusion criteria was 20: 15 with the histologic diagnosis of adenocarcinoma, three with neuroendocrine carcinoma and two with adenoma with high-grade dysplasia. The resection was complete in 18/20 (90%). Adverse events occurred in 7/20 (35%): the most frequent was bleeding (3/20 - 15%), followed by acute pancreatitis (2/20 - 10%). 14 (70%) of the selected patients keep monitoring and have no sign of the disease. Six patients were submitted to surgical treatment, and three of them had residual lesion (1 with pT1 and 2 with pT3) and metastatic lymph nodes in the surgical specimen (1 with pTxN1 and 2 with pT3N1). The main indication for surgery was the final diagnosis of EP product and the involvement of the lateral and deep margin of the lesion.

Conclusion: The EP is a safe and effective procedure for the treatment of papillary tumors. The involvement of deep and lateral resection margins was determinant to the surgical indication. To optimize the approach of the malignancies of major duodenal papilla endoscopically, we should expect a diligent patient selection, reference centers and specialized team.

Disclosure of Interest: None declared

P0695 OPTIMIZATION OF TISSUE ABLATION PARAMETERS FOR ENDOBILIARY RADIOFREQUENCY IN PORCINE LIVER, BILE DUCTS AND AMPULLA OF VATER

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Introduction: The extent of thermal tissue injury induced by endoscopic endobiliary radiofrequency ablation has been described only for a select set of parameters designed to treat malignant strictures of the common bile duct. Since potential indications of this therapeutic modality may also include shallow intrahepatic or ampullary lesions, we sought to determine the optimal generator settings for such indications.

Aims & Methods: Endobiliary radiofrequency ablation was performed in live swine on the ampulla of Vater, in the common bile duct and hepatic parenchyma. Radiofrequency ablation time, "effect", and power were allowed to vary. The animals were sacrificed 2 hours after the procedure. Histopathological assessment of the depth of thermal lesions was performed.

Results: Twenty-five radiofrequency bursts were applied in three swine. In the ampulla of Vater (n = 3), necrosis of the duodenal wall was observed starting with an effect set at 8, power output set at 10 W and a 30s shot duration, whereas superficial mucosal damage of up to 350μm in depth was recorded for an effect set at 8, a power output set at 6W and a 30 s shot duration. In the common bile duct (n = 4), a 1070 μm safe and efficient ablation was obtained for an effect set at 8, a power output of 8W, and an ablation time of 30 s. Within the hepatic parenchyma (n = 18), the depth of tissue damage varied from 1620μm (effect = 8, power = 10W, ablation time = 15 s) to 4480μm (effect = 8, power = 8W, ablation time = 90 s).

Conclusion: The duration of catheter application appeared to be the most important parameter influencing the depth of thermal injury during endobiliary radiofrequency ablation. In healthy swine, currently recommended settings of the generator may induce severe, supratherapeutic tissue damage in the biliary tree, especially in the high-risk area of the ampulla of Vater.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00-17:00
PAEDIATRIC: LIVER, BILIARY & PANCREAS - HALL 7

P0696 ROLE OF PROCALCITONIN AND C-REACTIVE PROTEIN AS BIOMARKERS OF INFECTION IN CHILDREN WITH LIVER DISEASE

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Introduction: Infection with organ failure is an important cause of mortality in patients with liver disease. Early and accurate identification of infection in these patients is challenging.

Aims & Methods: This study evaluated the role of procalcitonin (PCT) and C-reactive protein (CRP) as biomarkers of bacterial infection in children with liver disease.

Demographic and clinical data of consecutive children admitted with acute liver failure (ALF) or decompensated chronic liver disease (DCLD) were collected prospectively. Children were evaluated for infection at admission with hemogram including total and differential leukocyte count, PCT, CRP, blood and urine culture, chest X-ray and ascitic fluid analysis including culture in those with ascites. Systemic inflammatory response syndrome (SIRS) and severe sepsis were defined as per the International pediatric sepsis consensus definition[1].

Results: 164 children (113 boys, age 76(0.5 – 204) months, ALF = 69, DCLD = 95) were enrolled. 77 (47%) subjects had infection, most common site being ascitic fluid (AFI, n = 35), followed by urinary tract (UTI, n = 26), pneumonia (n = 22) and blood stream infection (BSI, n = 16). 21 children had multiple site infections, 18 had severe sepsis and 36 had SIRS.

Subjects with infection had significantly higher PCT (1.7 [0.1 – 38.1] ng/ml vs.0.3 [0.1 – 6.8] ng/ml; p = 0.00), CRP (1.82 [0.3 – 24] mg/dL vs. 0.33 [0.1 – 4.2] mg/dL, p = 0.00) and TLC (14,000 [3600 – 43800] /mm^3 vs. 8800 [3800 – 39600] / mm^3, p = 0.00) as compared to those without infection. Presence of fever did not

help in differentiating patients with and without infection (27/77 vs. 20/87, p=0.1). PCT and CRP values were not different in patients with various sites of infection i.e. BSI, AFI, UTI or pneumonia. PCT and CRP correlated with infection severity, highest in severe sepsis [8.3(3.5 – 38) ng/mL and 4.1(0.3 – 13.8) mg/dL] than infection [0.89 (0.1– 8) ng/mL and 1.7 (0.32-24) mg/dL] than no infection [0.3 (0.1 – 6.75) ng/mL and 0.3 (0.1 – 4.16 mg/dL). Sensitivity, specificity and likelihood ratio (LR) of CRP, PCT and TLC in identifying infection in children with liver disease is shown in Table 1. SIRS was commoner in patients with infection (31/77 vs. 5/87, p = 0.00). PCT (> 0.5 ng/ml) and CRP (>0.6 mg/dL) performed better in DCLD (AUC of 0.90 and 0.83) as compared to ALF patients (AUC of 0.73 and 0.69).

Conclusion: PCT and CRP are reliable markers of infection and correlate with infection severity in children with liver disease. Their diagnostic accuracy is better in DCLD than ALF cases. SIRS is significantly more common in patients with infection.

Reference

1. Goldstein B, Giroir B, Randolph A, et al. Definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005; 6: 2–8.

Disclosure of Interest: None declared

P0697 THE CLINICAL EFFECT AND CHANGES OF MICROFLORA UNDER PROBIOTIC SUPPLEMENTATION IN CHILDREN WITH BILIARY ATRESIA - A RANDOMIZED CONTROLLED TRIAL

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Introduction: Due to the modulatory effect on intestinal microflora, probiotics could be potentially used to prevent complication after hepatoportoenterostomy in children with biliary atresia, which can lead to progression of liver disease and require liver transplantation.

Aims & Methods: In this study we aimed at evaluating LGG probiotic treatment during the course of biliary atresia after the hepatoportoenterostomy in respect of clinical outcomes, liver function tests, gut microflora and intestinal barrier.

The patients were randomly assigned to two groups ingesting probiotic or placebo (1:1). The active preparation was the LGG probiotic (Lactobacillus GG) administered as capsuled powder (Dicoflor 60 preparation) for 6 months. Initially, after 3, 6 and 9 months the following parameters were assessed: A. anthropometric B. laboratory C. stool examination:- quantitative assessment of the gut microbiota composition by growing methods with the use of non-selective (differential) and selective growth media; quantitative assessment of the short-chain fatty acids (acetic, butyric and priopionic) and lactic acid; Alpha-1 Antitrypsin (A1AT) concentration in stool as a marker of intestinal barrier permeability.

The study included 30 children: 13 girls and 17 boys aged <4 months suffering from chronic cholestasis in the course of bile duct obstruction. In all patients, the bile duct obstruction diagnosis was intraoperatively confirmed and the Kasai portoenterostomy was performed.

Results: After 6 months there were 3 children in the LGG group suffering from at least one ascending cholangitis episode compared to 8 children in the placebo group, which was not statistically different. The number of all infections amounted to 6 in the LGG group and 12 in the placebo patients (ns). During the intervention, 7 out of 14 patients taking LGG and 5 out of 16 placebo patients were qualified for liver transplantation (no statistical difference).The level of conjugated bilirubin decreased below 2 mg/dl during the 6 months long trial in 6 patients in the LGG group and in 8 patients in the placebo group (ns) .After the intervention, clinical parameters (weight, height) and biochemical parameters (liver enzymes activity, the level of total and conjugated bilirubin, total protein and albumins, vitamin A and E) were similar both in the LGG and placebo groups. The level of Alpha-1 Antitrypsin (A1AT) concentration in stools was within normal limits. Also, the statistical differences between groups were not revealed.The gut microbiota and gut microbiota metabolisms of both groups measured with the use of SCFA did not differ after 6 months.

Conclusion: The LGG supplementation after the Kasai portoenterostomy in children suffering from the bile duct obstruction in the pilot study did not significantly influence the incidence of ascending cholangitis, the course of cholestatic liver disease, the death risk and the liver transplantation necessity.The LGG supplementation did not significantly influence gut microbiota and its metabolism.

Disclosure of Interest: None declared

P0698 PEDIATRIC PANCREATITIS. MULTICENTRE PROSPECTIVE DATA COLLECTION AND ANALYSIS BY THE HUNGARIAN PANCREATIC STUDY GROUP

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Introduction: The incidence of pediatric pancreatitis (PP) has increased in the last decade. Some of the recent studies showed that the occurrence of the disease has grown over 10/100,000 which is not much less than in adults. We have established the Paediatric Section of the Hungarian Pancreatic Study Group in order to organize nationwide data collection and improve themanagement of the disease.

Aims & Methods: Our aim was to analyse the epidemiology, risk factors, management and clinical outcome of PP in Hungary. 56 children suffering from PP were enrolled from 7 centres between 2012 and 2014.

Results: 61% of the children were female. 31 acute (AP), 11 recurrent acute (RAP) and 14 chronic pancreatitis (CP) cases were recorded in the registry. 84% of the AP patients had mild and 16% moderate episodes, however, no severe AP was observed. In RAP patients pancreatitis seemed to be more severe than in patients having isolated episodes (mild: 73% moderate: 18%, severe: 9%). Mortality was not observed at all. Without genetic testing we could identify the etiological factors only in 44% of the cases, the others remained idiopathic. In 17 cases, genetic analyses of PRSS1, SPINK1, CFTR and CTRC genes have been completed. Genetic alterations in PRSS1 were found in 3 cases (all CP), in SPINK1 in 4 cases (1 RAP and 3 CP), in CFTR in 1 case (CP) and in CTRC in 10 cases (3 AP and 7 CP). In 5 CP patients mutations in two genes were observed (3 SPINK1-CTRC, 1 PRSS1-SPINK, 1 CFTR-CTRC).

Conclusion: Genetic testing is essential to identify the etiological factors in children with pancreatitis.

Disclosure of Interest: None declared

P0699 RESULTS OF A PROSPECTIVE CLINICAL TRIAL IN PEDIATRIC PANCREATITIS (PINEAPPLE - PAIN IN EARLY PHASE OF PEDIATRIC PANCREATITIS)

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Introduction: The documented incidence of pediatric pancreatitis (PP) is very low, less than 1/100,000 in almost all European countries, whereas it is around 3.6-13.2 in the USA and Australia. Moreover, there are unexpectedly large differences between the incidences of PP among the countries and hospitals in Europe.

Aims & Methods: The aim of the PINEAPPLE study (ISRCTN35618458) is to understand the current practice of diagnosis of PP and to develop EBM guidelines that helps to evaluate (in a reliable and cost efficient way) the necessity of pancreatic enzyme measurement (PEM) and abdominal ultrasonography when a child has abdominal pain.

PINEAPPLE is a registered, multinational observational clinical trial. The PINEAPPLE-R subtrial is a retrospective review on children (patients under 18) records appearing at ER units, whereas, the PINEAPPLE-P subtrial is a prospective part of the study where detailed patients data (concerning medical history, complaints, symptoms, physical examination) are collected and PEM and abdominal imaging are performed in all cases. Until now 6012 patients records/PINEAPPLE-R and 90 patients/PINEAPPLE-P were enrolled from five pediatric centres.

Results: PINEAPPLE-R: 12% (710/6012) of the patients appearing at ER unit had abdominal pain. Only 2,5% (18/710) of them had PEM, whereas 30% (213/710) had transabdominal ultrasonograpy. Pancreatitis was diagnosed in one case only. PINEAPPLE-P: 1 pancreatitis of 90 patients with abdominal pain was diagnosed.

Conclusion: The PINEAPPLE-R study clearly shows that the number of PEM performed at ER units are unacceptably low in children, which could be the reason of low incidences of PP. More patients are crucially needed for PINEAPPLE-P in order to develop EBM guidelines.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00–17:00
PANCREAS II – HALL 7

P0700 IMPACT OF UPSIZING PERCUTANEOUS CATHETERS IN PATIENTS WITH SUSPECTED INFECTED NECROTIZING PANCREATITIS

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Introduction: Infected necrotizing pancreatitis is nearly always an indication for invasive treatment. Percutaneous catheter drainage (PCD) is now well established as the first intervention in a 'step-up approach'. It has been suggested that a drain upsizing strategy might obviate the need for additional surgical necrosectomy and improve clinical outcome, but studies on this topic are lacking.
Aims & Methods: We retrospectively identified patients with necrotizing pancreatitis from in-hospital databases (2004-2014) in four tertiary referral centers. Patients who underwent PCD as primary treatment for suspected infected necrosis were included. We compared patients' outcomes of a single center that attempted to routinely upsize in case of lack of clinical improvement with those of patients treated in the three centers where this strategy was not used routinely. Primary outcome was the need for additional surgical necrosectomy following PCD. Secondly, we compared complications including mortality and new onset (multi) organ failure.
Results: Of 1427 consecutive patients with acute pancreatitis, 369 patients (26%) were diagnosed with necrotizing pancreatitis, of which 117 patients (32%) underwent primary PCD for suspected infected necrosis. Infected necrosis was ultimately proven in 82 of these patients (70%). In total 42 patients (36%) were treated in the drain upsizing strategy center versus 75 patients (64%) in the non-upsizing strategy centers. Patient characteristics were similar in baseline, except for differences in age and timing of first PCD for which we corrected in the analyses. The median of drain procedures was 3 (interquartile range (IQR) 2-4) in the upsizing strategy center versus 2 (IQR 1-2) in the non-upsizing strategy centers, $P < .001$. The maximal drain size was median 16 French (IQR 14-20) compared to 14 French (IQR 12-14), $P < .001$, respectively. Additional surgical necrosectomy was required in significantly less patients in the upsizing strategy center, 29% vs. 52% $P = .045$. Mortality was comparable in both groups, 17% vs. 19%, $P = 0.79$. New onset (multi) organ failure after PCD occurred in 5% of patients in the upsizing strategy center compared to 20% of patients in the non-upsizing strategy centers, $P = 0.11$.
Conclusion: A PCD upsizing strategy for patients with suspected infected necrotizing pancreatitis appears to reduce the need for surgical necrosectomy. Future studies will have to demonstrate the true clinical value of PCD upsizing and whether this should be performed on indication or preemptively.
Disclosure of Interest: None declared

P0701 ELEVATED LEVELS OF IL-6 AND IL-8 PREDICT DEVELOPMENT OF RESPIRATORY FAILURE IN PATIENTS WITH ACUTE PANCREATITIS

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Introduction: Acute lung injury (ALI) is the commonest organ failure in patients with acute pancreatitis (AP). It is a major cause of early mortality in such patients and cytokines play a major role in its pathophysiology.
Aims & Methods: Aim & Methods: To study the predictive role of inflammatory cytokines in development of ALI in patients with AP.
In this prospective study between July 2013 and December 2014 consecutive eligible patients of AP underwent complete demographic, clinical, biochemical and radiological evaluation. Severity classification was done using revised Atlanta classification and also systemic inflammatory response score (SIRS) and Bedside Index of Severity of Acute Pancreatitis(BISAP), CT Severity Index (CTSI) and APACHE II scores were used. Serial arterial blood gas (ABG) analyses were done and ALI severity defined as per Berlin Classification using PaO_2/FiO_2 ratio. Development of ALI was monitored in all the patients. Serum levels of interleukin (IL)-6, IL-8, IL-10, IL-1b and TNFa were measured at baseline (day 1) for all patients and on day 3 in those who had ALI. For comparative analysis patients were divided into 2 groups: with and without ALI. The ALI cohort was further subdivided into persistent ALI (P-ALI) and transient ALI (T-ALI). A subgroup of ALI patients who developed ALI later during hospital stay was defined as "late onset" ALI (LO-ALI) to devise a predictive model for ALI using cytokine levels. Statistical analysis was done using SPSSv22.0
Results: Of the 107 patients (mean age of 38.4 yrs, 64.5% males, etiology: alcohol 36.4% gallstone disease 26.2% and others 51.4%), ALI developed in 51 (47.7%) of whom 40(78.4%) had ALI on admission while 11(21.6%) had LO-ALI. T-ALI was seen in 16(31.4%) while 35 (68.6%) had P-ALI. Patients with ALI had significantly higher IL-1b ($p < 0.0001$), IL-6 ($p < 0.0001$), IL-8 ($P < 0.001$) and TNFa ($P < 0.0001$) and lower IL-10 ($p < 0.0001$) levels on day 1, when compared to non-ALI group. In the ALI group, day 3 levels of IL-1b ($p = 0.001$), IL-6 ($p = 0.02$), IL-8 ($p = 0.006$) and TNFa ($p = 0.006$) were significantly higher than day 1 levels. Significant rise on day 3 of only IL-1b ($p = 0.04$) was observed in T-ALI group as compared to both IL-1b ($p = 0.001$) and TNFa ($p = 0.02$) in the P-ALI group. Day 1 levels of IL-6 and IL-8 had strong positive correlation with severity indices such as SIRS ($p < 0.001$), BISAP ($p < 0.001$) and CTSI ($p < 0.0001$) as also with outcome measures such as need for intervention ($p < 0.0001$), hospital stay ($p < 0.0001$) and intensive care stay ($p < 0.0001$). LO-ALI group had significantly higher levels of IL-6 ($p < 0.0001$), IL-8 ($p < 0.0001$), TNFα ($p < 0.0001$) and IL-1β ($p < 0.006$). IL-6 at cut off levels of 84.85 pg/mL (AUC = 0.94, sensitivity & specificity 91%) and IL-8 at cut off level of 112.5 pg/mL (AUC = 0.909, sensitivity 91% specificity 94.6%) predicted subsequent development of ALI.
Conclusion: Rising levels of IL-1b and TNFα suggest development of persistent ALI. IL-6 and IL-8 levels at admission can predict the future development of late onset ALI.
Disclosure of Interest: None declared

P0702 STUDY OF LUNG FUNCTION TESTS TO PREDICT DEVELOPMENT OF ACUTE LUNG INJURY IN PATIENTS WITH ACUTE PANCREATITIS

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Introduction: The commonest organ failure in patients with acute pancreatitis (AP) is acute lung injury (ALI). Data on pulmonary function tests (PFT) in AP is limited.
Aims & Methods: To study PFT in patients with AP and evaluate the role of PFTs in predicting ALI.
In this prospective study between July 2013 and December 2014 consecutive patients of AP underwent complete demographic, clinical, biochemical and radiological evaluation. Severity classification was done using revised Atlanta classification and also systemic inflammatory response score (SIRS) and Bedside Index of Severity of Acute Pancreatitis (BISAP), CT Severity Index (CTSI) and APACHE II scores were used. Serial arterial blood gas (ABG) analyses were done and ALI severity defined as per Berlin classification using PaO_2/FiO_2 ratio. Development of ALI was monitored in all the patients. PFTs were done by spirometry as soon as possible after admission. Forced expiratory volume in first second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio were used as basic parameters for interpretation and all measurements were expressed as a percentage of their predicted values (FVC%, FEV_1%). Patients were divided into 2 groups: with and without ALI. The ALI cohort was further subdivided into persistent ALI (P-ALI) and transient ALI (T-ALI). A subgroup of ALI group which developed ALI later during hospital stay was defined as "later onset" ALI (LO-ALI) to devise a predictive model for ALI with PFT parameters. Statistical analysis was done using SPSSv22.0
Results: Of the 107 patients (mean age of 38.4 yrs, 64.5% males, etiology: alcohol 36.4% gallstone disease 26.2% and others 51.4%), ALI developed in 51 (47.7%) patients of whom 40 (78.4%) had ALI on admission while 11 (21.6%) had LO-ALI. T-ALI was seen in 16 (31.4%) while 35 (68.6%) had P-ALI. PFT could be performed in 87 patients (52 non-ALI, 35 ALI including 9 from LO-ALI subgroup). ALI group had significantly lower FVC% ($p < 0.0001$) and FEV_1% ($p < 0.0001$) signifying higher lung dysfunction compared to those without ALI. Similarly, P-ALI had lower FVC% (58.9 ± 14.8 vs. 69.6 ± 17.2, $p = 0.06$) and lower FEV_1% ($p = 0.04$) than T-ALI. A significant correlation existed between PaO_2/FiO_2 ratio and FVC% ($r = 0.513$, $P < 0.0001$) and FEV_1% ($r = 0.488$, $p < 0.0001$). Both FEV_1% and FVC% showed significant correlation with other severity parameters such as SIRS ($p < 0.0001$), BISAP ($p < 0.00011$), CTSI ($p < 0.0001$) and APACHE II ($p < 0.002$) and also with need for intervention ($p = 0.04$), hospital stay ($p < 0.0001$) and intensive care stay ($p = 0.001$). LO-ALI (9) had significantly lower FVC% ($p = 0.02$) and FEV_1% ($p = 0.03$) as compared to those without ALI, but a predictive cut off could not be achieved (AUC = 0.257, $p = 0.021$) due to small numbers.
Conclusion: Patients who eventually develop ALI later have more severe lung dysfunction at baseline than those who do not and PFTs can act as a tool to predict it.
Disclosure of Interest: None declared

P0703 USE OF A NEW PLASTIC PANCREATIC STENT TO FACILITATE BILIARY CANNULATION IN DIFFICULT ERCP

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Introduction: Use of a pancreatic stent (PS) to facilitate biliary cannulation is one of the so called pancreatic techniques in which the pancreas serve as a step to gain the Common Bile Duct (CBD). We report on the performance characteristics of using a new plastic PS to facilitate CBD cannulation in difficult ERCP.
Aims & Methods: CBD cannulation was attempted with a sphincterotome loaded with a guidewire controlled by the endoscopist. In cases of difficult biliary access in which the Pancreatic Duct was cannulated, an straight Advanix PS (Boston Scientific), having 5 french, and 4 cm in length without inner barbs was placed. This PS has a proximal radiopaque marker that facilitates recognition of the indwelling position. After this, physician-controlled guidewire was attempted by using the PS to direct the sphincterotome into the CBD.
Results: Among 98 ERCPs in patients with naïve Papilla, 16 (16.3%) received an Advanix PS to facilitate biliary cannulation. Successful cannulation was achieved in 16 (100%) without the need of Needle-Knife-Precut. In one patient the PS dislodged from the Papilla during cannulation attempts. No postERCP pancreatitis was observed. There were eight patients with CBD stones, three with pancreatic head cancer and five with type I sphincter of Oddi dysfunction after cholecistectomy. On radiological follow-up, 7/15 (47%) PS had spontaneouly passed after two weeks, whereas 8/15 (53%) remained still in place and had to be removed by gastroscopy. No pancreatitis occurred after removal.
Conclusion: Endoscopist-controlled guidewire over this new PS facilitates biliary cannulation and appears to prevent from postERCP pancreatitis. The PS althougth has no inner barbs, remained in place for more than two weeks in half of the patients and had to be removed by gastroscopy. The inner radiopaque marker results very useful to know its position.
Disclosure of Interest: None declared

P0704 GHRELIN MOLECULAR SYSTEM IN THE PROTECTION OF PANCREATIC ACINAR CELLS

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Introduction: Ghrelin (GHRL), an endogenous ligand for the growth hormone (GH) secretagogue receptor (GHS-R) has been isolated from the stomach and identified in the pancreas. GHRL has been demonstrated to protect pancreatic tissue from caerulein-induced acute pancreatitis (CIP).
Aims & Methods: To investigate the effect of GHRL and caerulein on gene expressions and on protein signals of GHRL, GHS-R1 and of an antioxidant enzyme: superoxide dysmutase (SOD) in the isolated pancreatic acini.
Pancreatic acini were isolated by collagenase digestion from control rats and from rats pretreated with GHRL (50,0 μg/kg i. p.) administered 48 hours before the isolation. Isolated acini were incubated with high concentration of caerulein (10^{-8}M). The gene expressions were determined by RT-PCR, whereas the protein contents were assessed employing Western-blot.
Results: Protein expressions and mRNA signals for GHS-R1a receptor, GHRL and for SOD-3 have been detected in the pancreatic acini under basal conditions and have been significantly upregulated following application of GHRL to the rats. Incubation with caerulein markedly downregulated signals of GHS-R1a and SOD-3 in pancreatic acini, but failed to affect these for GHRL. Pretreatment of rats with GHRL prevented caerulin-induced suppression of GHS-R1a and SOD-3 signals.
Conclusion: Caerulein overstimulation is able to modify the GHS-R1a receptor in the pancreatic acini and this effect could be prevented by pretreatment of rats with GHRL. Protective effect of GHRL on caerulein-induced pancreatitis could be dependent, at least in part, on the activation of SOD and improvement of antioxidant system in the pancreas.
Disclosure of Interest: None declared

P0705 ENDOSONOGRAPHY-GUIDED NECROSECTOMY VERSUS SURGICAL TREATMENT OF INFECTED WALLED-OFF PANCREATIC NECROSIS: A COMPARATIVE STUDY

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Introduction: The surgical necrosectomy (SUR-N) of walled-off pancreatic necrosis (WOPN) has high morbidity and mortality rates. The new options of treatments have been increasingly used such as step-up approach and endoscopic drainage. The endoscopic approach is not yet defined as a first option for this treatment, but have been increasingly used for its efficacy, safety and the possibility of necrosis approach in any situation with the aid of endoscopic ultrasonography (EUS).
Aims & Methods: The objective was to study and compare the characteristics, clinical course, the immediate and late adverse events in patients with WOPN treated by SUR-N and EUS-guided necrosectomy (EUS-N). 63 patients with WOPN were treated by SUR-N (35) and EUS-N (28) from Aug/90 to Jul/2014.
Results: The mean age was higher in the EUS-N ($p < 0.01$). Sex, ASA index, diabetes, obesity, and cardiovascular risk factor before treatment were similar to the SUR-N and EUS-N groups ($p > 0.05$). Cause of AP ($p = 0.06$), infected necrosis ($p = 0.13$) and median time from onset of symptoms to treatment ($p = 0.34$) were similar for both groups. The Marshal ($p < 0.01$) and CT Balthazar score ($p < 0.01$) were significantly higher for SUR-N. Acute adverse events were statistically significant for the EUS-N vs SUR-N (71% vs 37%, $p < 0.01$). Despite the occurrence only in SUR-N group of sepsis, post-operative hernia, bowell obstruction, pneumonia, fistula (pancreatic and biliary) and chylous ascites there was no statistical difference compared to EUS-N group. The late adverse events were statistically significant for patients undergoing SUR-N vs EUS-N in relation to bowell and biliary obstruction (21% vs 0%, $p = 0.04$ and 27% vs 0%, $p = 0.01$, respectively) and required surgery (36% vs. 8%, $p = 0.02$, respectively). The average follow-up was 493 days, there was no difference between patients who underwent SUR-N and EUS-N in relation to pancreatic sequelae, including pseudocyst ($p = 0.62$), cases of onset diabetes ($p = 0.31$) or need for pancreatic enzymes ($p = 0.29$).
Conclusion: Compared to SUR-N, the EUS-N showed a lower rate of adverse events. EUS-N appears to be a safe and effective procedure must be included in the therapeutic algorithm patients with WOPN.
Disclosure of Interest: None declared

P0706 ETHANOL AND ETHANOL METABOLITES DECREASE THE ACTIVITY AND EXPRESSION OF CFTR CL- CHANNEL AND IMPAIR EXOCRINE PANCREATIC FLUID AND BICARBONATE SECRETION

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Introduction: Excessive ethanol consumption is one of the most common causes of acute and chronic pancreatitis. It is also documented that genetic defects of CFTR can lead to pancreatitis, however the effects of alcohol consumption on CFTR function in the pancreas is not known.
Aims & Methods: Our aim was to investigate the effects of ethanol and ethanol metabolites on the exocrine pancreatic fluid and bicarbonate secretion and on CFTR function and expression. Intra/interlobular pancreatic ducts were isolated from guinea pigs to study the effects of ethanol and ethanol metabolites on the *in vitro* pancreatic fluid and bicarbonate secretion. In vivo exocrine pancreatic secretion of anesthetized mice has been investigated using magnetic resonance cholangiopancreaticography (MRCP). The effects of ethanol and ethanol metabolites on CFTR activity pancreatic ductal epithelial cells (PDEC) was measured by patch clamp. CFTR expression in human tissue samples were assessed by immunohistochemistry in control human pancreatic tissue and in acute and chronic alcohol-induced pancreatitis. The mechanism of the decreased CFTR expression has been characterized in MDCK cell by western blot, cell surface elisa and pulse chase experiments.
Results: The administration of 100mM ethanol, or the non-oxidative ethanol metabolite palmitoleic acid (POA; 200μM) markedly reduced the *in vitro* fluid and bicarbonate secretion of isolated guinea pig pancreatic ducts. Moreover MRCP showed that the total excreted volume (used as a marker of the *in vivo* pancreatic fluid secretion) was significantly decreased after the i.p. injection of 1.75g/kg ethanol and 750mg/kg palmitic acid (PA). Exposure of guinea pig PDEC to 100mM ethanol or 200μM POA significantly decreased the forskolin-stimulated CFTR currents. Next we evaluated the effect of ethanol on the CFTR expression. Using human tissue samples we showed that CFTR expression was significantly decreased in acute or chronic alcohol-induced pancreatitis both at mRNA and protein levels. Similar decrease of pancreatic ductal CFTR expression has been observed in guinea pigs after the i.p. injection of 1.75g/kg ethanol and 750mg/kg PA. Experiments on MDCK-II cell expressing WT human CFTR revealed that ethanol and its metabolites decrease CFTR expression and plasma membrane density via accelerated channel plasma membrane turn over and damaged protein folding.
Conclusion: The findings indicate that alcohol and alcohol metabolites induce a loss of CFTR function and expression, which in turn impairs pancreatic ductal fluid and bicarbonate secretion. We suggest that the correction of CFTR function and expression should offer therapeutic benefit.
Disclosure of Interest: None declared

P0708 EXTENT OF NECROSIS AS KEY DETERMINANT OF OUTCOME IN PATIENTS WITH ACUTE NECROTIZING PANCREATITIS

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Introduction: Necrosis in patients of pancreatitis can be either pancreatic, peripancreatic or both. However the impact of site of necrosis over collection location and disease outcome is still unknown.
Aims & Methods: To evaluate the impact of site of necrosis upon location of collections and outcome in patients of Acute Necrotizing Pancreatitis (ANP).
161 Patients with ANP (Mean age-39.91 ± 13.78 yrs) were classified according to the site of necrosis [Pancreatic (Group I), Peripancreatic (Group II) or both (Group III)]. They were managed as per institute protocol (Step up), followed up for development of fluid collections and then categorized according to locations of collections within the abdominal cavity [Pancreatic (A), Peripancreatic (B), both (C), Peripancreatic with distant (D) and at all sites (E)]. Outcome variables were hospital stay, ICU stay, need for pigtail drainage, surgery and mortality. Data was recorded in excel sheet and statistical analysis was done using SPSS v17.0.
Results: Type III necrosis was the commonest type of necrosis (n = 69, 42.8%), followed by type II (n = 46, 28.57%) and type I necrosis (n = 46, 28.57%). Type I necrosis was significantly associated with collection location C [32(82.6%)], whereas type II necrosis had significant association with location D [20(43.47)] and Type III necrosis had association with location E [59(85.5%)] ($p < 0.001$). Surgery, mortality and need for percutaneous drainage were exclusively seen in type III necrosis [7(10.14%), 14(20.28%), 54(78.26%)]. Duration of hospital and ICU stay were significantly associated with type III compared to type I necrosis (34.28 ± 24.88 vs. 13.26 ± 7.46 days, 8.17 ± 12.96 vs. 0.89 ± 2.72 days, $p < 0.001$).
Conclusion: Collections develop in a compartment more than the area of necrosis. Outcome of patients with necrosis involving both pancreas and peripancreatic region is worst followed by only peripancreatic necrosis and pancreatic necrosis alone in sequence.
Disclosure of Interest: None declared

P0709 COFILIN-1-MEDIATED GROWTH REGULATION IN PANCREATIC CANCER CELLS IS ASSOCIATED WITH DOWNREGULATION OF GLI1 AND INCREASED ACTIVITY OF THE MAL/SRF TRANSCRIPTION FACTOR COMPLEX

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Introduction: We have previously described a multi-step high-content screening approach to identify novel functionally relevant target genes in pancreatic ductal adenocarcinoma (Buchholz et al. 2015, *PLoS-One*, 10:e0122946). The results of these analyses predicted an unexpected and previously undocumented role for the small actin-binding protein cofilin-1 in growth control of pancreatic cancer cells.
Aims & Methods: Multiple tissue arrays, RNAi, cell proliferation and viability assays, FACS analysis, Western blot, inducible shRNA clones, reporter gene assays.
Results: Cofilin-1 is strongly overexpressed in human pancreatic ductal adenocarcinoma both at the mRNA and at the protein level. RNAi-mediated knockdown of cofilin-1 gene expression in four different pancreatic cancer cell lines resulted in significantly reduced cell viability and proliferation rates, while apoptosis was not induced. Further, the capacity for anchorage-independent growth was strongly reduced in the absence of cofilin-1 expression. Moreover, stable repression of cofilin-1 expression in pancreatic cancer cell clones significantly decreased the growth of xenograft tumors *in vivo*. Flow cytometric analyses indicated that these effects were primarily mediated by attenuation of G1/S transition during cell cycle. Mechanistically, CFL1 knockdown resulted in simultaneous overactivation of the MAL/SRF transcription factor complex and downregulation of expression of the Hedgehog pathway effector Gli1, which is well known to regulate pancreatic cancer cell growth.
Conclusion: In addition to its previously known roles in actin dynamics and cell motility, cofilin-1 has a direct and essential role in growth regulation of pancreatic cancer cells. The clinical significance of this observation is emphasised by the strong and widespread overexpression of cofilin-1 in human PDAC.
Disclosure of Interest: None declared

P0710 A FAST ASSAY TO GAUGE FOR TAA-REACTIVE T-CELLS IN PBMCS FROM PATIENTS WITH PANCREATIC CANCER

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Introduction: Active cellular therapy (ACT) using *ex-vivo* expanded T-cells from patients with cancer, obtained by apheresis, can represent a viable source for anti-cancer directed cellular therapy. The objective was to establishe a T-cell expansion protocol using two rounds of re-stimulation with TAA peptides along with IL-2, IL-15 and IL-21. In order to gauge the ex-vivo cellular reactivity as well as the potential to successful expand antigen-specific T-cells from patients with pancreatic cancer, a screening assay using whole-heparin blood, to gauge for TAA reactivity (NY-ESO-1, survivin, mesothelin) and control antigens (EBNA-1, EBNA-3, CMVpp65) was established.
Aims & Methods: Fresh blood samples were obtained from 24 patients with pancreatic cancer and from 6 individuals with pre-malignant lesions and tested for anti-TAA reactivity defined by CD3 + CD4+/CD3 + CD8+ T-cell proliferation and IFN- γ production. T-cells were expanded without cytokines, with IL-2 and IL-7, or with IL-2, IL-15 and IL-21. For T-cell expansion, PBMCs were expanded by adding cytokine and TAA peptides. CD3, CD4, CD8, CD45RA and CCR7 were determined by flow cytometry and TAA-reactive T-cells were identified by ICS (IL-2, TNF, IFN and IL-17).
Results: IFN-γ responses were detected in 90% (27 of 30) in blood samples for mesothelin, 55.3% (16 of 30) for survivin and 43.3% (13 of 30) for NY-ESO-1 (without adding cytokines). Cellular responses could be augmented by adding cytokines, i.e. IL-2 and IL-7 (to favor CD4+ T cell proliferation) or IL-2, IL-15 and IL-21 (to favor CD8+ T cell proliferation). IFN-γ responses were detecetd in 100% (30 of 30) in blood samples for EBNA1, 100% (30 of 30) for EBNA3 and 93.3% (28 of 30) for CMV without the addition of cytokines and the cellular responses could be augmented by adding cytokines. TAA-reactive T cells could be successfully expanded ex vivo and exhibited TAA-specific production of IFN-γ and TNF-α and a CD8 + CD45RA-CCR7+ phenotype.
Conclusion: A TAA-specific whole blood assay can be used to gauge the potential for expansion of TAA-reactive T-cells in peripheral blood from patients with pancreatic cancer. TAA-reactive T-cells can be successfully expanded in IL-2, IL-15 and IL-21 and could represent a viable source for the cellular therapy of patients with pancreatic cancer.
Disclosure of Interest: None declared

P0711 GENERATION OF TUMOR-INFILTRATING LYMPHOCYTE CULTURES FROM PANCREATIC CANCER FOR ADOPTIVE TRANSFER THERAPY

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Introduction: The generation of T-lymphocyte cultures with specific reactivity against autologous tumor is a prerequisite for effective adoptive transfer therapies – among the most successful of immune therapies. Pancreatic cancer-specific tumor-infiltrating lymphocyte (TIL) cultures are difficult to obtain, but can represent a viable T-cell source for cellular therapy of patients with pancreatic cancer. The objective was to optimize the method for generation of T-lymphocyte cultures from pancreatic cancer TILs.
Aims & Methods: Pancreatic cancer tissue was obtained by excision or core biopsy from the fresh surgical specimens of 30 patients and cultured for 10 days with cytokines (IL-2, IL-15, and IL-21). TILs were extracted and expanded using OKT-3 and irradiated allogenic peripheral blood mononuclear cells. The specific activity of TILs for recognition of tumor-associated antigens (mesothelin, survivin, and NY-ESO-1) was evaluated by IFN-γ production and intracellular cytokine production and detected by ELISA and ICS. Clonal T-cell populations were tested by a panel of TCR Vβ-specific antibodies and by TCR CDR3 PCR-guided analysis, along with T-cell differentiation and exhaustion markers by flow cytometry.
Results: TILs from all 30 patients, up to 10e11 cells, could successfully be expanded using the combination of IL-2/15/21. Even the core biopsy specimens yielded at least 1.5 x 10e9 CD8 + TILs. Four-week TIL-cultures showed up to 90% CD8 + T-cells, yet one culture exhibited exclusively CD4 + TILs with a CD45RA-CCR7+ phenotype. The majority of the CD8+ and CD4+ TILs resided in the central memory and effector memory subsets (CCR7 + CD45RA- and CCR7-CD45RA-). Some TIL cultures showed preferential expression of TCR-Vβ families - in CD8 + TILs 99.3% in Vβ13.2, 77% in Vβ1, 68.7% in Vβ22, 64% in Vβ14 for individual patients. 30% of the expanded Vβ families were monoclonal. ICS analysis showed a low frequency (up to 2.5%) of mesothelin, survivin or NY-ESO-1 reactive CD8 + TILs. TILs from one patient showed up to 15% NY-ESO-1 specific IFN-γ and TNF-α production in CD4+ and CD8 + TILs. Specific T-cell killing of autologous tumor cells could be demonstrated by chromium-51 release essay – up to 70% cancer cell death with 25:1 TIL-to-tumor cell ratio.
Conclusion: The methods for the robust and fast TIL-generation from pancreatic cancer tissue were optimized using a cytokine cocktail of IL-2/IL-15/IL-21 even for small biopsies. TILs show a central-memory and effector memory phenotype and are monoclonal, which is a good prerequisite for efficient T-cell therapy.
Disclosure of Interest: None declared

P0712 GASTROKINE AS A NOVEL POTENTIAL BIOMARKER FOR PREMALIGNANT PANCREATIC LESIONS

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Introduction: Pancreatic cancer is a uniformly lethal disease that is difficult to diagnose at an early stage and even more difficult to cure. The current methods for diagnosing pancreatic cancer are ineffective and/or impractical for identifying smaller, potentially curable lesions. Gastrokine (GKN1-3) is a secreted auto-/paracrine protein in the gastric mucosa which shows growth factor or 'cytokine-like' activity toward gastric epithelial cells. GKN expression has so far been shown predominantly in the stomach, except for trace levels in the uterus and placenta and in the duodenum. In the stomach, GKN expression is confined to the gastric epithelium, where individual paralogs (GKN1-3) manifest remarkable cell-type-specific localization on different mucus-secreting epithelial lineages. Definitive physiological functions have not been formally ascribed to GKNs. The limited published evidence suggests fundamental roles in regulating gastric epithelial homeostasis and tumor suppression. While current research focuses on the exploration of tumor-suppressive properties of GKN1 regarding gastric tumors, nothing is known about GKN expression and function in other organ systems. Within the frame of a whole genome microarray analysis of a mouse model for pancreatic carcinogenesis (KrasxPtf1a), we have found gastrokines strikingly upregulated in the pancreas during pre-neoplastic conversion.

Aims & Methods: The aim of the study is to investigate gastrokine expression and function during pancreatic carcinogenesis. Gastrokine mRNA expression was confirmed by RT-PCR in human patients and different mouse models (pancreatitis and pancreatic carcinogenesis). Data mining of human microarray results focused on benign and malignant pancreatic diseases. Gastrokines were visualized by immunohistochemistry. The presence of GKNs in different stages of pre-malignant lesions was defined by IHC and mucin co-expression analysis. Secretion of GKNs in mouse pancreatic juice was shown by proteomic analysis. In vitro acinar assays were performed to analyze GKN expression during acinar transdifferentiation.

Results: Gastrokine expression is highly upregulated during the early stages of mouse pancreatic carcinogenesis. GKN transcripts are also increased in human patients in peri-tumoral tissue and in benign pancreatic tumors. GKN expression is neither detected in healthy pancreas nor in samples with pancreatic inflammation. Immunohistochemistry reveals strong GKN expression in pre-malignant PanIN lesions. GKN1 is abundant in the cytoplasm of dysplastic epithelium whereas GKN2 is localized to associated inflammatory cells. GKNs are absent from mouse and human PDAC. GKNs are co-expressed with Muc5ac and Muc2 in human patients indicating an expression on intestinal type IPMNs. ELISA and proteomic analysis in mice confirmed the secretion of GKN1 into pancreatic juice but not serum.

Conclusion: We identified for the first time gastrokine expression in neoplastic human and mouse pancreatic tissues. GKN expression is specific for premalignant PanIN lesions and it is secreted into the pancreatic juice during pancreatic carcinogenesis. Therefore, gastrokine could serve as a potential biomarker for early pancreatic pre-neoplastic lesions and benign tumors. Furthermore, determination of GKNs in pancreatic juice may provide a tool to identify patients at risk.

Disclosure of Interest: None declared

P0713 THE EFFICACY AND PITFALLS OF ENDOSCOPIC ULTRASOUND IN THE DIFFERENTIAL DIAGNOSIS OF PANCREATIC CYSTS

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Introduction: Pancreatic cystic lesions (PCL) are increasingly being diagnosed in clinical practice. However the efficacy of several methods in differential diagnosis is still uncertain and differs between centers. We investigated the role and contribution of endosonography (EUS) and EUS-guided fine needle aspiration (EUS-FNA) in the differential diagnosis of PCL.

Aims & Methods: We identified all patients who underwent EUS and EUS-FNA for PCL in our center from 2011 to 2014. Data were collected on demographics, clinical, laboratory and imaging, the results of biochemical and cytological evaluation of cyst fluid, in case it is available.

Results: There were 379 patients (45% male, mean age 57,6 ± 14,6 years, range 17-90). PCL were more commonly diagnosed between the ages of 60-69: 28% and 50-59: 23%. Three in four of the patients were symptomatic (excluding pseudocysts, 42%) and diabetes mellitus was present in 1/3. The mean cyst size was 38.2 ± 31,1 mm (median: 30 mm, range; 4-220 mm). A total of 268 FNAs were attempted, 3 of which were unsuccessful. In cytology, 15(10%) showed insufficient, and 41 (27%) non-specific findings. Out of 154 cytological examination, a specific diagnosis was reached in 98 (63%). Overall, out of 379 cases, a specific diagnosis could be reached in 274 (73%) patients: 95 (25%) were pseudocysts, 78 (21%) mucinous cysts, 40 (11%) cystic tumors, 38 (10%) serous cystadenomas (SCA), and 23(6%) other cystic lesions. In 51 cases surgery was performed. Diagnosis included, mucinous cystic tumor (MCN) (6), intraductal papillary mucinous neoplasm (10), cystic neuroendocrine tumor (2), SCA (3), solid pseudopapillary tumor (4), pseudocyst (4), cystic tumor (12), solid tumours with cystic degeneration, and cysts of different origin (10). The kappa value for the diagnosis of mucinous cyst between imaging-surgery were 0.688 and EUS-surgery, 0.658, respectively.The kappa level between EUS vs. imaging in making a diagnosis of pseudocyst was %77,7 (p: 0.001). In all serous cysts, the cyst amylase level was below 2000 U/L and CEA was below 5 ng/ml but the levels of amylase and CEA showed a wide variation in all other types of cysts. In 9% of pseudocyst, the amylase were below 2000 U/L. In two surgically diagnosed MCN, the cyst CEA were below 5 ng/ml, and in one of them amylase was over 20.000 U/L. In another MCN, CEA was 40 ng/ml and amylase was over 20.000 U/L. While in all serous cysts the serum CA19-9 was below 37 U/L. In 80 % of cystic malignancies it was over 37 U/ml.

Conclusion: The diagnostic value of imaging and EUS towards PCL seems to be similar. EUS-FNA obtained cyst cytology reached a specific diagnosis in 63% of the cases. While cyst CEA and amylase levels showed a variable diagnostic capacity and were sometimes, misleading, serum CA 19-9 level seemed to be discriminatory between benign and, already, malignant lesions.

Disclosure of Interest: None declared

P0714 NEUROGENESIS AND ANGIOGENESIS IN PANCREATIC CANCER BEHAVE CONCORDANTLY AND EXHIBIT DISTINCT TRANSCRIPTIONAL PROFILES

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Introduction: Pancreatic cancer (PCa) is characterized by increased intratumoral nerve density and nerve hypertrophy. Conversely, the density of vessels and tumor perfusion in PCa were reported to be decreased when compared to normal pancreas, creating a hypoxic tumor microenvironment. This observation raises the question whether neurogenesis and angiogenesis in PCa behave oppositely or even suppress each other.

Aims & Methods: The current study aimed to elucidate the interaction between neurogenesis and angiogenesis and to decipher the molecular actors that drive generation of nerves and vessels in PCa. Human PCa specimens (UICC stages II-III, n = 57) were analyzed for the density of all ($CD31^+$) vessels and all ($S100^+$) nerves in the whole tumor area via a novel triple immunofluorescence/immunohistochemistry analysis that additionally co-labeled cancer cells via cytokeratin-19 (CK19). The density of nerves and vessels were correlated to each other and to the severity of neural invasion (NI) and angioinvasion. The transcriptomic profile within tumor tissue of patients with strong neurogenesis or strong angiogenesis was compared to that of patients with little neuro- or angiogenesis via profiler PCR arrays.

Results: 41 out of 57 patients exhibited NI, whereas angioinvasion was detected in only one out of 57 patients. The mean vessel size and mean nerve size correlated positively (Sperman's coefficient $r = 0.43$, $p = 0.0013$), and the total area of nerves increased in parallel with the total area of vessels in the analyzed specimens ($r = 0.28$, $p = 0.04$). The frequency of NI increased in concordance with the amount of tumor innervation ($r = 0.25$, $p = 0.059$). There was no association between vessel density and NI. Patients with more pronounced tumor angiogenesis had greater intratumoral amounts of matrix metalloproteinase (MMP9), beta-III-integrin, TgfbetaR1, CXCL9, and lower levels interferon-alpha-1 (Ifna1) and LECT1. Furthermore, patients with more neurogenesis exhibited intratumoral upregulation of interleukin-6, TrkA, Nr1I2, NGF, CXC3CR1, and Neurotrophin-3, and downregulation of ciliary neurotrophic factor (CNTF).

Conclusion: Angiogenesis and neurogenesis behave concordantly in PCa. Interleukin-6 and neurotrophic factors may be responsible for the remarkably high prevalence of NI in PCa.

Disclosure of Interest: None declared

P0715 TM4SF1 PROMOTES INVASION AND METASTASIS OF PANCREATIC CANCER VIA REGULATING THE EXPRESSION OF DDR1

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) has increasingly mortality rates because it has highly invasion and metastasizes rapidly. We previously found that Transmembrane-4-L-six-family-1(TM4SF1), a four-transmembrane L6 family member, was highly expressed in human pancreatic cancer tissues and PDAC cell lines. Also, TM4SF1 promoted cancer cells invasion and metastasis *in vitro* and *in vivo*. Here, we investigated the mechanism of TM4SF1-mediated invasion and metastasis in PDAC.

Aims & Methods: We used small interfering RNAs in PANC-1, AsPC-1 to study the function of TM4SF1 on regulating invadopodia, which mediated the extracellular matrix (ECM) degradation to support cancer cells invasion. We investigated the ability of TM4SF1 to regulate the expression of discoidin domain receptor 1 (DDR1) using real-time PCR, immunoblot, immunofluorescence and coimmunoprecipitation analyses. And the effects on cell migration and invasion were analyzed by Transwell chambers and Matrigel invasion chambers. Finally, the clinical relevance of TM4SF1 and DDR1 was investigated using adjacent normal pancreatic tissues and pancreatic cancer specimens.

Results: In human PDAC cell lines, TM4SF1 facilitated the activation of matrix metalloproteinase 2 (MMP2) and matrix metalloproteinase 9 (MMP9) by western blot and gelatin zymography analysis. We found that the number of invadopodia reduced by 73% and the area of the ECM degradation decreased by 63% in PANC-1 when TM4SF1 was silenced compared to the control cells. Silencing of TM4SF1 reduced the percentage of cells with invadopodia by approximately 70% and decreased the ECM degradation by 46% in AsPC-1.

Also, TM4SF1 silencing down-regulated the expression of DDR1 and inhibited cancer cells migration and invasion. TM4SF1 expression colocalized with DDR1 in PANC-1 and AsPC-1 cells by immunofluorescence analysis. Coimmunoprecipitation assays showed an interaction between TM4SF1 and DDR1. Overexpressed DDR1 rescued the inhibitory effect of TM4SF1 silencing on PDAC cell lines migration and invasion, suggesting that DDR1 was involved in TM4SF1-mediated migration and invasion. When DDR1 was overexpressed in PANC-1 and AsPC-1, MMP2 and MMP9 protein expression levels increased. Moreover, TM4SF1 and DDR1 mRNA expression levels were both found to be almost 2 fold high in PDAC compared with adjacent normal pancreatic tissues. The scatter plots showed that TM4SF1 and DDR1 mRNA expression levels were positively correlated in PDAC tissues.
Conclusion: Taken together, our data suggest that a novel regulatory pathway involving TM4SF1, DDR1, MMP2 and MMP9, which mediates the ECM degradation and promotes invasion and metastasis in PDAC. Thus, TM4SF1 may be a potential therapeutic target.
Disclosure of Interest: None declared

P0716 NOVEL BIOMARKER PANEL FOR THE EARLY DETECTION OF PANCREATIC CANCER IN THE BLOOD

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Contact E-mail Address: Novel biomarker panel for the early detection of pancreatic cancer in the blood.
Introduction: Current pancreatic cancer marker, CA19-9 has limited diagnostic accuracy. In this study, we aimed to identify a multi-marker panel capable of detecting early stage pancreatic cancer eligible for surgical treatment, with high sensitivity and specificity. We conducted a thorough candidate marker screening and then validated the final panel in a large multicenter clinical study.
Aims & Methods: Pancreatic cancer biomarker candidates from data mining of commercial and public databases were listed. Additional candidates were recruited by identifying differentially expressed genes from our tissue microarray experiments. Initially 1000 candidates with supporting evidence from more than two sources were selected and their serum protein levels were measured using Multiple Reaction Monitoring Mass Spectrometry (MRM-MS) in 50 resectable pancreatic ductal adenocarcinoma (PDAC) samples and 50 healthy or benign samples. Of the candidates, 54 proteins with high ranked diagnostic performance were selected for further investigation. Using MRM-MS, the candidate markers were evaluated in blood samples from five major clinical centers in Korea. The study subjects included 401 cases of PDAC patients (232 in stage I-II), and 458 controls (300 normal individuals and 158 benign diseases including pancreatitis and non-malignant pancreas cystic tumors). All the possible biomarker combinations consisted of up to 5 proteins among 54 candidates were investigated using Support Vector Machine. Then, 7 multiple marker combinations were selected by 10 fold cross-validation to have sensitivity greater than 0.85 at a fixed specificity of 0.9. The final panel was selected by considering biological relevance with cancer development, dynamic ranges in the blood and reliability of the measurements. The panel was validated using ELISA and an automated immunoassay system in the 859 multicenter case-control samples and additional 149 other cancer samples.
Results: A panel comprising CA19-9, LRG1 and TTR was determined to be the best biomarker. This triple marker panel significantly improved diagnostic performance of CA19-9 and we obtained consistent results from the immunoassay analyses. The area under the ROC curve (AUC) of the panel was 0.941 and the sensitivity was 0.850 whereas those of CA19-9 alone were 0.847 and 0.746, respectively. Even in cancer samples of stage I-II, the performance was significantly improved to AUC 0.921 and sensitivity 0.820 whereas CA19-9 had 0.82 and 0.677 respectively. The increase in AUC was greater than 10% (Delong's test p-value < 0.001). Additionally, the panel was highly selective for PDAC and had AUC of 9% greater than CA19-9 in the analysis of PDAC vs. other cancers.
Conclusion: A new diagnostic panel showed advantages over CA19-9 in terms of sensitivity and specificity as a pancreatic cancer specific tumor marker. Noticeably, this panel consistently performed well for detection of relatively early stage pancreatic cancer samples, which suggests potential of the panel as a screening test for early detection of PDAC.
Disclosure of Interest: None declared

P0717 THE ANTI-DIABETIC DRUG METFORMIN INHIBITS PANCREATIC CANCER CELL PROLIFERATION IN VITRO AND IN VIVO: STUDY OF MICRORNAS ASSOCIATED WITH THE ANTI-TUMOR EFFECT OF METFORMIN

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Introduction: Recent studies suggest that metformin, which is a commonly used oral anti-hyperglycemic agent of the biguanide family, may reduce cancer risk and improve prognosis, but the detailed mechanisms by which metformin affects various cancers, including pancreatic cancer, remain unknown.
Aims & Methods: The goal of the present study was to evaluate the effects of metformin on human pancreatic cancer cell proliferation *in vitro* and *in vivo*, and to study microRNAs (miRNAs) associated with metformin's anti-tumor effect. We used the human pancreatic cancer cell lines Panc1, PK1 and PK9 to study the effects of metformin on human pancreatic cancer cells. Athymic nude mice bearing xenograft tumors were treated with or without metformin. Tumor growth was recorded after 5 weeks, and the expression of cell cycle-related proteins was determined. In addition, we used miRNA array tips to explore the differences among miRNAs in Panc1 cells bearing xenograft tumors treated with or without metformin *in vitro* and *in vivo*.
Results: Metformin inhibited the proliferation of Panc1, PK1 and PK9 *in vitro*. Metformin blocked the cell cycle in G0/G1 *in vitro* and *in vivo*. This blockade was accompanied by a strong decrease of G1 cyclins, especially in cyclin D1, cyclin-dependent kinase 4 (Cdk4), and Cdk6, and by a decrease in retinoblastoma protein (Rb) phosphorylation. In addition, metformin reduced the phosphorylation of EGFR and IGF-1R *in vitro* and *in vivo*. Moreover, metformin reduced the phosphorylation of EGFR at Tyr845. The miRNA expression was markedly altered by the treatment with metformin *in vitro* and *in vivo*. Various miRNAs altered by metformin may also contribute to tumor growth *in vitro* and *in vivo*.
Conclusion: Our results revealed that metformin inhibits human pancreatic cancer cell proliferation and tumor growth, possibly by suppressing the cell-cycle-related molecules via alteration of miRNAs.

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P0718 EPITHELIAL-TO-MESENCHYMAL TRANSITION (EMT) IN HUMAN PANCREATIC CANCER: ASSOCIATION WITH DISEASE DISSEMINATION AND RECURRENCE

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Introduction: EMT is an emerging mechanism underlying cancer cell dissemination. EMT is driven by transcription factors (TFs; *TWIST1*, *ZEB2*, *SLUG*) coupling the expression of M genes (*VIMENTIN, CDH2*) with the repression of E ones (*CDH1*), thus conferring to cancer cells fibroblast-like morphology and enhanced migratory properties. Although EMT occurs early in mouse model of pancreatic cancer (PC), evidence in human PC remain scattered.
Aims & Methods: Human PC cell-lines (HPAF-II, HPAC, PANC-1, MIAPaCa-2) were characterized as to the expression of *CDH1-2* and EMT-TFs mRNA. In tissue specimens from PC patients, the presence of stromal cells expressing TWIST1 was assessed by immunohistochemistry at the tumor center (^{CT}; n = 99) and at the posterior resection margin (^{PRM}; n = 79). Association between TWIST1+ cells, clinical-pathological features, and disease-free survival (DFS) were assessed by logistic regression, Cox model (N-adjusted, stage IV and DFS < 90 days excluded), and Kaplan-Meier curves. The levels of EMT-TFs mRNA in the bloodstream of PC patients were measured by qRT-PCR (n = 45; heathy controls, n = 30), and circulating tumor cells (CTCs) were searched by combining in-situ hybridization (chromosome 7 and 20) with VIMENTIN/CDH1 immune-reactivity (n = 10).
Results: *CDH1*+ PC cells (HPAF-II, HPAC) did not show EMT-TFs, while *CDH1*-negative cells (PANC-1, MIAPaCa-2) expressed *TWIST1* and *SLUG*. Most (71/99; 72%) specimens harbored TWIST1^{CT+} cells; the only pathological feature associated with TWIST1^{CT+} cells was neural invasion [71/71 TWIST1^{CT+} cases *vs* 23/28 (82%) negative ones; p = 0.001]. In pathological specimens, the presence of TWIST1^{PRM+} (51/79; 64.5%), was significantly lower than that of TWIST1^{CT+}cells (42/51, 82%, showing TWIST1$^{CT+/PRM+}$, but 14/28, 50%, TWIST1 $^{PRM\text{-}negative}$ harboring TWIST1^{CT+}; p = 0.003). TWIST1^{CT+} cells had no prognostic value [(HR&95%CI) 1.27, 0.65-2.48; p = .47], while TWIST1^{PRM+} cells increased the risk of recurrence (3.12, 1.35-7.26; p < .008), either local (3.35, 1.25-9.0; p = .017), either metastatic (5.8, 1.32-25.6; p = .02), and were associated with a worse DFS (log-rank test, p = 0.002). In patient bloodstream, we detected increased mRNA levels of *CDH1* ($2^{-\Delta CT}$median, 2.03E-07 *vs* 8.37E-08, in controls; p = 0.03), but also of *TWIST1* (3.95E-08 vs 2.06E-08; p = 0.06), *ZEB2* (1.52E-05 vs 3.63E-06; p = 0.006), and *SLUG* (2.36E-08 vs 9.09E-13; p < 0.001). Eventually, aneuploid CTCs expressing VIMENTIN (1.7 cells/ml) or CDH1 (2.1/ml) were detected.
Conclusion: A set of established PC cells, shows no E but M hallmarks and expresses EMT-TFs. The association between TWIST1^{PRM+} cells and disease recurrence suggests the involvement of EMT in PC progression. EMT-TF mRNA levels and aneuploid M-CTCs in the bloodstream indicate ongoing EMT in a subset of PC cells into the circulation. PC comprises cell populations with M features, ignored so far but likely relevant for local and distant dissemination.
Disclosure of Interest: None declared

P0719 IMPACT OF PHARMACOLOGICAL MACROPHAGE DEPLETION ON THE PROGRESSION OF PANCREATIC NEUROENDOCRINE NEOPLASMS

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Introduction: Pancreatic neuroendocrine tumors (PNETs) are a heterogeneous group of neuroendocrine neoplasms with distinct biological behaviour and response to treatment. Efforts have been taken to improve the survival for patients at advanced stage, however, conventional chemotherapy is still recommended as standard treatment with limited efficacy. Previous reports indicate that the infiltration of tumor-associated macrophages (TAMs) in PNETs strongly correlates with proliferation and metastases.
Aims & Methods: Evaluation of the impact of the liposomal clodronate as pharmacological tool for macrophage depletion *in-vitro* and *in-vivo*.
The effect of liposomal clodronate on cell-viability was analysed in J774 and RAW myeloid cells and isolated murine bone macrophages as well as CD11b+cells of RIP1-Tag2 pancreata which were evaluated by FACS. RIP1-Tag2 mice were treated with either clodronate or liposomes alone to evaluate tumor progression, proliferation, angiogenesis and macrophage infiltration by FACS and immunohistochemistry.
Results: Liposomal clodronate inhibited the proliferation of monocytic J774 and RAW cells and murine bone macrophages. In contrast, cell-viability of neuroendocrine BON-1 and QGP-1 cells was not affected by this treatment. FACS analyses of RIP1-Tag2 mice treated with clodronate confirmed the selective depletion of macrophages. In RIP1-Tag2 mice liposomal clodronate reduced the evolution of invasive beta-cell tumors. Furthermore, proliferation of tumor cells and angiogenesis within the tumors were markedly reduced.
Conclusion: Liposomal clodronate selectively depletes macrophages and disrupts tumor progression in the RIP1-Tag2 neuroendocrine tumor model associated with reduced angiogenesis.
Disclosure of Interest: None declared

P0720 THE HIGH FREQUENCY OF PD-1 IN PERIPHERAL CD4+ T CELLS OF PANCREATIC DUCTAL ADENOCARCINOMA IS POTENTIALLY USEFUL FOR DEVELOPMENT OF THE NOVEL DIAGNOSTIC METHOD AND PREDICTION OF CHEMOTHERAPY RESPONSIVENESS

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is the lethal malignancy with extremely poor prognosis due to difficulty of diagnosis in early stage as well as the high grade of malignant potential. Therefore, detailed biological features including the immune-pathology are to be examined for development of the novel diagnostic method and therapeutic approach including immunotherapy.
Aims & Methods: We here examined the peripheral blood of PDAC patients in the context of programmed cell death-1 (PD-1) molecule, which is expressed on activated lymphocytes and regulate host immune response, and their clinical features. Fifty PDAC patients (Age; 68.0 ± 10.1, Gender; Male/Female = 29/21, Stage I/II/III/IV = 7/12/13/18) and twenty seven healthy volunteers (Age; 64.1 ± 8.7, Gender; Male/Female = 13/14) were enrolled with the informed consent of the study. Peripheral blood mononuclear cells (PBMCs) were isolated from heparinized venous blood using Ficoll-Hypaque density gradient centrifugation. Obtained PBMCs were incubated with fluorescent antibodies, PD-1, CD4, CD8, CD25, CD127, and these expression levels were analysed using flow cytometry. Furthermore, we extracted RNA from CD4+ T cells using anti-CD4 magnet beads from PBMCs, and examined the expression level of PD-1 and FoxP3, which is transcriptional factor for regulatory T cells, on these cells.
Results: Flow cytometry analysis showed that the frequency of CD4 + PD-1+ cells, not CD8 + PD-1+ cells, was significantly increased in the PBMCs of PDAC patients ($6.4 \pm 2.9\%$), compared to healthy volunteers ($3.8 \pm 2.1\%$, $p = 0.001$). Then, PD-1 mRNA expression level was also increased in CD4+cells of PDAC patients. On the other hand, CD4 + CD25 + CD127low/- cells, which is representative regulatory T cells, was increased in the PBMCs of PDAC patients ($3.8 \pm 1.4\%$), compared to healthy volunteers ($2.9 \pm 1.4\%$, $p = 0.022$), while FoxP3 mRNA expression level was not increased in CD4+cells of PDAC patients.
We observed that the frequency of CD4 + PD-1+ T cells and regulatory T cells was no correlation with clinical stages as well as serum CEA and CA19-9 values in PDAC patients. We examined whether the frequency of these populations were correlated with clinical outcome of PDAC patients or not, among the enrolled 35 PDAC patients who underwent chemotherapy. The frequency of CD4 + PD1+ T cells was significantly increased in patients with poor response to chemotherapy ($p = 0.002$), although the frequency of regulatory T cells was not. There was no significant difference in overall survival among the frequency of CD4 + PD1+ T cells as well as regulatory T cells populations.
Conclusion: The frequency of CD4 + PD-1+ T cells was increased even in early stage of PDAC patients, implying assessment of the frequency of CD4 + PD-1+ T cells in PBMCs is the possible novel diagnostic approach in early stage. In addition, the high frequency of CD4 + PD-1+ T cells population of PDAC patients was predictive of poor response of chemotherapy.
Disclosure of Interest: None declared

P0721 FACTORS ASSOCIATED WITH CANCER WORRIES IN INDIVIDUALS PARTICIPATING IN ANNUAL PANCREATIC CANCER SURVEILLANCE

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Introduction: There is growing interest in surveillance for pancreatic cancer (PC) in high-risk individuals to detect early stage PC or precursor lesions. When assessing the feasibility of such surveillance, it is important to also address participants' psychological burden. Previously, we reported that repeated participation in annual surveillance imposes low psychological burden. However, a subgroup of individuals showed intermediate to high levels of cancer worry. The aim of this study was to evaluate possible factors associated with these cancer worries.
Aims & Methods: High-risk individuals (estimated lifetime risk of PC $\geq 10\%$), participating in an annual prospective multicenter Dutch EUS-MRI based PC surveillance program, were invited to complete an annual questionnaire to assess their cancer worries with the Cancer Worry Scale (CWS). The questionnaire was sent after genetic counseling (T0), after intake for participation but prior to the first MRI and EUS (T1), and thereafter annually after MRI and EUS (T2-T7). Individuals who scored ≥ 12 points on the CWS on each available questionnaire were defined as having intermediate to high cancer worries.
Results: A total of 688 out of 763 questionnaires were returned (90%) by 166 out of 178 participants (93%): 41, 92, 149, 123, 106, 81, 64 and 32 questionnaires at each of the eight time points respectively. The mean age of participants was 52 years with a mean follow-up of 49 months. The mean CWS-score was 12.8 (range 8-26). A total of 66 individuals (40%) scored ≥ 12 points on the CWS at each available questionnaire. Both univariate and multivariate analysis showed three factors to be associated with intermediate to high cancer worries: proven carriers of a PC-associated gene mutation (as opposed to familial pancreatic cancer individuals in whom no known gene mutation could be detected) ($P = 0.04$); scoring ≥ 20 points on the Hospital Anxiety and Depression Score (HADS) at least once ($P = 0.05$); and having a family member affected with pancreatic cancer < 50 years of age ($P < 0.01$). Not associated were gender, education level, marital status, a personal history of cancer, the detection of a cystic lesion nor a shortened interval during surveillance.
Conclusion: A total of 40% of individuals participating in annual pancreatic cancer surveillance had intermediate to high cancer worries at all available psychological questionnaires. We identified three factors to be associated with these worries: carriership of a pancreatic cancer associated gene mutation, a high HADS score, and a family member affected with pancreatic cancer under 50 years of age. These associated factors can help to identify patients 'at risk' for experiencing cancer worries who might benefit from psychosocial support.
Disclosure of Interest: None declared

P0722 PREVALENCE AND PROGRESSION OF CYSTIC PANCREATIC PRECURSOR LESIONS DIFFER BETWEEN TWO GROUPS AT HIGH RISK OF DEVELOPING PANCREATIC CANCER

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Introduction: Individuals at high risk of developing pancreatic ductal adenocarcinoma (PDAC) are (1) carriers of a mutation that predisposes to PDAC, and (2) individuals who have no known gene mutation but who have a strong family history of PDAC (familial pancreatic cancer, FPC). The genes involved in the

development of FPC are unknown. Consequently, given the presumed autosomal dominant inheritance pattern of FPC, by definition half of these FPC-individuals are not at increased risk. It is still unclear whether the prevalence and natural progression of cystic precursor lesions are equal in both risk groups. The aim of our study was therefore to compare prevalence and progression of lesions between the two groups.

Aims & Methods: Individuals with an estimated lifetime risk of developing PC ≥10% underwent annual pancreatic surveillance with magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) in an ongoing prospective multicenter study. Individuals included are (1) first degree relatives (FDR) of FPC cases, defined as families with PDAC in ≥2 FDR, in ≥3 relatives, or in ≥2 relatives with ≥ 1 case aged < 50 at diagnosis, and (2) mutation carriers of PC-prone gene mutations (all *CDKN2A* mutation carriers and Peutz-Jeghers patients; *BRCA1* or *2* mutation carriers, *p53* mutation carriers and Lynch syndrome patients with ≥2 family members affected with PDAC). Progression of a lesion was defined as growth ≥4 mm or the development of malignant features.

Results: We included 172 individuals, of whom 90 (52%) were mutation carriers and 82 (48%) were FPC individuals. There was no significant difference in follow-up between groups (mean 41 months vs 44 months respectively, $P = 0.35$). A total of 36 cysts were detected in 90 mutation carriers (40%) and 47 cysts in 82 FPC-individuals (57%, $P = 0.12$). Significantly more cysts ≥10 mm were detected in FPC individuals than in mutation carriers (15% vs 4%, $P = 0.05$). However, the cystic lesions detected in mutation carriers were significantly more likely to progress than those in FPC individuals (19% vs 2%, $P = 0.04$). The number of lesions per individual, the presence and number of chronic pancreatitis features, and the age of individuals at diagnosis of a cystic lesion did not differ between both groups.

Conclusion: FPC individuals had a higher prevalence of cystic lesions ≥10 mm, which is remarkable given the fact that half of these FPC individuals are probably not at increased risk to develop pancreatic neoplasia (presumed autosomal dominant inheritance of unknown mutation). However, the lesions in mutation carriers were more likely to progress during follow-up. These results could lead to better tailored surveillance strategies, to identify high-grade dysplastic lesions or PDAC more adequately.

Disclosure of Interest: None declared

P0723 HOW TO DEAL WITH INCIDENTAL PANCREATIC CYSTIC NEOPLASM; DETECTION OF MALIGNANCY

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Introduction: Careful selection for surgical intervention or radiologic and clinical surveillance is important in the management of patients with pancreatic cystic neoplasms (PCNs). Although some PCNs require surgical resection, they are slow growing and have a favorable prognosis in contrast to ductal adenocarcinoma.

Aims & Methods: We aimed to evaluate natural course of PCNs and the detection of malignant transformation during follow-up according to the risk factors. We retrospectively reviewed the records of 301 patients with PCN incidentally diagnosed by using abdominal US, CT, or MRI. Cyst size was recorded as the maximum dimension measured on cross-sectional imaging. Presence of cyst features that are known potential risk factors for malignancy, such as thickened enhanced cyst walls, main pancreatic duct size > 5 mm, non-enhanced mural nodules, abrupt changes in the main pancreatic duct caliber with distal pancreatic atrophy, and enhanced solid component, were also recorded. Patients were followed-up after an initial 3-month interval and then followed-up at 6 months and 12 months, followed by an annual follow-up. Malignant transformation of PCN during follow-up was defined as either histologic confirmation after surgical resection or evidence of metastatic or invasive disease from a suspected primary PCN on radiologic imaging.

Results: Of 301 patients, 19 were excluded (15 less than 1 year of follow-up, 4 underwent surgery for malignancy at initial diagnosis). Data from 282 patients were analyzed (mean age: 59.4 years, median follow-up: 28.5 months); 97 patients had risk factors such as cyst > 3 cm or the presence of mural nodule. During surveillance, 41 patients showed changes in cysts (median duration: 24 months); 32 showed an increase in cyst size, and 9 showed a change in cyst characteristics. Cyst-related malignancy occurred in 5 patients (2.5%, 5/203), all who had risk factors and whose cysts showed changes. Post-operative morbidity was observed in 30 of 93 patients (32.3%); 2 died (1, intra-abdominal infection; 1, mechanical obstruction). Mortality was observed in 9 patients, with disease-specific death in only one.

Conclusion: Although the risk of malignant transformation was higher in patients with incidental PCNs than in the general population, the detection of malignancy or disease-specific mortality during surveillance was low, even in the high-risk group. Continued surveillance is important whether there are significant changes in PCNs.

Disclosure of Interest: None declared

P0724 EFFICACY OF PROPHYLACTIC GASTROJEJUNAL BYPASS IN PREVENTING GASTRIC OUTLET OBSTRUCTION SYMPTOMS IN UNRESECTABLE PERIAMPULLARY CANCER

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Introduction: Up to 33% of patients with preoperatively considered resectable periampullary cancer are deemed unresectable at laparotomy due to unexpected locally advanced or metastasized disease. The conversion from curative to palliative intent usually leads to the construction of a concomitant prophylactic gastrojejunal bypass (PGJB) as part of a double bypass to prevent eventual duodenal / gastric outlet obstruction (GOO) symptoms that may occur with further tumour progression. How PGJB subsequently affects the adequacy of oral intake in a palliative setting has not been fully clarified.

Aims & Methods: To investigate the effect of PGJB on GOO symptoms using established scoring systems. Observational study on patients with periampullary adenocarcinoma found to be unresectable at exploratory laparotomy between 2004 and 2014. The patients were grouped according to the palliative surgical management they had received into PGJB or exploration (EXP) alone. Data on oral intake before operation, at discharge and at follow up was retrieved from the patient's medical records and classified according to the GOO scoring system. Postoperative complications were classified according to Dindo-Clavien and delayed gastric emptying (DGE) according to the ISGPS consensus definition.

Results: A hundred-eight patients were included, 94 underwent PGJB (14 EXP). The groups were comparable regarding demographical data and and, except for severe complications (17% PGJB vs 7% EXP), had similar postoperative outcomes and long-term survival. Clinically significant DGE occurred in 18 % of the PGJB group and in 7.7 % of the EXP group. Length of hospital stay was longer in the PGJB group (9 vs 6 days). Improved rates of oral intake could not be demonstrated for PGJB when compared to EXP. Regarding therapeutic efficacy, 40 % of patients with preoperative GOO symptoms had improved oral intake at discharge after PGJB and 46 % had full oral intake on follow up. 43 % had a sustainably improved oral intake (at discharge and follow up). Regarding prevention of GOO symptoms, 32 % of the non-symptomatic patients developed a temporarily decreased and 7% a prolonged decrease of oral intake. At a median follow-up time of 47 days, 73 % of patients had regained full oral intake; however, only 49 % had full oral intake at both discharge and follow-up after PGJB compared to 73 % with full oral intake at discharge and follow-up after EXP.

Conclusion: Prophylactic gastrojejunal bypass, usually part of a double bypass, is a major surgical procedure with high rates of associated morbidity and mortality. For this procedure, the present study failed to demonstrate acceptable results for the treatment and effective short-term / long-term prevention of gastric outlet obstruction symptoms. Since primary gastric outlet obstruction develops in only 10-20 % of all patients with periampullary cancer, less invasive on-demand strategies may be discussed as alternatives to prophylactic surgery.

Disclosure of Interest: None declared

P0725 VALIDATION OF THE FUKUOKÁS INTERNATIONAL CONSENSUS FOR INTRADUCTAL PAPILLARY MUCINOUS TUMOR OF THE PANCREAS

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Introduction: The anatomic classification of intraductal papillary mucinous tumor (IPMT) is difficult to understand. Despite the involvement of the main pancreatic duct (MPD) having a greater chance of malignancy, the branch duct remains a major challenge in relation to diagnosis and the decision of the treatment to be performed. There are several factors to predict the presence of malignancy, but they are still intense debate about, and there are many questions regarding which is the best malignancy predictor?

Aims & Methods: The aim of this study was to evaluate the effectiveness and accuracy of the latest international consensus to predict malignancy of IPMT. Data from 203 patients with pancreatic mucinous neoplasm identified by imaging and referred to the endoscopy department were prospectively collected to undergo endosonography-guided fine needle aspiration (EUS-FNA), between January 2008 and April 2014. We evaluated and compared the malignancy predictors factors described by the Fukuokás International Consensus described in 2012.

Results: According to the EUS images, results of laboratory tests and microhistology obtained by EUS-FNA, it was observed that the larger cysts > 2.5 cm have a higher chance of malignancy (50% versus 19%; $p < 0.001$), with sensitivity and a specificity of 70% and 69.2%, respectively. The solid component was present in 30% of malignant tumors compared to 11.9% of benign ($p = 0.006$). The presence of solid component cysts larger than 2.5 cm has preditive positive value (PPV) 68% ($p = 0.001$) while his absence of cysts of any size has a PPV of 88% ($p = 0.006$). The MPD was normal in patients with no invasion (86% vs 60%, $p < 0.0001$). The BD-IPMT had more results benignity (88.1%) while the MD-IPMN had the highest frequency among malignant lesions (41.2%) [$p < 0001$]. The presence of one major criteria is associated with the presence of tumor by 55% ($p < 0.001$).

Conclusion: The frequency of malignancy found in patients with MPD diameter between 5-9mm and also in cysts 2.5cm in diameter suggests that there is space for discussion of reducing the cutoff for the diameter lesions were classified as at high risk for malignancy. Furthermore, the presence of vegetation within cysts larger than 2.5 cm has a high PPV for the presence of malignancy, validating the proposed consensus.

Disclosure of Interest: None declared

P0727 EXPRESSION OF HEDGEHOG SIGNALING PATHWAY IN PANCREATIC DUCTAL ADENOCARCINOMA (PDAC) AND CHRONIC PANCREATITIS (PC)

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Introduction: The involvement of the Hedgehog pathway in pancreatic carcinogenesis has been suggested. Hedgehog signaling molecules, such as Sonic hedgehog (Shh), Smoothened (Smo) and Glioblastoma transcription factor 1 (Gli1) are proposed as biomarkers for cancer detection and prognosis.
Aims & Methods: The aim of the study was to evaluate the Hedgehog signaling pathway molecules, α smooth muscle actin (αSMA) and Ki67 in patients with PDAC and CP.
We enrolled 114 patients undergoing pancreatic resection: 83 with PDAC and 31 with CP. Normal control pancreatic tissue was obtained from autopsy material from 21 patients. The immunoexpression of Shh, Smo, Gli1, αSMA and Ki67 were detected in tissue specimens by immunohistochemistry (Abcam antibodies, GB). The intensity and extend of staining of Shh, Smo, αSMA were recorded semi-quantitatively and for nuclear expression of Gli 1 and Ki67 labeling index was calculated.
Results: Mean Shh staining score in PDAC was: 2.24 (+0.57), which was significantly higher than in CP patients: 1.17(+0.25) and in control group: 0.79(+0.34) ($p = 0.000$). Smo protein expression was 2.62(+0.34) in PDAC, 1.21(+0.23) in CP and 0.94(+0,15) in control group ($p = 0.000$). Likewise Gli1 protein expression was higher in PDAC: 1.74(+0.74) than in CP: 1.15(+0.72) and in control group: 1(+0) ($p = 0.000$). In addition, Shh and Smo immunoreactivity in CP was significantly higher than in the control group ($p = 0.024$; $p = 0.007$ respectively). Significant correlation was found between immunoexpression of Shh, Gli and Ki67 in PDAC group ($r = 0.379$; $r = 0.28$, respectively; $p < 0.05$).
Conclusion: Presented findings support the hypothesis on the role of Hedgehog pathway in pancreatic carcinogenesis as well as cell hyperproliferation in CP.
Disclosure of Interest: None declared

P0728 POOR SURVIVAL IN PANCREATIC MALIGNANCY ASSOCIATED WITH TROPICAL PANCREATITIS. IS IT A BIOLOGICALLY DIFFERENT DISEASE?

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Introduction: Malignancy in tropical pancreatitis is associated with high chance of mortality and has higher rates of hepatic and or distant metastasis. In a prospective cohort with pancreatic malignancy, we studied the tumor size and survival.
Aims & Methods
Aims: To evaluate the operability, risk factors and survival of pancreatic malignacy in tropical pancreatitis.
Methods: In this prospective study, 1480 subjects with tropical pancreatitits were studied in a tertiary referral centre attached to Trivandrum Medical College in S India recruited between January 1980 and March 2006. On follow up, 164 developed malignancy. The diagnosis was estalished by CT/MRI and MRCP followed by either FNAC pancreas or at surgical resection. Abdominal pain, diabetes and duration, alcohol abuse, tobacco smoking were evaluated in detail. Univariate analysis, Cox Proportional Hazard regression and Kaplan Meir Survival curves were plotted and analysed.
Results: Pancreatic malignacy occured at an younger age of 45 ± 12.4 years. The tumor was confined to head region in 130 subjects and tail and or body in the rest. Mean size was 4.2 cms and lymph node metastasis was present in 60%. 38 percent had hepatic/ distant metastasis and were inoperable. CA 19-9 level was over 1000 units in 80%. Duration of diabetes and abdominal pain didnot affect survival.The relative risk of mortality for: age over 50 was 4.97 (95% CI 3.7-6.67); for smoking 1.39 (95% CI 1.01-1.89). KM survival probability were 0.55 (95% CI 0.42-0.66) at 3 months; 0.24 at 6 months and 0.13 at 9 months.
Conclusion: The survival in pancreatic malignancy associated with tropical pancreatitis is poor and the biological behaviour is different; there was high regional and distant metastasis.
Disclosure of Interest: None declared

P0729 IS SCREENING FOR PANCREATIC CANCER IN HIGH-RISK GROUPS COST-EFFECTIVE?

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Introduction: Pancreatic cancer (PC) is the fourth leading cause of cancer death worldwide, symptoms are few and diffuse, and when the diagnosis has been made only 10-15% would benefit from resection [1]. Surgery is the only potentially curable treatment for PC, and the prognosis seems to improve with early detection [2]. A hereditary component has been identified in 1-10% of the PC cases [3]. To comply with this, screening for PC in high-risk groups with a genetic disposition for PC has been recommended in research settings [4].
Aims & Methods: Between January 2006 and February 2014 31 patients with or with a disposition for HP and 40 first-degree relatives of patients with FPC were screened for development of PDAC with yearly endoscopic ultrasound and fine needle aspiration when needed. Total pancreatectomy was performed when 1) PDAC 2) PanINIII or 3) Main-duct IPMN was verified by histology. The cost-effectiveness of screening in comparison with no-screening was assessed by the ICER.
Results: By screening the FPC group we identified 2 patients with PDAC who were treated by total pancreatectomy. One patient is still alive, while the other died after 7 months due to cardiac surgery complications. The cost per PDAC identified was 132.899 US$, the cost per life-year saved was 37.994 US$ and the cost per QALY gained was 50.329 US$. Stratified analysis of patients with HP and FPC provided ICERs of 47.156 US$ vs. 35.493 US$ per life-year and 58.647 US$ vs. 47.867 US$ per QALY. Including only PDAC related death changed the ICER to 31.722 US$ per life-year and 42.128 US$ per QALY. The ICER for patients with FPC was estimated at 28.834 US$ per life-year and 38.785 US$ per QALY.
Conclusion: With a threshold value of 50.000 US$ per QALY this screening program appears to constitute a cost-effective intervention although screening of HP patients appears to be less cost-effective than FPC patients. These results are sensitive to appropriate stratification of the patients and the effectiveness of the treatment modalities offered. Both screening and surgery should be performed in specialized, research-based centres with many patients and a dedicated multidisciplinary approach and expertise.

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Disclosure of Interest: None declared

P0730 EUS-GUIDED INTRATUMORAL INJECTION OF CHST15 DSRNA FOR UNRESECTABLE PANCREATIC CANCER: AN INVESTIGATOR-INITIATED TRIAL

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Introduction: The glycosaminoglycan chondroitin sulfate E (CS-E) is known to promote tumor invasion by cleaving CD44 on pancreatic cancer cells. Interference with CS-E has been shown to inhibit tumor invasion and metastasis in nonclinical studies. CS-E is upregulated in pancreatic cancer tissue and its biosynthesis is mediated by specific enzyme carbohydrate sulfotransferase 15 (CHST15). CHST15 mRNA is reported to be upregulated and to correlate with poor prognosis in several types of cancer. We have shown that synthesized CHST15 dsRNA can inhibit the expression of CHST15 mRNA in human pancreatic cancer cells in vitro. In this study, we conducted an investigator initiated trial of CHST15 dsRNA through EUS-guided intratumoral injection in patients with unresectable pancreatic cancer.
Aims & Methods: Primary outcome measures were safety, feasibility, and tolerability. Secondary outcome measures were response in tumor size, overall survival (OS) and disease-free survival. Histopathologically, tumor specimens were also evaluated with CHST15 immuno-stain before and 1 month after injection.
Results: A total of five stage IV pancreatic cancer patients with a median age of 75.8 years (male: female = 3:2) were enrolled. Four of them had undergone standard chemotherapy including gemcitabine or S-1 regimen, and the other patient refused chemotherapy. For all patients, a total of 16 ml (250nM) of dsRNA was successfully injected into the tumor under EUS guidance using a 22 gauge needle without related adverse events. Mean tumor size changed from 29.0 (21-39) mm to 29.6 (23-45) mm in diameter one month after the first injection. Histopathologically, all patients (100%) were CHST15 positive in the primary specimen, and one patient's specimen revealed CHST15 weakness

one month after the first injection, suggesting the effectiveness of dsRNA injection.
Conclusion: This was the first-in-patient trial of EUS-guided injection of dsRNA against glycogene in unresectable pancreatic cancer in the world. A single-dose administration of CHST15 dsRNA showed no drug-related adverse effects at the tested concentration. High safety and feasibility were demonstrated, which will contribute to further clinical trials investigating this anti-tumor agent.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00–17:00
ENDOSCOPY AND IMAGING II – HALL 7

P0731 PER ORAL ENDOSCOPIC PYLOROMYOTOMY AFTER SUBMUCOSAL TUNNEL FOR THE TREATMENT OF REFRACTORY GASTROPARESIS: A CLINICAL CASE SERIES

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Introduction: Gastroparesis is a motility disorder affecting 4% of the population with symptoms related to pathological gastric emptying. Therapeutic options remain limited with many patients refractory to the medical treatment. 2 series reported the effectiveness of laparoscopic pyloroplasty. Recently, endoscopic per oral pyloromyotomy after tunnel creation (G-POEM) has been attempted (3 cases: US, Brazil and our team) with excellent results.
Aims & Methods: Five patients, 3 men and 2 women, with mean age of 58 years old [42 – 76], were managed in our center for refractory gastroparesis. Two were due to diabetes, two were post operative consequences (Heller), and one idiopathic. All the patients underwent a G-POEM procedure after multidisciplinary discussion and giving informed consent. Four of them have had a pre-operative gastric emptying scintigraphy. The procedures were performed by an endoscopist expert in esophageal POEM, on patients under general anesthesia, intubated and in supine position. We used a large operating channel gastroscope (Pentax, Japan) with CO_2 and a Triangle Tip knife (Olympus, Japan). The steps of the procedure were: 1/ mucosal incision after submucosal injection (posterior wall, 5cm upstream the pylorus); 2/ Tunnel creation by dissection (Swift Coag 35 W); 3/ Pyloric 3cm complete incision; 4/ Closure of the mucosal flap. An antibiotic prophylaxis and PPI were administrated daily. They were followed-up clinically at 1 month and associating a gastric emptying scintigraphy at 3 months.
Results: A complete procedure could be performed on all the patients but one (4/5). The failed patient had a fibrotic stomach and was mistakenly performed with a regular channel scope resulting in difficult access to the pylorus. The mean duration was 100 minutes without per- or post-operative complication. All the patients could drink at POD 2, eat gradually at POD 3, and were discharged at POD 6. The patients with technical success reported a mean improvement of quality of life of 73% [65-90%] and of gastric emptying symptoms of 60% at 1 month, persisting at 3 months. Regarding the scintigraphy, the baseline evaluation showed a mean half gastric emptying time (HGET) of 139 min [104-188] and a mean residual percentage at hour 4 (RPH4) of 25% [6-45%]. After the G-POEM, the mean HGET and RPH4 were normalized, decreasing to 81 min [77-85, $p = 005$] and 4% [1-9, NS], respectively.
Conclusion: Endoscopic pyloromyotomy with the G-POEM technique is feasible, reproducible, and safe. This approach seems effective clinically in terms of quality of life and specific symptoms, which was confirmed by the scintigraphy. A prospective study will soon start in our department to clearly confirm its great potential on patient with refractory severe gastroparesis.

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Disclosure of Interest: None declared

P0732 PREDICTORS OF MORTALITY IN CAUSTIC INGESTION: A SINGLE, TERTIARY CENTER STUDY

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Introduction: Caustic ingestion, whether accidental or intentional, causes severe injury to the esophagus and the stomach, and may be associated with significant morbidity and even mortality. The severity of caustic injury depends on the following factors: corrosive properties of the ingested substance, amount, concentration, and physical form of the agent and duration of contact with the mucosa.
Aims & Methods: This is a retrospective cross-sectional study which included all adult patients who ingested caustic agents who were admitted at the Philippine General Hospital Acute Care Unit from January 1, 2008 to December 31, 2012. This study aimed to determine the predictors of mortality; determined the incidence of caustic ingestion and surgical and mortality rates; and characterized patients admitted for caustic ingestion.
Results: There were 303 cases of caustic ingestion admitted over a five-year study period. The mean age was 36 ± 13 years. There were slightly more male patients. Ingestion of acidic corrosive agents was more common than alkaline substances Majority were intentional in nature. The average amount of ingested substance was 74.9 ± 84.9 ml. Psychiatric disorder was the most commonly identified co-morbidity and was the only co-existing illness recognized among patients who expired. The most common symptoms were vomiting and abdominal pain. Among 154 patients who underwent esophagogastroduodenoscopy, half had mild (Zargar grades 1-2b) mucosal injury. One-third had severe (Zargar grade 3) mucosal injury. Around 10% had no signs of mucosal injury. Metabolic acidosis and leukocytosis were common laboratory findings. There were 13 cases of perforation (perforation rate of 4.5%). Surgery was performed in 56 (19.2%) patients. There were 23 recorded cases of death (8.1% mortality rate). Only metabolic acidosis, presence of a psychiatric disorder, need for surgical intervention, and presence of documented perforation were significantly different between patients who expired and who survived. On univariate analysis, presence of psychiatric abnormality did not show significant association with mortality (Table 1). Multivariate analysis revealed that surgery was the most consistent predictor of mortality. Perforation had no effect in the absence of metabolic acidosis.

TABLE 1: Univariate Analyses on the Effects of Metabolic Acidosis, Presence of Psychiatric Disorder, Need for Surgery, and Perforation on Mortality

Clinical /Parameter	Odds Ratio	95% CI	P-value
Metabolic Acidosis	10.6	2.17, 76	0.006
Presence of Psychiatric Disorder	4	0.55, 20.4	0.108
Need for Surgery	13.3	3.9, 44.6	< 0.001
Perforation	22.2	8.3, 70.4	< 0.001

Conclusion: The clinico-demographic profiles of the adult subjects, distribution of severity of mucosal injury, all-cause mortality rate and surgery rate in this study are similar to the other publication. Patients with metabolic acidosis on admission, undergoing surgical intervention, and with perforation are at higher risk of death. Among these, institution of surgical intervention was the most consistent predictor of mortality. We recommend that these patients be closely monitored during their hospital stay in order to lower the possibility of mortality.
Disclosure of Interest: None declared

P0733 ENDOSCOPIC PREDICTORS FOR UNDIFFERENTIATED HISTOLOGY IN DIFFERENTIATED GASTRIC NEOPLASMS PRIOR TO ENDOSCOPIC RESECTION

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Introduction: Endoscopic submucosal dissection (ESD) has been widely accepted as an established treatment modality for gastric neoplasms. With regard to patient selection for ESD, an exact histologic diagnosis before treatment is essential. However, there is often a discrepancy between results from endoscopic forcep biopsy and resected specimen.

Aims & Methods: We aimed to identify endoscopic predictors for undifferentiated histology in differentiated gastric neoplasms prior to endoscopic resection. Medical records of the patients who underwent ESD for biopsy-proven differentiated gastric neoplasms at Seoul National University Hospital between July 2005 and July 2014 were retrospectively reviewed. The lesions were divided into two groups based on the histologic result of ESD: differentiated adenocarcinoma (DA group) and undifferentiated histology (UDH group). The discordant rate, clinicopathologic characteristics and endoscopic factors were analyzed.

Results: A total of 1,641 early gastric cancers from 1,615 patients were included. Of these, 1,556 (94.8%) were diagnosed as DA and 85 (5.2%) as UDH. The mean age was significantly lower and number of women was higher in the UDH group than in the DA group. On multivariate analysis, age <65 years (odds ratio [OR] 1.75, 95% confidence interval [CI] 1.10–2.80), female sex (OR 3.19, 95% CI 2.00–5.08), endoscopic size >10 mm (OR 1.81, 95% CI 1.12–2.92), depressed type (OR 2.85, 95% CI 1.56–5.21), nodularity (OR 2.83, 95% CI 1.59–5.05), and whitish discoloration (OR 19.64, 95% CI 6.98–55.25) were independent predictors.

Table 1: Multivariate analysis of clinicopathologic and endoscopic characteristics associated with undifferentiated histology in endoscopic submucosal dissection

Characteristics	OR (95% CI)	*P* value
Age		
≥65	1.00 (reference)	
<65	1.75 (1.10 – 2.80)	0.019
Sex		
Male	1.00 (reference)	
Female	3.19 (2.00 – 5.08)	< 0.001
Endoscopic size		
≤10 mm	1.00 (reference)	
>10 mm	1.81 (1.12 – 2.92)	0.016
Macroscopic type		
Elevated	1.00 (reference)	
Flat	1.49 (0.70 – 3.14)	0.298
Depressed	2.85 (1.56 – 5.21)	0.001
Gross morphology		
Ulcer	1.97 (0.76 – 5.07)	0.161
Erosion	0.71 (0.41 – 1.26)	0.241
Whitish discoloration	19.64 (6.98 – 55.25)	< 0.001
Nodularity	2.83 (1.59 – 5.05)	< 0.001

Conclusion: Female sex, age <65 years, large endoscopic size, depressed morphology, surface nodularity, and whitish discoloration were predictors for UDH. Meticulous attention should be paid to the lesions with these endoscopic predictors for determining the risk of UDH prior to endoscopic resection.

Disclosure of Interest: None declared

P0734 CLINICAL OUTCOMES OF NO RESIDUAL DISEASE IN THE SPECIMEN AFTER ENDOSCOPIC RESECTION FOR GASTRIC NEOPLASMS

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Introduction: Endoscopic resection (ER) has been widely accepted as a curative treatment strategy for early gastric cancer and gastric adenoma. However, no residual disease (NRD) can be found in the specimen after ER of biopsy-proven gastric neoplasm.

Aims & Methods: This study aimed to evaluate the endoscopic and pathologic characteristics of patients with NRD, and identify the cause and long-term prognosis. Medical records of patients who underwent ER for biopsy-proven gastric neoplasms at a single tertiary hospital between January 2005 and November 2014 were retrospectively reviewed. Patients whose post-ER histology was revealed as NRD were included in the study. Overall incidence, clinicopathologic characteristics, cause, and long-term prognosis were analyzed.

Results: NRD was detected in 138 (3.2%) of 4,318 cases of gastric neoplasms treated with ER. Mean endoscopic size of the initial lesion was 8.27 ± 6.73 mm; in 92 cases (66.7%), the lesion was located in the lower third of the stomach. Initial pathologic diagnosis was as follows: adenoma (n = 108), carcinoma (n = 26), and atypical gland (n = 4). The causes of NRD were minute lesions removed by biopsy in 135 patients, pathologic misdiagnoses in 2, and localization error in 1. Local recurrence was detected in 5 patients (3.7%) with minute lesions during follow-up and treated with argon plasma coagulation (n = 4) or re-ER (n = 1). Synchronous (n = 5, 3.7%) and metachronous gastric lesions (n = 6, 4.4%) were also detected during follow-up.

Conclusion: The main cause of NRD was minute lesions, which might be completely removed by initial diagnostic biopsy; these cases showed a minimal rate of local recurrence and synchronous or metachronous gastric neoplasms. Careful follow-up is also mandatory for detection of residual disease.

Disclosure of Interest: None declared

P0735 ENDOSCOPIC FULL-THICKNESS RESECTION WITH DEFECT CLOSURE USING AN OVER-THE-SCOPE CLIP FOR GASTRIC SUBEPITHELIAL TUMORS

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Introduction: Endoscopic full-thickness resection (EFTR) is a mini-invasive technique for gastric subepithelial tumors originating from the muscularis propria, which enables a full-thickness resection of tumors and can provide a complete basis for pathological diagnosis. Gastric fistula closure after EFTR is a challenge for endoscopists. In this study we introduced EFTR with fistula closure using the over-the-scope clip (OTSC) system for gastric subepithelial tumors originating from the muscularis propria.

Aims & Methods: Objectives: To evaluate the feasibility and safety of fistula closure with OTSC by a retrospective analysis on the cases of EFTR with defect closure using OTSC for gastric subepithelial tumors originating from the muscularis propria in our hospital.

Methods: The patients were selected who underwent EFTR for gastric subepithelial tumors originating from the muscularis propria (tumor diameter ≤2cm) in our hospital from October 2013 to March 2014. After a full-thickness resection of tumors, the OTSC was released to close the defect. The success rate of defect closure with OTSC was observed and the endoscopic follow-up was performed at 1 week, 1 month and 6 months after operation to check OTSC closure.

Results: Totally 23 patients were included into the study. The full-thickness resection rate of gastric tumors in the muscularis propria was 100% (23/23), the success rate of defect closure was 100%, and the average time of defect closure was 4.9 min (range: 2-12 min). All patients experienced no postoperative complications such as bleeding and perforation. The postoperative follow-up time was 1-6 months (mean: 3 months), and no OTSC detachment was found.

Conclusion: OTSC can be used to perform EFTR with defect closure for gastric tumors in the muscularis propria (tumor diameter ≤2cm). It is simple, convenient, safe and effective.

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P0736 FINDINGS IN GASTROSCOPY WITH BIOPSY AS A PREDICTOR OF RESECTABILITY OF GASTRIC CANCER

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Introduction: Gastric cancer diagnosis is usually performed by gastroscopy with biopsies, but reports about its predictive value for cancer resectability are scarce.
Aims & Methods: To analyze endoscopy findings predictive value concerning resection possibilities with curative intention in gastric cancer.
264 gastric carcinomas, consecutively diagnosed by endoscopic biopsy, were retrospectively reviewed. Non operated cases due to causes not related to the tumor (age and/or comorbidities) were excluded. Thus, frequency of the following parameters were compared between resected and non resected cases: Size > 5cm, macroscopic type (Japanese classification of gastric carcinomas), Lauren histological subtype and differentiation grade (I-IV). The group of variables with $p < 0.05$ was considered as a predictive diagnostic test for resectability and its sensitivity (S), specificity (Sp), positive (PPV) and negative predictive value (NPV) and diagnostic accuracy (DA) were calculated.
Results: 154 patients were operated with curative intention. Of the rest, 11 were operated without resection and 62 were inoperable due to their tumoral stage. 37 inoperable cases were excluded for the statistical analysis because of their age and/or comorbidity. No significant differences in resectability were registered regarding tumoral location: p= 0.25 or histological type. Tumors < 5cm showed a higher resectability rate: 88.2% versus 48.7%; [OR = 7.69; IC95% = (3.85-128.2); p = 0.000]. Carcinomas with an infiltrative component (ulcerated infiltrative-diffuse infiltrative) registered a lower resectability rate: 53% vs the rest: 73.9%.[OR = 2.51; IC95% = (1.32-4.77); p = 0.002]. According to the differentiation grade the resectability was: grade I-II (well-moderately differentiated) = 86% vs III-IV (poorly-undifferentiated) = 56.4% [OR = 5; IC = (2.38-111.1); p = 0.000]. If tumors < 5cm, with no macroscopically infiltrative type and well-moderate differentiation grade were considered as positive diagnostic test for resectability we obtained a S = 0.80; Sp = 0.95; PPV = 0.98; NPV = 0,63 y DA = 0.84.
Conclusion: 1. Among all parameters which can be evaluated with a gastroscopy plus biopsies, size < 5 cms, a macroscopically non infiltrative type and a well-moderate differentiation grade showed a significant predictive value for gastric cancer resectability with curative intention.
2. High specificity rate and positive predictive value were registered considering as a positive diagnostic test for resectability the presence of a tumor < 5cm, with no endoscopic infiltrative component and with a well-moderate differentiation grade.
Disclosure of Interest: None declared

P0737 GENTAMICIN SUBMUCOSAL LAVAGE DURING PER ORAL ENDOSCOPIC MYOTOMY (POEM): IS IT NECESSARY?

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Introduction: Per oral endoscopic myotomy (POEM) is an evolving therapeutic modality for achalasia. According to the original Inoués technique, lavage with gentamicin (80 mg) into the submucosal tunnel before starting the myotomy has been practiced due to the fear of infection. Since the number of infectious complications during POEM has been negligible, several centers (including our own) discontinued the use of gentamicin. However, there is no data assessing the clinical utility of gentamicin lavage yet.
Aims & Methods: The aim of this study was to compare outcomes of patients who received gentamicin lavage vs. patients who did not.
A retrospective analysis of prospectively collected data. POEM was performed in 86 patients (median age 46). Before the procedure, all patients were given intravenously ceftriaxone 2 g and metronidazole 500 mg; ceftriaxone was further administered on POD 2 and 3. In 60 patients (69.8%), a lavage with 80 mg of gentamicin diluted in 10 mL of normal saline was performed into the submucosal tunnel before starting the myotomy (= group A). In 26 patients (30.2%), gentamicin lavage was not performed (= group B). The main outcome variables were CRP level, WBC level, infectious complications and postprocedural fever and pain.
Results: The treatment success at 12 months (defined as an Eckardt score < 3) did not differ between the two groups (group A 98.3% vs. 100% group B). We did not experience any clinically significant infectious complications, such as mediastinitis, peritonitis or abscesses, in either group. In group A (with gentamicin), there was a trend for lower CRP levels and lower WBC count after POEM (POD 1, median with IQ range: CRP: 52.6 (34.8) mg/L vs. 68.2 (34.1) mg/L, p= 0.1; WBC: (10.9 (3.3) vs. 12.4 (3.7) (p= 0.05). Regarding all remaining parameters, we did not detect any differences between the two groups (group A vs. group B, median with IQR: RBC 4.2 (0.6) vs. 4.3 (0.7), Hb 129.5 (18) vs. 133 (22), length of hospitalization 2.0 (1) vs. 2.0 (0) days. The post POEM fever was present on POD 1 and/or POD 2 in 10% of patients in the group A and in 11.5% of patients in the group B (NS).
Conclusion: During POEM, submucosal lavage with gentamicin prior to myotomy does not seem to play a role in the prevention of clinically significant infectious complications, although the systemic inflammatory response may be decreased.
Disclosure of Interest: None declared

P0738 ENTERAL ACCESS FOR DUODOPA INFUSION: THE ROLE OF THE ENDOSCOPIST

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Introduction: In patients with advanced Parkinson's disease, the continuous delivery to the jejunum of levodopa/carbidopa (Duodopa) represents a new therapy, which results in less motor fluctuations than oral administration, but requires insertion of a percutaneous endoscopic gastrostomy with a jejunal extension (PEG-J). In this study, outcome of patients undergoing PEG-J placement for Duodopa infusion was analysed.
Aims & Methods: A prospective trial regarding Duodopa treatment is on-going in our institution. All patients had a nasojejunal tube placed initially to assess Duodopa efficiency and dosage, following by a PEG-J after 9 weeks, which was used exclusively for Duodopa infusion. We report the results (technical success, complication rate and outcome), regarding endoscopic management. Complications were defined as adverse effects that required specific treatment (surgery, endoscopy) and/or prolonged hospitalisation.
Results: 27 patients (17 men, median age: 64 (42-80)) were included for long-term Duodopa treatment requiring PEG-J placement, from June 2007 to April 2015. The nasojejunal tube (Freka intestinal tube CH15) was inserted under sedation (n = 11) or general anaesthesia (n = 16). This was performed either from the nasal route with a paediatric scope and the use of a guidewire (n = 17), either with a standard scope and a biopsy forceps (n = 10). No complications were noted. The PEG-J (Freka PEG CH15) was placed under general anaesthesia in all patients. The jejunal extension was inserted during the same procedure in the majority of the patients (n = 25, 93%).
Complications (n = 17) were reported in 12 patients (44%) including J-tube migration (n = 4, during first 3 months after insertion), J-tube impaction in the jejunum (n = 1), J-tube dysfunction (n = 5), Buried Bumper Syndrome (n = 2), duodenal ulcer (n = 2), covered duodenal perforation (n = 1), peritonitis (n = 1), and jejunal perforation with duodenal fistula (n = 1). Complications occurred after a mean follow-up of 17 months (0-54 months). All complications were managed successfully medically (n = 3), by endoscopy (n = 13), or by surgery (n = 1).
The mean number of repeat endoscopy was 2.60 (0-9) (including scheduled procedures for tube replacement and procedures for complications management) during a mean follow-up of 51 months (1-94 months).
All patients responded well to Duodopa regarding neurological outcome. There were no mortalities related to nasojejunal tube or PEG-J during follow-up.
5 patients required PEG-J definitive removal because of cognitive defect (n = 2), psychological trouble (n = 1) and gastrointestinal complications (n = 2, jejunal perforation with duodenal fistula; duodenal ulcer). This PEG-J withdrawal occurred after a mean follow-up duration of 27 months (1-72 months).
Conclusion: Placement of a PEG-J tube for Duodopa jejunal treatment in patients with advanced Parkinson's disease is an effective and noninvasive technique but which carries a high risk of gastro-intestinal complications, probably linked to the overall fragility of these patients. Patients should be fully informed of procedure-related complications and should be followed-up accordingly in referral centres.
Disclosure of Interest: None declared

P0739 RECURRENCE OF ZENKER'S DIVERTICULUM IS MORE FREQUENT IN MEN WITH SEVERE SYMPTOMS

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Introduction: Zenker's diverticulum (ZD) is an illness of the middle-aged and elderly, with a 1.5-fold predominance in men. It develops over time through increased pressure at the Kilian triangle due to impaired relaxation of the upper esophageal sphincter. Nowadays, endoscopic treatment is well established offering various techniques. However, some 20 – 30 % of patients experience recurrence of symptoms after successful treatment. The objective of this study was to identify predictive factors for development of recurrence in order to optimize surveillance for patients at risk.
Aims & Methods: A patient cohort of 25 male and 21 female patients, mean age 67 years, with symptomatic ZD was retrospectively analyzed for pre-treatment differences between patients who experienced or did not experience recurrence. In this cohort 12 out of 47 patients experienced recurrence of symptoms. We examined descriptive factors such as sex, age, multimorbidity, prior treatment and altered local anatomy, as well as severity, duration and frequency of pre-treatment clinical symptoms and complications due to ZD.
Results: Most strikingly, we observed a higher pre-treatment prevalence of severe symptoms such as vomiting (frequency score 2.25 vs. 0.26; $p < 0.01$) and symptom-related insomnia (1.71 vs. 1.04, n. s.) in the recurrence group. Likewise, the dysphagia score was markedly higher (2.27 vs. 1.61, n. s.). Upon further stratification of the recurrence group by No. of sessions (2 or 3 sessions total), the patients with 3 sessions had even more pronounced symptoms. However, due to the small number of these cases there were no significances. Also, duration of symptoms was longer (24.1 vs. 19.6 months, n. s.) and weight loss was more pronounced (3.6 vs. 0.9 kg) in the recurrence group. Analysis of the descriptive

factors showed more male patients in the recurrence group (80 % vs. 47 %; $p < 0.05$), whereas old age and multimorbidity did not show a relevant difference.
Conclusion: Male patients with a high dysphagia score and high frequency of severe symptoms are more likely to experience recurrence of symptoms from ZD and should be monitored more closely following successful endoscopic treatment.
Disclosure of Interest: None declared

P0740 EFFICACY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR CANCER OF THE OPERATED STOMACH

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Introduction: Cancer can develop in the operated stomach after partial gastrectomy and in the reconstructed gastric tube after surgery for esophageal cancer. It is considered that endoscopic therapy is more safe and suitable for the early gastric cancer developed in such stomah than opration. To investigate the efficacy of endoscopic submucosal dissection (ESD) for cancer of the operated stomach.
Aims & Methods: Subjects were 669 gastric cancer patients who underwent ESD: 22 patients (23 lesions) had surgically altered gastric anatomy, whereas 647 patients (727 lesions) had normal gastric anatomy. In the altered gastric anatomy group, 13 patients, 6 patients and 3 patients had previously undergone distal gastrectomy, gastric tube reconstruction, and proximal gastrectomy, respectively. Rates of complete *en bloc* resection and curative resection were compared between the two groups. Influence of an anastomotic site and/or a suture line on ESD outcomes was examined in the altered gastric anatomy group.
Results: The rate of complete *en bloc* resection by ESD was 82.6% (19/23) in the altered gastric anatomy group and 92.3% (671/727) in the normal gastric anatomy group. The rate of curative resection and incident rates of complications were not significantly different between the groups. In the altered gastric anatomy group, the rate of complete *en bloc* resection was significantly lower when a lesion had spread across an anastomotic site and/or a suture line ($P = 0.0372$). Furthermore, duration of ESD was significantly longer ($P = 0.0276$), and resection efficiency was significantly lower (13 mm^2/min, $P = 0.0283$), when treating lesions with an anastomotic site and/or a suture line than when treating isolated lesions.
Conclusion: Outcome of ESD for cancer of the operated stomach compares with that in normal stomach anatomy. Anastomotic site/suture line within a lesion influenced the ESD procedure.
Disclosure of Interest: None declared

P0741 METHYLENE BLUE CHROMOENDOSCOPY AND MAGNIFICATION ENDOSCOPY ARE NOT USEFUL FOR DIFFERENTIATING TYPES OF INTESTINAL METAPLASIA IN THE STOMACH

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Introduction: Intestinal metaplasia (IM) in the stomach is a precancerous state often presenting as foci. IM can be divided into complete and incomplete, the latter bears greater risk of malignant transformation. Methylene blue (MB) chromoendoscopy can detect IM in the stomach, but sensitivity of this method is low. We hypothesised that those two types of IM have different ability to absorb MB which may be the cause of false negative results of chromoendoscopy. Previous studies suggested that complete and incomplete IM in the stomach present with different mucosal surface pit patterns.
Aims & Methods: We aimed to check if absorption of MB depends from the type of IM and if mucosal pit pattern evaluation may be helpful to discern complete and incomplete IM in the stomach. 37 patients with previously diagnosed IM in the stomach underwent gastroscopy with 0.5% MB staining and evaluation of gastric mucosal pit pattern in magnification up to x115 (Olympus GIF Q160Z). Biopsies were collected from antrum and corpus of the stomach, separately from the areas that stained and did not stain with MB. If intestinal metaplasia has been found in H&E histology, it was further differentiated into complete and incomplete by histochemistry (Alcian Blue PAS pH 2,5).
Results: We collected biopsies from 127 areas (34 stained and 93 unstained). Intestinal metaplasia was found in 57 bioptates (44.9%). IM was found more often in specimens collected from areas stained with MB (27 out of 34 – 79.4%) than in specimens collected from areas that did not stain with MB (30 out of 93 – 32.3%), $p < 0.001$. MB chromoendoscopy had 47.4% sensitivity and 90.0% specificity in detecting IM. There was no difference in the frequency of positive MB staining between complete and incomplete IM ($p = 1.0$). Comparing specimens containing IM collected from stained and unstained areas, the percentage of metaplastic cells in gastric mucosa was significantly higher in the first group (56.06%) than in the latter (28.17%, $p < 0.001$). IM was significantly less common in dot pit pattern (7.1%) than in tubular (38.9%, $p < 0.05$), villous (48.7%, $p < 0.0005$), foveolar (53.3%, $p < 0.005$) and cobblestone pit pattern (67.7%, $p < 0.0005$). The differences in frequency of IM between tubular, villous, foveolar and cobblestone pit patterns were not significant. The proportion of complete and incomplete intestinal metaplasia was similar in all pit patterns.
Conclusion: Positive MB staining and other than dot pit pattern correlate positively with the presence of IM. Positive or negative MB staining of metaplastic areas in the stomach may depend from percentage of metaplastic cells in gastric mucosa. Neither MB chromoendoscopy nor mucosal pit pattern evaluation are helpful in discerning complete and incomplete IM in the stomach.
Disclosure of Interest: None declared

P0742 IS THERE ANY VALUE OF ENDOSCOPY FOR GORD IN PATIENTS UNDER 45?

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Introduction: For gastro-oesophageal reflux (GORD), upper endoscopy may be indicated in men older than 50 years with chronic GORD symptoms (symptoms for more than 5 years) and additional risk factors (nocturnal reflux symptoms, hiatal hernia, elevated body mass index, tobacco use, and intra-abdominal distribution of fat) to detect oesophageal adenocarcinoma and Barrett oesophagus. In addition, upper endoscopy is indicated in patients with heartburn and alarm symptoms, such as dysphagia, bleeding, anaemia, weight loss, and recurrent vomiting. However, upper endoscopy is not an appropriate first step in most patients with GORD symptoms and is indicated only when empirical PPI therapy for 4 to 8 weeks is unsuccessful. Furthermore, inappropriate use of upper endoscopy does not improve the health of patients, exposes them to preventable harms, may lead to additional unnecessary interventions and results in unnecessary costs with no benefit.
Aims & Methods: The aim of the study was to assess the findings at upper endoscopy in patients under 45 years endoscoped for reflux without alarm symptoms. A single centre retrospective analysis in a North London NHS Trust Hospital was performed. Patients endoscoped for reflux were identified using the Unisoft Endoscopy reporting software, across a period of 10 years (June 2005 - May 2015). Data from the patients' electronic records were scrutinized if Barrett's was detected.
Results: A total of 1772 patients underwent upper endoscopy for reflux within the study period. 478/1772 patients were under 45 years of age. 124/ 1772 were found to have Barretts (7%). The age distribution was: under 45 years old: 16 patients (13%), 45-55 years: 20 patients (16%), 55-65 years old: 31 patients (24.8%), over 65: 57 patients (45.6%).
Out of the 478 patients under 45 undergoing endoscopy, 16 had Barrett's (3%), and no patient had cancer of oesophagus/stomach. All the 16 patients with Barrett's under 45 years had a short segment Barrett's without dysplasia (8 patients with 1 cm, 7 patients with 2 cm maximal length, 1 patient with 3 cm maximal length.
Conclusion: From this study, no patients under 45 undergoing upper endoscopy for GORD had upper GI cancer and only 3% had Barrett's, all short segment (<3 cm). The yield of upper GI endoscopy in this group is very low. In austere times where supply of endoscopy is overstretched it is important not to overburden the service with unnecessary procedures. From this study, we do not advocate performing upper GI endoscopy in patients under 45 years of age with reflux without alarm symptoms.
Disclosure of Interest: None declared

P0743 PREDICTIVE FACTORS FOR INTRACTABILITY TO ENDOSCOPIC HEMOSTASIS IN THE TREATMENT OF BLEEDING GASTRODUODENAL PEPTIC ULCERS IN JAPANESE PATIENTS

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Introduction: Acute upper gastrointestinal (UGI) ulcers is a major cause of morbidity and mortality, as well as a common medical emergency. Endoscopic hemostasis is the first treatment for UGI ulcer, and it can avoid emergency surgery. However, it can be difficult to completely achieve in some patients, and excessive hemorrhage from UGI ulcers can be fatal. Endoscopic treatment of UGI bleeding has recently advanced along with the administration of high dose intravenous proton pump inhibitors. Despite improvements in endoscopic hemostasis and pharmacological therapies, UGI ulcers repeatedly bleed in 10% to 20% of patients, and those without early endoscopic reintervention or definitive surgery might be at a high risk for mortality. Therefore, determining which factors are involved in rebleeding after an initial endoscopic hemostasis is extremely important for patients with bleeding UGI ulcers. In addition, understanding the factors that contribute to intractable or in sufficient initial endoscopic hemostasis is needed to advance the management of such ulcers.
Aims & Methods: This study aimed to determine the risk factors for intractability to initial endoscopic hemostasis. We analyzed 558 patients who underwent emergency endoscopic for bleeding UGI ulcers within 24 hours of arrival at our hospital between April 2000 and October 2014. We retrospectively documented the patients' backgrounds, and evaluated the ulcer location, size of exposed vessels on the bottom of the ulcer size, and Forrest bleeding patterns. To determine the factors involved in intractability to the initial endoscopic hemostasis, we compared patients whose bleeding UGI ulcers were successfully treated with the hemostasis with those who were intractable.
Results: Durable hemostasis was achieved in 477 patients (84.5%) by using initial endoscopic procedures. Seventy-six patients (14.6%) with Forrest types

Ia, Ib, IIa, and IIb at the second look endoscopy were considered intractable to initial endoscopic hemostasis. Three patients (0.6%) who underwent emergency surgery because of failure to the initial endoscopic hemostasis and two patients (0.4%) who died right after the initial endoscopic hemostasis because of heart failure were also considered intractable to initial endoscopic hemostasis. Multivariate analysis indicated that smoking (odds ratio [OR], 1.94; 95% confidence interval [CI], 1.16 to 3.24), shock on admission (OR, 2.68; 95% CI, 1.35 to 5.31), hemoglobin upon admission < 8.0 mg/dl (OR, 1.87; 95% CI, 1.02 to 3.42), serum albumin upon admission < 3.3 g/dL (OR, 2.05; 95% CI, 1.07 to 3.90), exposed vessels with a diameter of ≥ 2 mm on the bottom of ulcer (OR, 2.79; 95% CI, 1.65 to 4.72) predicted intractable endoscopic hemostasis, but Forrest types Ia was not the predictive factor of intractable endoscopic hemostasis.

Conclusion: Smoking, shock upon admission, hemoglobin < 8.0 mg/dL, serum albumin < 3.3 g/dL, and exposed vessels ≥ 2 mm on the ulcer bottom were identified as independent risk factors associated with initial intractable endoscopic hemostasis in patients with peptic UGI bleeds. Careful observation after initial endoscopic hemostasis is important for patients at a high risk for incomplete hemostasis.

Disclosure of Interest: None declared

P0744 PREDICTIVE FACTORS FOR OUTCOMES OF THROUGH-THE-SCOPE GASTRODUODENAL STENTING IN PATIENTS WITH GASTRIC OUTLET OBSTRUCTION; A LARGE MULTICENTER RETROSPECTIVE STUDY IN WEST JAPAN

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Introduction: Gastric or pancreatobiliary cancer patients sometimes suffer from gastric outlet obstruction due to gastric or duodenal stenosis. Recently the through-the-scope gastroduodenal stenting for malignant gastric outlet obstruction has become more effective, but the gastroduodenal stenting is sometimes ineffective, and stent dysfunction and complications occur. Many previous studies have analyzed the clinical efficacy, but not much has been available on the predictive factors.

Aims & Methods: The purpose of the present study was to retrospectively evaluate the clinical effectiveness of the gastroduodenal stenting with malignant obstruction and to identify predictive factors associated with ineffectiveness, stent dysfunction and complications. Between March 2009 and March 2014, 278 patients who underwent through-the-scope gastroduodenal stenting at four tertiary medical centers in west Japan were analyzed retrospectively. Primary aim was to investigate predictive factors for the outcomes such as clinical ineffectiveness, stent dysfunction and complications. The ineffective group was defined as the group without achievement of the GOOSS of 2 or more and relief of symptoms of GOO after stenting on the day 7 after stenting.

Results: The mean age of patients was 71.7 ± 11.4 years old. The patient etiology was; pancreatic cancer in 121 (43.5%) and gastric cancer in 87 (31.3%). Technical success was achieved in 277 of 278 patients (99.6%). Clinical effectiveness was achieved in 242 of 277 patients (87.4%), while stenting was ineffective in 32 patients (11.6%) and 3 patient (1.1%) died within 7 days after stenting. Stent dysfunction (ingrowth, overgrowth, migration and others) occurred in 46 patients (16.6%) (16, 11, 11 and 8 patients, respectively). Complications (jaundice, bleedings, perforation and others) occurred in 54 patients (19.5%) (23, 15, 6 and 10 patients, respectively). Number of stenosis regions ≥ 3 (odds ratio 6.11; 95% CI 2.16-17.30; $p < 0.01$) and KPS ≤ 50 (odds ratio 6.63; 95% CI 2.89–15.20; $p < 0.01$) were the significant predictive factors for clinical ineffectiveness. KPS ≤ 50 (hazard ratio 4.10; 95% CI 1.80–9.32; $p < 0.01$) and covered stent (hazard ratio 2.05; 95% CI 1.07–3.93; $p = 0.03$) were the significant predictive factors for stent dysfunction. Type II stenosis (hazard ratio 40.94; 95% CI 2.58-649.90; $P < 0.01$), covered stent (hazard ratio 87.14; 95% CI 6.16-1232.81; $P < 0.01$) and ascites (hazard ratio 0.13; 95% CI 0.02-0.96; $P < 0.05$) were the significant predictive factors for stent migration. Deployment of 2 stents in the same session (hazard ratio 1554.78; 95% CI 12.63-191364.4; $P < 0.01$) was the significant predictive factor for perforation.

Conclusion: The gastrodudenal stenting tends to be ineffective in patients with poor performance status and long stenosis regions. Stent dysfunction occurs more frequently with using covered than uncovered stents and in patients with poorer performance status. Uncovered stent is recommended in case of type II stenosis and non-ascites. We have to pay attention to prevention of perforation during deployment of 2 stents.

Disclosure of Interest: None declared

P0745 ENDOSCOPIC ENBLOC RESECTION OF SUB EPITHELIAL TUMORS: A SINGLE-CENTRE STUDY

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Introduction: Sub epithelial tumors (SETs) are soft tissue tumors arising from the sub mucosal or muscluaris propria layers of luminal organs. Enbloc resection of these lesions is desirable; often using surgical methods. Endoscopic techniques for resection of these lesions include endoscopic submucosal dissection (ESD) for lesions originating in the sub mucosal layer or endoscopic full thickness resection (EFTR) or submucosal tunneling endoscopic resection (STER) for lesions arising in the muscularis propria layer. This study describes our experience of endoscopic treatment of SETs.

Aims & Methods: Data of all consecutive patients undergoing endoscopic resection of SET in the period 2012 – 2014 was analyzed. All patients underwent pre procedure screening esophagogastroduodenoscopy (EGD) and endoscopic ultrasound (EUS) for assessment of the SET. One of following 3 procedures – ESD, EFTR or STER was performed for resection of the SET. ESD was performed for SET's arising in sub mucosal layer whereas EFTR or STER was performed for lesions in the muscularis propria layer. All patients underwent follow up EGD at 4 - 6 weeks. Parameters recorded were – location of lesion, layer of origin, procedure performed (ESD, EFTR or STER), technical success, margin positivity on histology, complications and their management, final histopathology.

Results: 29 consecutive patients with sub epithelial tumors underwent endoscopic resection during study period. Mean age – 56 years (range 29-78) and 21 male patients. ESD was performed in 23 patients, EFTR in 4 and STER in 2. Location of SET's was stomach (14), colon (6), duodenum (5), esophagus (3) and rectum (1). The mean area of sub epithelial tumors was 14.11 cm^2 (range 1-110). Histology was neuroendocrine tumors – 9, lipoma – 7, gastrointestinal stromal tumors – 6, leiomyoma – 5, ectopic pancreatic rest – 1 and duplication cyst – 1. Technical success of resection was 100%. 3 complications: perforation – 2 patients, 1 required surgery; bleeding – 1 patient, managed endoscopically. Histopathology of all specimens showed en-bloc excision with negative tumor margins.

Conclusion: Endoscopic en-bloc resection using ESD, EFTR or STER is a safe and effective therapy for SETs. Pre procedure EUS must be used to detect the layer of origin of SET. Based on EUS findings, the appropriate excision procedure can be selected.

Disclosure of Interest: None declared

P0746 PREDICTIVE FACTORS FOR LYMPH NODE METASTASIS AND LONG TERM OUTCOMES IN NON-CURATIVE PATIENTS WITH EARLY GASTRIC CANCER AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) is now widely employed and accepted in Japan as a less invasive treatment for early gastric cancer.

Aims & Methods: Endoscopic submucosal dissection (ESD) for gastric cancer has been familiarized broadly and rapidly. However risk factors and long-term outcomes in patients with non-curative resection after ESD remain to be elucidated. We evaluated predictive factors for lymph node metastasis (LNM) and long-term outcomes for these patients.

We analyzed 859 patients with early gastric cancer (1074 lesions) who underwent endoscopic submucosal dissection (ESD) from June 2001 through August 2011 in Hiroshima Citizens Hospital. Among 128 patients of non-curative resection, pathological factors have been analyzed. Ninety-nine patients (group A) have undergone an additional surgical gastrectomy with lymph node dissection and 29 patients (group B) have received no additional surgical gastrectomy due to their comorbidities. Seven hundred thirty one patients have had curative resection (group C). We have revealed risk factors for LNM and compared long-term outcomes in three groups.

Results:

The incidence of LNM was 8% (8/99) in group A. Pathological factors such as size, histology (pure differenced type, dominant type, pure undifferenced type), depth of submucosal invasion, ulceration, lymphatic involvement (LI), and venous involvement (VI) were examined for LNM. Decision tree analysis showed that the highest LNM risk combination was LI and ulceration. The frequency of LNM was 31% (3/9) in the patients LI and ulceration. Univariate analysis revealed that LI was only significant prognostic factor ($p = 0.005$). Kaplan-Meier demonstrated that there was a significant difference of group A and Group B ($p = 0.0002$) to group B and group C ($p = 0.005$).

Conclusion: LI was a only risk factor for LNM in patients with non-curative resection after ESD and additional surgical gastrectomy with lymph node dissection was recommended to them if possible.

Disclosure of Interest: None declared

P0747 CREATING AND ASSESSING EX-VIVO MODELS FOR SIMULATION ENDOSCOPIC TRAINING

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Introduction: While virtual reality and plastic models are essentially similar for all training centers, ex vivo models are centers' proprietary work, making it impossible for a student to assess the quality of a center's model before taking the course. At the same time, lack of standards in the area of ex-vivo modelling directly affects the quality of trainings provided. In view of this, standards must be set to maximize the quality of ex-vivo models, both in terms of the organ and pathology representation and imitation of surgical manipulations.

Abstract number: P0747 Ex-vivo Model Assessment Chart: Gastrointestinal Hemorrhage

Criteria		Not achieved	Partially achieved	Fully achieved
Organ modeling	Organ integrity			
Mucous membrane of natural color, with changes corresponding to the simulated pathology				
Pathology modeling	Hemorrhage intensity true to type			
Vessel wall condition				
Surgery simulation	Supporting the whole range of surgical techniques			
	Ease of access			
Model supporting several types of hemorrhage				

Aims & Methods: To optimize the process of creation of ex-vivo models (illustrated with the example of the gastrointestinal hemorrhage model), we have developed the following methods:
1. Organ modeling: A) To ensure the stomach integrity, we recommend forming an artificial gastroesophageal sphincter imitation from polymers. B) To preserve the natural colour of the mucous membrane, we recommend treating it with NaCl isotonic solutions and storing the abdominal organs in a 20% ethanol, 10% glycerine solution, at -10 to -15 C.
2. Pathology modeling: A) To simulate Forrest I arterial hemorrhage, we recommend using a pulse pump, and a drip set to imitate a vein hemorrhage. B) We recommend using the vessels: animal's own spleen artery and vein to imitate the vascular wall condition for this pathology.
3. Surgical manipulations imitation: A) The model supports the whole range of surgical techniques owing to the properties of the mucous membrane treatment solution and the natural properties of the animal's vessels, which ensure good contact between the tissue and a plate electrode, and adequate electrocoagulation. B) To provide access to the abdominal organs, we recommend forming a polymer port in the upper esophagus, wide enough in diameter to the surgical tools to be used. C) To create a model that would support several types of gastrointestinal hemorrhage, we recommend modeling up to 20 Forrest Ia/b bleeding points in the organ's wall.
Results: Based on four years of surgical gastroenterology work at the Training Center and on the feedback received individually and through polls from RNRMU professors, our international partners (including World Endoscopy Organization (WEO) experts) and students, we developed a set of performance criteria for ex-vivo models for each type of training.
Conclusion: Based on these criteria, the key requirements to each ex-vivo model were identified and have been implemented in a targeted manner.
This paper exemplifies successful use of feedback from simulation training students to find solutions to the key problems of biomodelling.
Disclosure of Interest: None declared

P0748 CLINICAL OUTCOME IN PATIENTS TREATED WITH A NEWLY-DESIGNED SEMS IN CERVICAL ESOPHAGEAL STRICTURES AND FISTULAS

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Introduction: Using a self-expandable metallic stent (SEMS) in the cervical esophagus is controversial due to increased risk of complications. Here we assessed a new type of SEMS purpose-designed for the cervical esophagus area.
Aims & Methods: This study included patients with malignant or benign stenosis within 4 cm distance of the upper esophageal sphincter (UES) who underwent placement of an SEMS with a shorter proximal funnel (Niti-S Esophageal Covered Stent—Cervical-type, NSCSC), Taewoong Medical). Main outcome measures were functional outcome, tolerance, complications, recurrent dysphagia and survival.
Results: 37 patients had a NSCSC placed between April 2008 and June 2013 for esophageal stenosis (20 malignant = 20, benign = 17), 5 with associated tracheoesophageal fistula. Average distance between UES and upper taper of the stenosis was 1.86 ± 1.27 cm. Median follow-up was 150 days. Dysphagia improved in 27/37 cases (73%). Short-and long-term tolerance without needing stent removal was 92% and 82%, respectively. Complication rate was 59% (22/37): 32% (n = 12 patients) major complications (fistula (3), perforation (3), aspiration pneumonia (5), laryngeal dyspnea (2) and bleeding (1)), and 27% (n = 10 patients) pain (7) or dysphonia (3). 84% of major complications occurred after 49 days. Multivariate analysis found a higher risk of major complications in cases of benign stenosis ($p = 0.04$). Recurrent dysphagia occurred in 15 (40%) patients due to obstruction (7) or migration (8).
Conclusion: NSCSC placement in the cervical esophagus effectively palliates dysphagia and is well-tolerated, but carries a high rate of complications. It does not seems to be less morbid than standard SEMS in this indication. The use of this device in benign strictures beyond six weeks is not recommended.
Disclosure of Interest: None declared

P0749 WHEN TO DRIVE SAFELY AFTER SEDATED ENDOSCOPY: A PROSPECTIVE PILOT STUDY ACCESSING THE DRIVING SKILLS RECOVERY AFTER ENDOSCOPIC SEDATION BY DRIVING SIMULATOR

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Introduction: Patients after endoscopic sedation were recommended not driving in 24 hours.
Aims & Methods: Assessing patients driving skills recovery after endoscopic procedures with propofol sedation to determine when to drive safely. Outpatients range in age from 20 to 70 years old and hold legitimate licenses. Volunteers were recruited to have a gastroscopy or colonoscopy under intravenous anesthesia with propofol, and measured driving ability by driving simulator before, and 2h, 4h after endoscopy. Meanwhile, blood samples were collected respectively before, and 2h, 4h after endoscopy for propofol concentration, which was determined by High Performance Liquid Chromatography. Driving simulation scenes were designed as low, moderate and high risk. The low risk scene simulated S curve driving, the moderate risk scene evaluated overtaking ability, and the high risk one assessed emergency collision avoidance capacity.
Results: Thirty volunteers met the inclusion criteria and participated in preoperative driving simulation, but eight of them had symptoms of dizziness, nausea or vomiting in the driving simulation test and were excluded from the study. The rest twenty two cases completed preoperative driving simulation test, but four of them refused the next gastrointestinal endoscopy. Eventually, eighteen cases completed gastroscopy or colonoscopy with propofol sedation, the driving simulation and blood collection 2h, 4h after endoscopy. Repeated measures was used for analyzing the variables of low risk, medium risk and high risk driving scenes. In low risk S curve scene, average acceleration (cm/s2) before endoscopy, 0.016 ± 0.010 VS 2h after endoscopy, 0.029 ± 0.016, $P = 0.001$; the average lane deviation (cm) before endoscopy, 42.50 ± 16.91 VS 2h after endoscopy, 53.80 ± 18.85, $P = 0.014$; the maximum lane shift (cm) before endoscopy, 113.70 ± 31.91 VS 2h after endoscopy, 157.00 ± 62.27, $P = 0.024$; the times of deviating from pathway before endoscopy, 0.83 ± 1.65 VS 2h after endoscopy, 2.06 ± 1.80, $P = 0.022$. In moderate risk scene and emergency collision avoidance high risk scene, there were no significant differences between before endoscopy and 2h after endoscopy. All variables of low, moderate and high risk scenes between before endoscopy and 4h after endoscopy, were no significant differences. The average blood concentration of propofol 2h after endoscopy was 0.81 ± 0.40 ug/ml, and propofol blood concentrations of blood samples collected 4h after endoscopy were below the limit of detection.
Conclusion: Subjects driving ability 2h after endoscopy was not recovered to baseline completely, but being fully restored 4h after endoscopy. Propofol had a certain impact on driving ability 2h after endoscopy.

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P0750 ENDOSCOPIC CLOSURE OF GASTRIC DEFECTS RESULTING FROM ENDOSCOPIC FULL-THICKNESS RESECTION BY APPLICATION OF NOVEL ENDOLOOPS AND METALLIC CLIPS, USING A SINGLE-CHANNEL SCOPE: A MULTICENTER CLINICAL STUDY

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Introduction: The key stage of the EFTR procedure is the successful closure of the gastric wall defect left after full-thickness resection and thereby avoid surgical intervention. This report presents a new method of closing large gastric defects left after EFTR, using LeClamp^{TM} endoloops and metallic clips by means of single-channel endoscope.
Aims & Methods: We retrospectively analyzed 68 patients who presented at four institutes between April 2014 and October 2014 with gastric fundus GISTs arising from the MP and who consequently underwent EFTR, with the resulting large gastric defects being closed using novel endoloops (Loop-20 and Loop-30, LeClamp^{TM}, Changzhou, China) and metallic clips (HX-600-135; Olympus). The key steps of closure were (1) An endoloop was inserted into the gastric cavity by forceps through the single-channel therapeutic endoscope; (2) The endoloop was anchored onto the full thickness of the defect's distal margin with the clip, followed by insertion of several additional clips to anchor the endoloop at different sides of the margin; (3) The delivery system was inserted and a removable hook was connected with the endoloop; (4) The endoloop was tightened by slight pulling of all the edges together; (5) Other clips were used if any clip was not accurately positioned or the purse-string suture was not tight. Patient characteristics, tumor size, en bloc resection, and postoperative complications were evaluated.
Results: A total of 68 patients (27 men [40%], 41 women [60%]; median age 55 years, range 38–67) were successfully underwent EFTR and the en bloc resection rate was 100%. Completely closure of all the gastric full-thinkness defects was achieved (success rate 100%). The median suture operation time was 13 minutes (range 9–21min). The mean maximum size of the lesions was 2.3cm (range 1.5–3cm). Pathological examination determined that all of the lesions were GISTs. The tumors were all low risk or very low risk, with a low mitotic index. No further treatment was given. The median hospital stay after the procedure was 5.4 days (range 3–9). None of the patients experienced severe complications, such as delayed bleeding, peritonitis or abdominal abscesses. Contrast roentgenography on post-procedure day 3 showed that no patients had gastrointestinal tract leakage or disturbed gastric emptying. None of the 68 patients underwent any surgical operations for the treatment of their lesions. All the patients had follow-up visits and the wounds were healed in all cases 1 month after the procedure. No residual tumor or tumor recurrence was observed during the follow-up period (range 6–12 months).
Conclusion: The use of LeClamp^{TM} endoloops and metallic clips is a relatively safe, easy, and feasible method for repairing gastric defects resulting from EFTR.

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P0751 ESD TRAINING IN CHINA: EXPERIENCE FROM HYBRID KNIFE HANDS-ON WORKSHOPS IN ZHONGSHAN HOSPITAL

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Introduction: Endoscopic submucosal dissection (ESD) is the gold standard technique for en bloc resection of superficial tumors of the gastrointestinal tract [1]. Hands-on endoscopy workshops are popular and valuable source for training of ESD. In China, ESD experience remains limited. Endoscopy Center, Zhongshan Hospital was the first endoscopy center to provide ESD in China back in 2006 [2], and has been a destination for ESD training since 2009.
Aims & Methods: The aim of the study is to evaluate the efficacy and safety of short-term hands-on workshops in ESD and to assess the progress of ESD practice in China following endoscopic training at the Zhongshan Hospital, with special attention to both short-term outcomes during the course and to the later ESD experience of the trainee's hospitals, in order to help setting the standards for adequate training and certification for ESD. From 2009 to 2013, ESD hands-on workshops have been held at Zhongshan Hospital. The workshops included lectures, ESD live demonstrations and hands-on training on live porcine models. Follow up questionnaires were sent to all 550 trainees at 464 hospitals in October 2014, with 460 trainees responding.
Results: There were 550 doctors who were trained during the 23rd hands-on workshops held Zhongshan Hospital, the median number of course trainees was 25 (ranging between 7-32). Completed questionnaires were returned by 460 (83.6%) trainees. There were 417 trainees who started performing ESD after the course. 28 doctors attended the workshop twice, and performed better than trainees who attended once in the hands-on practical session. Performance in the practical session has a significant difference both in the trainees GI experience ($>$ 5years vs$\leq$ 5years) and GI endoscopies ($>$4000 vs $\leq$4000). Following up the trainees within 1-year, there were 378 (82.2%) respondents from high-volume medical centers, with one-third of the respondents had experience in ESD.
Conclusion: Hands-on endoscopy workshops are useful in introducing ESD for trainees. Results showed that our training model is safe and enable novice endoscopists to start performing ESD. Requirements for starting ESD training include prior GI endoscopy experience, intensive learning and simulated ESD on live animal models under instructor's supervision. Essential requirements for trainees starting ESD remain to be established, but our system provides a step on the way.

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P0752 ENDOSCOPY IN VARICEAL BLEEDING: OPTIMAL TIME TO RESCOPING

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Introduction: Variceal haemorrhage is a common and potentially lethal complication of cirrhosis (1). Variceal rebleeding can occur in 20% of cases in the first week following the acute episode (2). BSG guidelines published in 2000 suggested endoscopy at weekly interval, whereas the AASLD guideline from 2007 suggest at 1-2 week interval and most recent ASGE guideline suggests optimal rescoping intervals of 1-8 weeks, a wide-ranging time scale recommendation classified as low-grade evidence (3,4,5). There is also primary literature that indicates that rescoping in less than 3 weeks might increase risk of harm (6).
Aims & Methods: We reviewed our practice to assess compliance with guidelines.
Method: We carried out a retrospective review of endoscopic procedures and follow up after oesophageal variceal bleeds at a DGH in the West Midlands over a 12-month period from August 2012 onwards. We recorded the date of their first variceal bleed (index bleed) and the scheduled follow up endoscopy procedure. We also recorded any adverse events such as rebleeds (bleeds in $<$7 days since the index bleed) or interval bleeds (bleeds that occurred $>$7 days post index bleed).
Results: 31 patients identified during 12month period had total 45 acute variceal bleeds, requiring urgent endoscopy. Haemostasis was achieved in all but one occasion 97.8% (44/45), with the majority (32) receiving band ligation and remaining receiving sclerotherapy or combination of therapies. 20% of total bleeds had rebleeds or died within 7 days. Of the remaining 36 bleeds, 14% had scheduled repeat endoscopy in $<$7 days as per last BSG guidelines, 29% had scheduled endoscopy between 1-8 weeks, which conforms to the standards suggested in new ASGE guideline, 20% had follow up endoscopy after 8 weeks, and 37% had no follow up endoscopy. The mortality rates of the people rescoped within 0-2 weeks and 2-8 weeks were 78% and 23% respectively with multiple reasons contributing.
Conclusion: There is inconsistency in the duration to follow up endoscopy practice perhaps due to wide discrepancy in available guidance and patient compliance. It is likely that in real-life practice in UK, rescoping interval is variable and inconsistent. It would be helpful to reassess current BSG guidelines and consider follow up endoscopy within 3-8 weeks after an index variceal bleed, with ongoing prospective review and audit to inform future adjustment.

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P0753 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC SUPERFICIAL NEOPLASTIC LESIONS: A EUROPEAN II LEVEL CENTER EXPERIENCE

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Introduction: Endoscopic dissection for the treatment of gastric superficial neoplastic lesions is an established first-line treatment in Eastern countries, its role has yet to be considered in Western guidelines, mostly due to a lack of long-term studies. The aim of this study was to describe the efficacy, safety and long-term outcomes for endoscopic submucosal dissection (ESD) in the treatment of gastric lesions in our center.
Aims & Methods: This was a single-center, retrospective, cohort study between November 2007 and November 2014. A total of 60 consecutive patients with 61 gastric superficial lesions underwent ESD and were followed up for a median of 27 months.
Results: In total 60 ESD were performed. 44 (73.3) lesions matched Extended Criteria, 16 (26.7%) Guideline Criteria (standard criteria). ''En bloc'' resection was feasible in 95%, with R0 resection rates of 86.6% (Ext-G 38/44 86.4% vs St-G 14/16 87.5% p:n.s). In total, 60 gastric lesions were classified as 33 (55%) adenocarcinomas intestinal type according to Lauren classification, 2 (3.3%) adenocarcinomas diffuse type according to Lauren classification, 7 (11.67%) adenomas with low-grade dysplasia (LGD), 10 (16.67%) high-grade dysplasia (HGD), 3 (5%) ectopic pancreas, 2 (3.3%) hyperplastic lesions, 3 (5%)

neuroendocrine tumors. Mean lesion size was 25.5 mm with a difference between two groups (Ext-G 28.77 vs St-G 16.50 mm, $p < 0.001$). 78.3% of lesions were located in third lower of stomach. Type 0-IIa + IIc according to Paris classification was the most frequent lesion in Extended group (54.5%). The recurrence rate was 18.18% (10/55 lesions of Ext-G, p:ns) at follow up of 27 months. We observed only 1 (1.6%) serious adverse events, a perforation treated with surgical resection. 9/10 complications were treated endoscopically without sequels. Surgery was performed in 7 cases (11.67%) : 5/7 after non curative endoscopic resection and 1/7 after histological evaluation (adenocarcinomas diffuse type according to Lauren classification), 1/7 due to complications.
Conclusion: ESD is a highly effective treatment for gastric superficial lesions, without compromising cancer survival. Endoscopic resection should also be considered as first-line treatment for gastric neoplasias in Western countries.
Disclosure of Interest: None declared

P0754 HEMOSPRAY AS A "RESCUE" ENDOSCOPIC TREATMENT IN GASTROINTESTINAL BLEEDING: A BINATIONAL OBSERVATIONAL STUDY

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Introduction: Hemospray is a novel hemostatic agent for the management of gastrointestinal bleeding (GIB). Herein we describe the experience with Hemospray in our cohort of patients with GIB.
Aims & Methods: This was a binational multicentre observational study done at three tertiary hospitals in Croatia and Bosnia and Herzegovina. Consecutive patients with GIB refractory to standard endoscopic hemostasis were included in the study. The patients referred for surgery, or in whom the informed consent for endoscopy was not obtained, were excluded from the study.
Results: There were 16 patients (median age 66.5 yrs, range 47-91, 11 males) with active GIB in whom Hemospray was applied. Lesions in the upper GI tract included: peptic ulcer bleeding (n = 4), Cameron lesion (1), Mallory-Weiss (1), GAVE (1), esophageal cancer (3). Lesions in the lower GI tract included: post-polypectomy bleeding (n = 5), bleeding polyp (1) Severity of bleeding was classified as spurting in 5 pts, oozing (7), visible vessel (1) and can't tell (3). A total of 6 patients were receiving anticoagulant or/and antithrombotic therapy. Bleeding with spurting vessel was in 31.25% of patients, in the form of oozing in 43.75%, and 25% of patients had visible blood vessel. Previous endoscopic treatment was recorded in 10 pts (clips = 7, nylon snare = 1, injection therapy = 1). Rebleeding at 7 days was noted in one patient (6%) with the post-polypectomy bleeding, who was referred to surgery. During the follow-up period (median 3 months, range 1-6), no re-bleeding episodes were recorded and two GIB-unrelated deaths occurred (12.5%). During study period we did not observe any side-effects of Hemospray.
Conclusion: In our cohorts of patients the use of Hemospray was efective treatment option for patients with GIB.
Disclosure of Interest: None declared

P0755 THE DEVELOPMENT OF A NOVEL DEVICE FOR TRANSPLANTATION OF CELL SHEETS IN THE FIELD OF THE PHARYNX

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Introduction: With the development of image-enhanced endoscopy and endoscopic diagnosis, the number of superficial cancer in the oropharynx and hypopharynx is increasing. The endoscopic submucosal dissection (ESD), endoscopic mucosal resection, or endoscopic laryngopharyngeal surgery is performed for these superficial squamous cell carcinomas. Because of complicated structure of pharynx, when ESD was performed for the lesion near the pyriform sinus, postoperative adhesion was observed. It impairs swallowing function and becomes the cause of aspiration pneumonitis. And similar to the esophageal ESD, postoperative stricture is observed when a large area of mucosa was removed. Some study showed the endoscopic transplantation of fabricated autologous epithelial cell sheets prevent postoperative stricture. It is expected same effect after the ESD of the oropharynx and hypopharynx. However, because of the narrow and complicated 3-dimensional structure of pharynx, we can transplant the cell sheets on only a limited area by using existing transplant method and devices. So, it was impossible to investigate an effect of the cell sheet transplantation in the field of the pharynx.
Aims & Methods: To transplant cell sheets to entire field of the oropharynx and hypopharynx after ESD, The novel devices were designed and developed with a computer-aided design system, and the three-dimensional data were transferred to a 3-D printer. And then, primary epidermal cells were isolated from the lower abdominal skin of miniature pigs, cultured for 14 days at 37°C on temperature-responsive culture inserts. Transplantable cell sheets were harvested from the inserts by reducing temperature to 20°C. We performed pharyngeal ESD and cell sheets transplantation with this device in a porcine, and investigated the feasibility of these in the field of the oropharynx and hypopharynx.
Results: Developed novel endoscopic delivery device was consisted of a cell sheet carrier and an air tube. A cell sheet carrier was spoon-shaped and covered by balloon, and connected to an air tube. It could attach the cell sheets by inflating the balloon that inflated only one side. It could deliver the cell sheets without contacting the mouth and laryngopharyngeal mucosa, and deliver the cell sheets on any areas of the pharynx after circumferential ESD. Required cell sheets were successfully transplanted to cover the ulcer site.
Conclusion: The novel device was very useful. Owe to this device, now we can investigate an effect of the cell sheets transplantation after pharyngeal ESD.
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P0756 SUCCESFUL TREATMENT OF ACHALASIA BY POEM IN ROMANIA: A REPORT ON THE FIRST 30 CASES

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Introduction: Peroral endoscopic myotomy (POEM) is now the proposed method to replace laparoscopic mytomy in the treatment of achalasia, being less aggressive, with lower morbidity and similar or even higher efficiency. Thus, POEM is reserved for expert endoscopists.
Aims & Methods: The main purpose was to analyze the efficacy and complications of the technique, while the secondary purpose was to evaluate the clinical, endoscopic and manometric improvement in patients after treatment. Endoscopic, radiological and manometric assessments were performed in all patients before and after the procedure. All POEMs were performed by a highly experienced endoscopist with no previous hands-on training. We evaluated the resolution of symptoms at 3 and 30 days after POEM using the Eckardt score. The technique, accessories and electrocautery settings used were those described by Prof. Inoue (1). An esophagography was performed in all patients after the procedure to rule out any leakage. All patients were allowed to eat 48 hours after POEM.
Results: From November 2013 to April 2015, thirty patients were treated by POEM, with a mean age of 43.7 years. Five patients had previous endoscopic balloon dilation. No patient had previous surgical myotomy. The average duration of the intervention was 87.5 minutes. We recorded five incidents, three in the form of esophageal and gastric mucosal microperforations, closed safely with endoscopic clips, one subcutaneous emphysema, for which temporary cessation of the intervention was necessary, and one pneumoperitoneum, for which transumbilical decompression using a Veress needle was necessary. We also recorded two complications in the form of postprocedural endoscopic clip slippage, which required endoscopic reintervention. We noted a decrease in Eckardt score from a mean 7,7 before POEM to a mean 0,8, 30 days after POEM. We also recorded a decrease in LES pressure from a mean 35,5 mmHg before the procedure to 3 mmHg, 30 days after the procedure.
Conclusion: POEM is an effective and safe technique. An experienced gastroenterologist can perform it without the need for hands-on training in advance, due to a reduced learning curve.

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P0757 OUTCOMES OF ENDOSCOPIC INJECTION OF MITOMYCIN C FOR REFRACTORY RECURRENT BENIGN ESOPHAGEAL STRICTURES

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Introduction: Benign esophageal strictures are a common problem characterized by luminal narrowing due to acid exposure, radiation, caustic injury, or post-surgical changes. The production of collagen and fibrous tissue stimulated by esophageal injury results in chronic stenosis. Up to 35% of benign strictures recur are recalcitrant. Mitomycin C is a chemotherapeutic agent that inhibits both DNA and protein synthesis following intracellular enzymatic reduction resulting in slowing of cell division and fibroblast proliferation [1]. Topical MMC has been used in children and adults to treat laryngeal and tracheal strictures [2,3]. Limited data of MMC topical mucosal therapy in children and adults suggests promising safety and efficacy for recalcitrant esophageal strictures [4].
Aims & Methods: We report the clinical outcomes of 9 patients with refractory benign esophageal strictures treated with endoscopic submucosal injection of MMC(0.4 mg/,l) after dilation[4].
Results: 9 symptomatic patients with 11 refractory esophageal strictures previously treated with numerous dilations (median 4), steroid injections and/or

stents underwent MMC treatment. A total of 16 intralesional endoscopic injections were made. 3 patients with complex strictures required more than 1 MMC treatment. Pre-MMC mean stricture length and diameter were 3.7cm (range 1-10cm) and 5.5mm (range 2-10mm), respectively. Mean patient follow-up time was 14 months (range 6.3-49.8 months). Symptomatic recurrence requiring unscheduled intervening therapy was observed in 4/9 patients within the first 3 months (2 dilation, 1 stent, 1 dilation + MMC). Partial response (post-MMC dysphagia score improved by at least 1 grade) was noted in all. A durable complete response was defined as no dysphagia and no intervening therapies at last follow-up. This was observed in all except 1 patient who required stenting within 6 months. MMC injection decreased pre-treatment intervention therapy from median 3.8 procedures per 6 months (interquartile range 3 to 4.5 per 6 months) to 0 procedures in 6 months ($p = 0.008$,Wilcoxon signed rank). There were no treatment-related adverse events with endoscopic injection of a total of 0.64 to 6.4 mg MMC per patient.

Conclusion: MMC injection for refractory recurrent benign esophageal strictures is safe, eliminates dysphagia, and significantly decreases symptom recurrence and the need for subsequent interventions.

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P0758 NITROUS OXIDE CRYOTHERAPY FOR TREATMENT OF ESOPHAGEAL SQUAMOUS CELL NEOPLASIA (ESCN): INITIAL EXPERIENCE WITH A NOVEL PORTABLE CRYOBALLOON FOCAL ABLATION SYSTEM (CBFAS)

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Introduction: Early esophageal squamous cell neoplasia (ESCN) can be successfully treated with radiofrequency ablation (RFA), endoscopic mucosal resection (EMR), or endoscopic submucosal dissection (ESD), but strictures can develop[1]. Endoscopic cryotherapy can successfully eradicate neoplastic Barrett's esophagus[2, 3], including those that failed other treatments[2, 4]. A new portable battery-powered contact cryotherapy system using nitrous oxide (cryoballoon focal ablation system, CbFAS) has been used for Barrett's esophagus[5] with promising early results[6].

Aims & Methods

Aim: To determine the feasibility of endoscopic eradication of ESCN with nitrous oxide cryotherapy using a CbFAS.

Methods: Patients with ESCN who had failed or were ineligible for EMR/RFA (stricture, esophageal varices) were treated with nitrous oxide cryoballoon ablation using the CbFAS, which consists of a small hand-held device containing liquid nitrous oxide, which converts to gas within a low pressure compliant through-the-scope balloon. It freezes targeted mucosa in contact with the balloon, resulting in ablations of approximately 2 cm^2. After chromoendoscopy, all Lugol's voiding lesions (LGLs) were treated with multiple focal ablations (8-10 seconds of ice per site). Post-procedure adverse events were recorded. Patients were treated every 6-8 weeks until targeted and random biopsies demonstrated eradication of neoplasia.

Results: 3 male patients (mean age 66, range 55-76) with multifocal low-grade intraepithelial neoplasia (LGIN), high grade intraepithelial neoplasia (HGIN), or flat type ESCC involving 3 cm (Pt1), 4 cm (Pt2), and 10 cm (Pt3) of the esophagus had 3, 8, and 10 ablations at the index procedure, respectively. Residual LGLs were treated in a second (Pt2) and third procedure (Pt3). No device malfunction was noted. Aiming the cryogen at LGLs was relatively easy. Median procedure time was 34 min (range 18-57). No major adverse events occurred. One patient had mild odynophagia and chest pain. No strictures or bleeding developed. Squamous regeneration was seen in all treated areas with no LGLs and complete pathologic response achieved in all patients with short term follow-up (mean 165 days, IQR 35-316).

Conclusion: Our initial experience suggests that multifocal cryoballoon ablation is a promising portable, technically simple, well-tolerated, safe and effective endoscopic therapy for ESCN, including extensive disease refractory to EMR and RFA. Prospective studies are needed to optimize cryogen dosimetry and assess safety and long-term efficacy.

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P0759 PERCUTANEOUS TRANSESOPHAGEAL GASTROTUBING (PTEG) FOR THE PATIENTS THAT PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) INSERTION IS IMPOSSIBLE – USEFULNESS OF ENDOSCOPICALLY ASSISTED PROCEDURE

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Introduction: Percutaneous transesophageal gastrotubing (PTEG) was developed as an alternative route to access the gastrointestinal tract for the patients that Percutaneous Endoscopic Gastrostomy was contraindicated with conditions such as prior gastrectomy, gastric anterior wall malignancies, or massive ascites. PTEG by endoscopic assistance may enhance the safety of the procedure.

Aims & Methods: The aim of this study is to evaluate the clinical usefulness of PTEG supported by endoscopy. A rupture-free balloon (RFB) catheter is inserted into the lower esophagus. Percutaneous balloon puncture with a specialized needle is then performed from the left side of patient's neck under ultrasonographic control. A guide wire is inserted through the needle into the RFB, followed by a dilator and sheath. A placement tube is then inserted through the sheath, and the sheath is removed. We started to perform PTEG under endoscopy or fluoroscopy in a total of 144 patients (93 men and 51 women, mean age 72.0 years) in whom PEG was not feasible. PTEG was performed for nutrition in 82 patients and for decompression in 62.Thirty patients were started by fluoroscopic assistance and 114 patients were started by endoscopic assistance.

Results: Satisfactory results were achieved in all 144 patients. Median follow-up was 64.0 days in patients who received decompression because of the obstruction due to malignancies and 255.5 days in those who received nutrition. Seven of 82 patients for nutrition were able to free from tube feeding due to PTEG tube feeding support. There was 1 patient with severe bleeding requiring blood transfusion in the fluoroscopy group. one patient had tracheal penetration, which was managed conservatively. Other complications were minor oozing bleeding in eight patients that did not require blood transfusion, subcutaneous emphysema in two patients, which were managed conservatively. The complication rate associated with fluoroscopically and endoscopically assisted PTEG was 20.0% and 14.1%, respectively. No patient required surgical treatment or died after PTEG.

Conclusion: PTEG is feasible, safe, and useful. PTEG could be an optimal procedure for long-term nutrition and/or decompression even for the patients who failed PEG insertion. The use of endoscopy enhances the safety of the procedure and allows better confirmation of each step involved.

Disclosure of Interest: None declared

P0760 A SELF-ASSEMBLING, MATRIX-FORMING PEPTIDE CAN BE USED TO PREVENT POST OPERATIVE BLEEDING AFTER ENDOSCOPIC RESECTION INCLUDING IN HIGH-RISK SITUATIONS

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Introduction: Endoscopic resections can remove superficial digestive neoplasia with low morbidity and mortality. Nevertheless, delayed bleeding has been reported in approximately 1, 5, 15 and 2% after resection in the esophagus, the stomach, the duodenum and the rectum, respectively, increasing with antiplatelet/anticoagulant therapy or in case of portal hypertension. A self-assembling peptide (SAP) forming a gel in appropriate conditions of ionization could protect the mucosal defect during the early phase of healing. The aim of this clinical trial was to assess the safety and efficacy of the SAP to prevent delayed bleedings after endoscopic resections.

Aims & Methods: Consecutive patients who underwent endoscopic resections for esophageal, gastric, duodenal or colic superficial lesions were enrolled in two university hospitals. We also included patients with high risk of bleeding like patients with antiplatelet agents, anticoagulation drugs with heparin bridge therapy and cirrhosis with portal hypertension. The SAP gel (Purastat®, 3D Matrix, Ltd) was apllied immediately after resection. The volume of gel depended of the resection size and was applied with a catheter aiming to cover all the ulcer bed.

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Table 1: Mean ESD time of cases with pathology and invasion depth

		InspectionTime(min)	IncisionTime (min)	DissectionTime (min)	CoagulationTime (min)	TotalTime (min)
Pathology	Adenoma	3.54	15.97	30.12	6.98	56.36
	Adenocarcinoma	3.81	19.41	47.44	8.08	79.09
	P value	0.051	0.013	0.001	0.566	0.001
Invasion depth	M	3.62	17.93	36.68	7.04	65.09
	MM	3.58	18.38	37.46	6.32	66.00
	SM	4.71	19.75	77.92	6.08	110.33
	P value	0.383	0.767	0.001	0.659	0.001

Subsequent patient management included oral PPI after esophageal, gastric and duodenal resections. The primary endpoint was the rate of post resection bleeding. Ease of use and safety were also assessed.

Results: 37 patients were included with 42 lesions (8 esophagus, 10 stomach, 8 duodenum, 3 ampullary, 13 colorectal tumors). Among those 42 lesions, 28 were resected in high-risk situations (8 non-discontinued anti-platelets drugs, 6 heparin bridge therapies followed by anticoagulant drugs at day 1, 9 with cirrhosis and portal hypertension, 1 with both cirrhosis and antiplatelet therapy, 3 large duodenal lesions and 1 lesion of the anal canal surrounded by large hemorroids). The resection technique was ESD in 22 cases, en-bloc EMR in 9 and piecemeal EMR in 5. The mean lesion size was 17.1 mm (SD 18.4) with a mean area of 2.94 cm^2 (SD : 3.2). The mean volume of Purastat® used was 3.1 ml (SD : 1.5 ml) in a mean time of 2.0 min (SD : 1.2). No difficulty was noted during application. Four delayed overt bleedings occured (9.5 %) (3 hematochezia, 1 hematemesis) needing endoscopic hemostasis in 3 cases. The mean hemoglobin drop off was 0.8 g/dl (-0.1to 2.1 g/dl). There were no adverse events related to the gel.

Conclusion: The use of this novel EMS may help to reduce the post endoscopic resection bleedings including in high risk situations. Its use is easy and safe but further comparative studies are needed to fully evaluate its effectiveness.

Disclosure of Interest: None declared

P0761 PRELIMINARY EVALUATION OF SUBMUCOSAL TUNNELING ENDOSCOPIC RESECTION FOR THE TREATMENT OF LARGE SYMPTOMATIC SUBMUCOSAL TUMORS ORINGINATING FROM THE MUSCULARIS PROPRIA LAYER IN THE ESOPHAGUS AND CARDIA

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Introduction: Submucosal tunneling endoscopic resection (STER) has been proved to have many advantages for small upper gastrointestinal (GI) submucosal tumors (SMTs) originating from the muscularis propria (MP) layer. Here, we report the clinical value of STER for huge (≥3cm) and symptomatic SMTs originating from the MP layer in the esophagus and cardia.

Aims & Methods: Our study aimed to evaluate the clinical value of STER for large symptomatic submucosal SMTs originating from the MP layer in the esophagus and cardia. A total of 72 large symptomatic SMTs originating from the MP layer in the esophagus and cardia were treated by STER between May, 2011 and December, 2013. Large symptomatic tumors referred to the tumors which were not less than 3 cm in maximum diameter and caused varying degrees of retrosternal or epigastric discomfort, regurgitation, odynophagia, and/or dysphasia. After located, a submucosal tunnel was created to expose the tumor. The lesion was then resected under direct endoscopic view and the tunnel entry was closed with several metal clips.

Results: STER was performed successfully in all cases, and the en bloc resection rate was 100%. The median maximum diameter of the specimens was 4.0 cm. Pathological results revealed 69 leiomyomas, 1 stromal tumor, 1 schwannoma and 1 cyst. STER-related complications were listed in Table 1. All of those complications were treated successfully after conservative treatments. No patient encountered massive and delayed bleeding, intra-tunnel infection or abscess, and procedure-related death. The symptoms of retrosternal or epigastric discomfort, regurgitation, odynophagia and/or dysphasia were relieved varying degrees after the procedures according to patients' subjective feelings. An objective relief of dysphagia was also achieved as assessed by Stooler's dysphagia score ($P < 0.001$). No tumor residual or recurrence was found during the follow-up period (range, 2-30 months)

Table 1 Clinicopathologic information of the 72 patients

. Patients N = 72

Age, median (range), years 46 (28-67)

Sex, n (%). Male 50 (69.4) Female 22 (30.6)

Lesion size, median (range) cm 4.0 (3.0-7.0)

Procedure time, median (range) min 70.0 (42-140)

Tumor location, n (%) . Esophagus 60 (83.3) Cardia 12 (16.7)

Chief complaint, n (%) . Retrosternal or epigastric discomfort 72 (100.0) Regurgitation 56 (77.8) Odynophagia 60(83.3) Dysphasia 72 (100.0)

EUS layer, n (%) . Superficial MP 31 (43.1) Deep MP 41 (56.9)

Pathologic diagnosis, n (%) . Leiomyoma 69 (95.8) GIST 1 (1.4) Schwannoma 1 (1.4) Cyst 1 (1.4)

Complications, n (%) .Substernal or epigastric pain Analgesics required Mucosal damage Closures required 41 (56.9) 3 (4.2) 4 (5.6) 4 (5.6)Pneumothorax Subcutaneous emphysema Diaphragmatic emphysema Pneumoperitoneum Pleural effusion Massive and delayed bleeding Intra-tunnel infection or abscess Surgical-related death Tumor residual or recurrence 9 (12.5) 18 (25.0) 19 (26.4) 9 (12.5) 34 (47.2) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0)

Conclusion: STER is safe and effective for large symptomatic SMTs originating from the MP layer in the esophagus and cardia. The procedure can significantly relieve symptoms without severe adverse events. High en bloc resection rate and accurate histopathologic outcomes can also be achieved with the technique.

Disclosure of Interest: None declared

P0762 ANALYSIS OF CLINICOPATHLOGIC FACTORS THAT AFFECT ON PROCEDURE TIME OF ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) has become a widely accepted therapeutic method for gastric adenoma and early gastric cancer. However, it takes a long time to perform ESD procedure because of technical difficulties. So there has been a lot of effort to analyze factors that have an affect on procedure time. Especially, in this study, we analyzed not only total procedure time but also subdivision of the time -inspection, incision, dissection, coagulation time.

Aims & Methods: We reviewed the data of 343 patients who underwent ESD for 378 lesions (gastric adenoma and early gastric cancer) from July 2006 to December 2012 by one skillful endoscopist. Clinical outcomes of ESD such as procedure time, location, pathology, size, invasion depth were analyzed.

Results:

Mean total procedure time was 64.9 min, and mean inspection, incision, dissection, coagulation time were 3.68, 17.27, 36.65, 7.32 min respectively. Univariate analysis showed the total ESD time was closely related to pathology ($p = 0.001$), tumor invasion depth ($p = 0.001$), location ($p = 0.002$), size ($p = 0.001$), ulceration ($p = 0.001$) and depression ($p = 0.001$). Especially, the pathology, location, tumor size, ulceration and depression were related to incision time and dissection time. Invasion depth was associated with dissection time ($p = 0.001$). When tumor size was controlled, incision time was positively correlated with dissection time ($p = 0.001$).

Conclusion: ESD procedure takes longer when the neoplasm is adenocarcinoma compared to adenoma. Deeper invasion depth, larger tumor size, presence of

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Pre-ESD biopsy result (No.)		Post-ESD result	No. (%)	Discrepancy group
Gastric adenoma (837)	Low grade dysplasia (688, 82.2%)	Non neoplasia	51 (7.4)	Downgrade
		Low grade dysplasia	511 (74.2)	Concordance
		High grade dysplasia	43 (6.3)	Upgrade
			Adenocarcinoma	83 (12.1)
	High grade dysplasia (149, 17.8%)	Non neoplasia	3 (2)	Downgrade
	Low grade dysplasia	28 (18.8)		
	High grade dysplasia	36 (24.2)	Concordance	
	Adenocarcinoma	82 (55)	Upgrade	

Abstract number: P0765

Table 1:: Predictors of clinical response after transpyloric stent placement

	Clinical Response (n = 20)	No Clinical Response (n = 7)	OR	P value	CI 95%
Age(yrs)(mean ± SD)	40.95 ± 16.36	40.28 ± 14.18	1.00	0.92	0.94-1.06
Female, n(%)	14(70)	5(71)	0.93	0.94	0.13-6.22
Etiology, idiopathic, n(%)	10(50)	4(57.14)	0.75	0.7	0.13-4.2
Predominant N/V, n(%)	19(95)	5(71)	7.6	0.12	0.56-101

ulceration or depression are predictors of a long ESD time, especially SM invasion is related with longer dissection time.

Disclosure of Interest: None declared

P0763 ANALYSIS OF DISCREPANCIES IN HISTOLOGIC DIAGNOSES OF GASTRIC NEOPLASM BETWEEN BIOPSY AND ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) has become a widely accepted therapeutic method for gastric adenoma and early gastric cancer. A preoperative histologic diagnosis of neoplasia is a requirement for ESD. But, histologic discrepancies between endoscopic forcep biopsy (EFB) and ESD specimens have been reported at rates ranging from 2.7–49%.

Aims & Methods: Aim of this study was to analyze the prevalence of paradoxical (upgrade and downgrade) and concordant pathology results on ESD specimens and to compare their endoscopic characteristics among the each groups. Between February 2005 and December 2011, 1186 ESDs were done at Ajou University Hospital in Suwon, South Korea. Among these cases, 837 cases was diagnosed as adenoma in endoscopic forceps biopsy. We retrospectively reviewed these cases from our original database of gastrointestinal therapeutic procedures. The following variables were analyzed to document endoscopic characteristics such as size of lesion, sampling ratio and coexistence lesions.

Results: Compared with upgrade and concordance group, the downgrade group showed a meaningful smaller tumor size, surface area, and lower sampling ratios ($P < 0.001$). On the other hand, compared with concordance group, the upgrade group showed a significant larger tumor size and more frequent prevalence of ulcerative lesion (14.3%, concordance;4.0%) and depressed lesion (48.8%, concordance; 32.2%) ($P < 0.001$).

Conclusion: The tumor size and sampling ratio can be predictable value of downgrade group of histologic discrepancy after ESD. And the coexistant endoscopic finding such as ulcerative lesion or depressed lesion could be predictable value of upgrade group of histologic discrepancy after ESD.

Disclosure of Interest: None declared

P0764 HEMOSPRAY IN ACUTE NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: FIRST EXPERIENCES IN A UK TEACHING HOSPITAL

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Introduction: Acute Upper GI Bleeding (AUGB) is a common and serious medical emergency with an incidence ranging from 50 to 190/10 000/year in the UK.[1] Hemospray (TC-325), a hemostatic powder licensed for the treatment of non-variceal upper GI bleeding, was launched in the United Kingdom in June 2013. We introduced Hemospray into our practice at University Hospitals of Leicester [UHL] in December 2013.

Aims & Methods: The aim of our study was to assess the use of hemospray and its impact on our practice at UHL. We retrospectively reviewed our endoscopy reporting database [Unisoft- GI reporting tool] for all patients who underwent Upper GI endoscopy for AUGB [indications: melaena and/or haematemesis] and were treated with Hemospray between December 2013 and March 2015. Data was analysed for patient age, gender, endoscopic diagnosis, Monotherapy vs. combination therapy, concomitant anti-thrombotic agent use, rebleeding rate and 30 day mortality.

Results: From December 2013 until March 2015, 1299 Upper GI endoscopies were performed at UHL for AUGB. Hemostatic interventions were performed in 233 procedures [17.9%]. 19 patients were treated with Hemospray (14 male) in 21 procedures. In 19 endoscopies (90.5%) Hemospray was used at index endoscopy, while it was used at two (9.5%) second look endoscopies for rebleeding. The average age was 72 years (Range 34-94). The cause of AUGB was peptic ulceration in 78% of patients (n = 14) {duodenal ulcer 78.6% (n = 11) ; gastric ulcer 21.4%(n = 3)}, 10.5 % oesophageal ulceration (n = 2), 10.5 % gastric malignancy (n = 2), 5.3% post-sphincteromy bleeding (n = 1). The main reasons for Hemospray use by procedure (n = 21) were: 66.7% difficult endoscopic access (n = 14), 23.8 % difficulty in visualising exact bleeding point (n = 5), 9.5% patient intolerance of procedure (n = 2). Amongst peptic ulcers (n = 14), the Forrest classification breakdown was: 1A (4, 28.6%), 1B (8, 57.1 %), 2A (2, 14.3%). Immediate hemostasis was achieved in 18/21 endoscopies (85.7 %). 9/19 patients (47.4%) were on anti-thrombotic therapy (aspirin 66.6% (n = 6), clopidogrel 22.2% (n = 2) and therapeutic enoxaparin 11.1% (n = 1). Hemospray was used as monotherapy in 5 (23.8%) endoscopies and in combination with traditional modalities (adrenaline injection, heater probe, haemostatic clips) in 16 (76.1%) endoscopies. 5/19 patients developed rebleeding (26.4%). The average time to rebleeding was 5.8 days (Range 2-14 days). The 30 day mortality was 31.3% (n = 6). 3 deaths (50%) were directly related to uncontrolled gastrointestinal haemorrhage. No adverse events as the result of Hemospray use were noted.

Conclusion: Hemospray is a safe and useful adjunct to traditional hemostatic therapies with a high rate of immediate hemostasis. In our series, Hemospray accounted for about 8% of all endoscopic interventions and was only employed in 1.5% of all patients presenting with AUGB. There was a significant rebleed rate of 26%, likely to be a reflection of a very sick patient cohort. The majority of cases had high rebleeding risk (Forrest 1A and 1B ulcers, GI malignancy). The average time to rebleed was 6 days, which suggests that Hemospray is a useful bridging therapy to non-endoscopic GI bleed therapy (angiography/surgery). A formal RCT comparing Hemospray to conventional haemostatic methods is indicated to evaluate its efficacy and effect on mortality.

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Disclosure of Interest: None declared

P0765 REFRACTORY GASTROPARESIS CAN BE SUCCESSFULLY MANAGED WITH ENDOSCOPIC TRANSPYLORIC STENT PLACEMENT AND FIXATION

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Introduction: Medical treatment options for gastroparesis are limited. Data from studies of botulinum toxin and pyloroplasty suggest that disruption of the pylorus can result in symptomatic improvement in some patients with refractory gastroparetic symptoms. We previously performed a pilot study that demonstrated improvement of symptoms in 4 patients with gastroparesis treated with transpyloric stent placement (TPS).

Aims & Methods: To (1) determine safety and efficacy of TPS placement for refractory gastroparesis; and (2) evaluate whether various stent fixation techniques had impact on stent migration rate and clinical outcome. Patients with gastroparesis refractory to medical treatment were referred for TPS. A through-the-scope fully covered self-expandable metallic esophageal stent was deployed across the pylorus. In fixation group, the stent was anchored to the gastric wall with either endoclips, over-the-scope clip (OTSC) or endoscopic suture (ES: placed in 2 locations between stent and gastric wall). Self-reported symptom improvement, stent migration rate and post-stent gastric emptying study (GES) results were collected. Time to migration was compared using Kaplan Meier estimate.

Results: A total of 29 patients (20 female, mean age 39yr) with refractory gastroparesis (idiopathic 16, diabetic 8, post-surgical 5) underwent 47 TPS procedures. Of these, 25/47 (53%) were performed in patients admitted to the hospital with intractable symptoms. Most (n = 24, 83%) had predominant symptoms of nausea (N) and vomiting (V). Successful stent placement was achieved during 46 (98%) procedures. Most stents were anchored to the gastric wall using ES (n = 23), followed by OTSC (n = 18) and endoclip (n = 2). Three patients did not receive stent fixation. Overall, 20/27 (74%) patients had clinical response (2 patients were lost to follow-up). All inpatients were successfully discharged after stent placement. Clinical success was higher in patients with predominant N/V compared with those with abdominal pain/bloating (95% vs. 71%, p = 0.12) (table 1). Repeat GES was performed in 16 patients: mean 4hr GE normalized in 5 patients (76% vs. 98%, p = 0.2) and significantly improved in 4 (54% vs. 73%, p = 0.02). Stent migration occurred in 59% of procedures: 100% in the no fixation group, 50% in the endoclip group, 71% in the OTSC group, and 48% in the ES group ($p > 0.05$ for all comparisons). During a mean follow up of 146d, time to stent migration was not different between ES and other groups (P = 0.9).

Conclusion: TPS is a promising novel endoscopic treatment modality for gastroparesis and improves both symptoms and gastric emptying in patients refractory to medical treatment, especially those with N/V. TPS can be considered as salvage therapy for inpatients with intractable symptoms. Questions regarding long-term durability and stent migration risk remain.

Disclosure of Interest: None declared

P0766 ACCELERATED TRAINING IN UPPER GI ENDOSCOPY - AN ANALYSIS OF SPRINT PROGRAMME OUTCOMES

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Abstract number: P0766
Table: Median (IQR) for time to training landmarks (weeks) by group

No.of UGI cases	50	75	100	125	150	175	200
SPRINT GROUP	10 (7.5 to 13.5)	14 (11 to 25.5)	20 (14.5 to 29.5)	23 (20.5 to 31.5)	27 (25 to 35)	29 (29 to 37.5)	35 (33.5 to 40.5)
HISTORIC CONTROLS	22.5 (15.3 to 29.3)	35 (20 to 40.5)	45 (26.5 to 48)	51.5 (29.5 to 57.3)	58 (32.5 to 63.8)	63 (39.8 to 70)	67.5 (45.8 to 78.8)
p value for difference	0.002	0.005	0.002	0.001	0.001	0.0007	0.0008

Introduction: In the UK novice endoscopists must attain JAG certification in UGI endoscopy (portfolio > UGI 200 cases, trainer DOPS, achievement of performance indicators and JAG basic skills course attendance). Cases are recorded on the JETS e-portfolio (1). Barriers include need for dual accreditation in general medicine, service pressure, difficulty accessing courses and variable quality of hands-on training. In Wales we designed an accelerated national training pathway - SPRINT programme –delivering core elements with integrated simulator and lesion recognition training.
Aims & Methods: Efficiency of SPRINT training was determined by time to achieve numerical milestones, compared to previous cohorts of Welsh trainees using procedure logs from the JETS e-portfolio. SPRINT trainees evaluated each component of SPRINT training (Simulator, Lesion Recognition, endoscopic non-technical skills [ENTS]) plus an overall rating using a Likert Scale (0 = no help to 10 = extremely useful). Seven novice trainees were selected by GI and GI surgery training programme directors. The training programme was commenced in Sept 2014 and comprised structured induction and simulator training, JAG Basic UGI course and regional 'Endoscopy school' days. Data from a historical cohort of 14 trainees was used for comparison. Differences between groups were measured using a one-sided t-test ($p < 0.05$ significance level).
Results: Median time to each landmark was significantly faster at all stages in the SPRINT group – shifting learning curves to the left (Table) with a reduced range in completion times in the SPRINT cohort. Mean Likert scores were Simulation 7.8; Lesion Recognition 9.2; ENTS 8.8; Overall program 9.4. Trainee evaluation highlighted the main benefits as peer learning and support, faculty discussion, feedback and access to training opportunities.
Conclusion: A well-structured training pathway, incorporating evidence-based training methods can enhance training quality and experience for trainees and improve efficiency of training – in this case halving training time in UGI endoscopy compared to historic controls. All elements were valued by trainees. Regular contact with regional trainers acts to standardise training, improves discussion and feedback, allowing early identification and targeted support where progress is slower than expected.

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Disclosure of Interest: None declared

P0767 THE DIFFERENCES BETWEEN MAGNIFYING ENDOSCOPIC IMAGING OF EARLY GASTRIC CANCER WITH BLI AND NBI WERE CAUSED BY THE PATHOLOGICAL FINDINGS AS THE DEPTHS OF CRYPTS

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Introduction: We formerly presented about the efficacy of magnifying endoscopy with blue laser imaging (M-BLI) in the diagnosis of early gastric cancers at this meeting (UEGW 2012). BLI is a novel image-enhanced endoscopy with two different lasers. In our previous presentation, we have showed that M-BLI can detect microsurface (MS) pattern at the same level of M-NBI and additionally, 75% of lesions which were showed absent MS pattern in NBI were detected irregular MS pattern in BLI. However, we couldn't quite understand the cause of that until now.
Aims & Methods: The aim of the present study is to clarify the pathological differences among these lesions which were showed absent MS pattern in NBI and irregular MS pattern in BLI. We retrospectively analyzed 20 early gastric cancers that were examined with M-BLI and NBI at the Hospital of Kyoto Prefectural University of Medicine between September 2011 and March 2014. All gastric cancers had been treated by endoscopic submucosal dissection. The following were selected on the basis of their appearance revealed by M-BLI and NBI performed beforehand: 11 lesions showing irregular MS pattern by M-BLI but absent MS pattern by M-NBI (Group A), 4 lesions with irregular MS pattern by both methods (Group B), and 5 lesions with absent MS pattern by M-BLI and NBI (Group C). The resected specimens were observed by a stereoscopic microscope, then photographed microscopic images were compared with endoscopic images. In all cases, it had been confirmed that the histological areas examined corresponded to the parts observed by both methods very closely. We examined the characteristics of the histopathological findings of each group. Furthermore, in Group A and B, the depths of three crypts in each lesion were measured using a viewer soft according to the method by Yagi (*Diagn Ther Endosc* 2012).
Results: In Group A, 6 of 11 lesions show histological feature that crypts were shallow, 3 lesions had histological feature that number of the ducts opens in the surface layer were few and 2 lesions had winding crypts. In Group B, all 4 lesions had deep and straight crypts. In Group C, 3 of 5 lesions were replaced with signet ring cell carcinoma in all mucosal layer, one lesion had very short intervening part and one lesion had pseudostratified cancer cells. Average depth of crypts of 6 lesions (65 ± 20 μm) in group A was significantly shallower than it of 4 lesions (265 ± 64um) in Group B ($p < 0.01$). Yagi reported that the depths of crypts in areas where the white zones were indistinct or invisible and those in lesions where the white zones were distinct were 81μm and 182μm, respectively in NBI. Since MS pattern is almost synonymous with white zone, it may be also that M-BLI can visualize even shallower crypt compared with M-NBI.
Conclusion: BLI may be useful for diagnosis of an extent and a submucosal invasion of early gastric cancers by visualizing the shallower crypt compared with NBI. Further study is necessary to clarify what differences of pathological findings except depth of crypts cause the differences in MS pattern findings between with BLI and NBI.
Disclosure of Interest: None declared

P0768 THE DIAGNOSIS OF INVASION DEPTH IN SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA: A COMPARISON BETWEEN A MAGNIFYING NARROW-BAND IMAGING OBSERVATION AND EUS

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Introduction: The diagnosis of cancer invasion depth is crucial for selecting the optimal treatment strategy for esophageal cancer. Endoscopic ultrasonography (EUS) is regarded as the standard modality for diagnosing invasion esophageal cancer depth in the West. In Japan, magnifying endoscopy has been used for diagnosis by observing the architecture of the esophageal microvasculature. This modality represents a rapid and simple diagnostic procedure without the need for any additional equipment. However, the accuracy of magnifying endoscopy has not been compared with that of EUS for the diagnosis of cancer invasion depth.
Aims & Methods: Patients with esophageal squamous cell carcinoma (SCC) suspicious for muscularis mucosa or submucosal invasion in non-magnifying white light imaging were included. All patients received white-light imaging (WLI), magnifying narrow-band imaging (NBI) observation followed by EUS. Magnifying NBI observation was performed by endoscope with magnification (GIF-Q240Z, or H260Z; Olympus, Tokyo, Japan). EUS was performed using a high-resolution probe by jelly-filled method. Before examination, several syringes (5 mL) containing sufficient amounts of jelly (K-Y Lubricating jelly, Johnson and Johnson, k. k.) were prepared. After endoscope insertion (GIF-2TQ260M; Olympus) into the target area within the esophagus, a 30 or 20-MHz miniature probe was then inserted through the left channel of the endoscope and 30 to 40 mL of echo jelly was instilled through the right channel until the esophageal lumen was filled. Cancer invasion depth was diagnosed as T1a or T1b using both modalities. The diagnostic accuracy of magnifying NBI observation was compared with that of EUS while the histologic diagnosis of resected specimen served as reference standard.
Results: From January 2011 to March 2014, 204 patients with esophageal SCC suspicious for muscularis mucosa or submucosal invasion in non-magnifying WLI were examined using the two modalities. Of the 204 patients, 108 treated with chemoradiotherapy or photodynamic therapy were excluded from analysis because histologic specimens were not obtained. Ninety-six patients with 97 lesions treated either by esophagectomy (n = 25) or endoscopic resection (n = 72) were included in the final analysis. Histologic diagnosis was T1a in 48 lesions, T1b in 47 lesions, and T2 in two lesions. 4 lesions couldn't be diagnosed by magnifying NBI because intra-epithelial papillary capillary loop couldn't be observed. The overall accuracy of diagnosing invasion depth was 67.7% (63/93 lesions) by magnifying NBI and 71.1% (69/97 lesions) by EUS ($P = 0.364$). The accuracy of diagnosing invasion depth in lesions with protrusions was 63% (29/46 lesions) and 80% (40/50 lesions) by magnifying NBI and EUS, respectively ($P = 0.07$).
Conclusion: EUS and magnifying NBI exhibited high diagnostic accuracy in esophageal SCC. Considering its simplicity of use, magnifying NBI has the potential to be the standard modality for diagnosing invasion depth of esophageal SCC. However, the diagnostic accuracy for esophageal SCC is not sufficient only with magnifying NBI. Compared with magnifying NBI, EUS has the potential to diagnose invasion depth more accurately lesions with protrusion.
Disclosure of Interest: None declared

P0769 COLON PREPARATIONS WITH PEG 4000 AND LACTULOSE: A PROSPECTIVE RANDOMIZED DOUBLE BLINDED TRIAL

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Introduction: Colonoscopy represents nowadays one of the best diagnostic methods for colorectal diseases and for colorectal cancer screening. Good colon preparation is essencial for a high quality diagnostic examination and for the necessary therapeutic approaches. This study aims to compare two preparations regarding efficacy: The PEG 4000 preparation, which is the gold standard in the United States, and the 10% lactulose solution. Lactulose is an osmotic laxative still without formal indication as colon preparation.

Aims & Methods: It is a prospective randomized double blinded trial with 400 patients included, submitted to elective out-patient colonoscopies in private clinic. The patients were randomized in two 200 patients groups and in each one preparation was used. The Boston Bowel Praparation Scale was used in order to measure the colon preparation quality.

Results: In only 13 patiens the preparation was considered inadequate. In PEG patients only six (3%) and in lactulose patiens seven (3.5%) were considered inadequate. There was no statistical difference between both groups regarding efficacy ($P = 0.778$).

Conclusion: The study concluded that lactulose solution is as effective as PEG 4000 as bowel preparation for colonoscopic exams. The lactulose solution can be indicated as an option for colon preparation for colonoscopic exams. Its restrictions and contra-indications should be respected.

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Disclosure of Interest: None declared

P0770 THE EFFICACY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING THE "CLIP-FLAP METHOD" FOR LARGE SUPERFICIAL COLORECTAL TUMORS

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Introduction: Endoscopic submucosal dissection (ESD) is technically difficult because of poor visualization and instability in the cutting area. Although the mucosal flap formation improves visualization of the cutting area, it is difficult to achieve, especially in colorectal ESD. To facilitate the mucosal flap creation, we developed the "clip-flap method" by initially substituting an endoclip for the mucosal flap until the flap is completed (K. Yamamoto, et al., *Endoscopy* 2012·2015).

Aims & Methods: We retrospectively studied 200 cases, in which ESD for large superficial colorectal tumors was performed at Toyonaka Municipal Hospital between 2009 and 2013. We compared the treatment outcomes after the adoption of the clip-flap method (Clipflap-ESD: 100 cases) with those before the adoption of the clip-flap method (Conventional-ESD: 100 cases) to evaluate the efficacy and safety of the clip-flap method. The procedure of the clip-flap method is as follows. After submucosal injection, the mucosa around the lesion on the anal side was incised with an adequate margin, and then the submucosal layer was cut deeply. The edge of the exfoliated mucosa was clipped with an endoclip (EZ CLIP, HX-610-135; Olympus). The distal attachment was inserted under the endoclip as well as under the mucosal flap, and then the submucosal layer was dissected with the endoknife. A single endoclip was generally used, and the cross pattern of endoclips, created by attaching one endoclip to another endoclip, was also used according to the situations. We mainly used a short-needle electrosurgical endoknife with a water-jet function (FlushKnifeBT; Fujinon), and also used other endoknives in some cases.

Results: Median tumor diameter, resected specimen diameter, procedure time, *en bloc* resection rate, and perforation rate of Conventional-ESD and Clipflap-ESD were 27mm vs 30mm, 34mm vs 37mm, 97minutes vs 70minutes, 91% vs 97%, and 4% vs 1%, respectively. The procedure time of Clipflap-ESD was statistically significantly shorter than that of Conventional-ESD ($P < 0.01$), and the differences in other parameters were not significant. Perforation was conservatively treated by clipping in 5 of 5 cases. In all cases which the clip-flap method was used, the exfoliated mucosa was lifted by the endoclip attached to the exfoliated mucosa after the distal attachment was inserted under the endoclip, allowing for clear visualization and efficient dissection of the submucosal layer, and effective creation of the mucosal flap.

Conclusion: The clip-flap method very effectively enabled the mucosal flap creation and allowed our treatment outcomes to be greatly improved. The present study demonstrates that the clip-flap method is a simple, safe, and very effective option for colorectal ESD.

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Disclosure of Interest: None declared

P0772 PREVALENCE AND ASSOCIATED FACTORS OF INTERVAL COLORECTAL CANCERS AT TAIWAN

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Introduction: Interval colorectal cancer is an emerging issue in cancer screen and surveillance. The frequency and associated factors have not been well studied in Taiwan.

Aims & Methods: We plan to clarify the prevalence and associated factors with interval colorectal cancer. The Colorectal cancer with negative colonoscopy 6 months to 36 months before cancer diagnosis was defined as interval colorectal cancer. Patients' characteristics, past history, colon preparation, colonoscopy finding and pathology were retrospective evaluated. 670 patients with colorectal adenocarcinoma from Jan. 2005 to Nov. 2014 and who underwent colonoscopy before the diagnosis were recruited.

Results: Colorectal cancer with negative colonoscopy 6 months to 36 months before cancer diagnosis was defined as interval colorectal cancer. Patients' characteristics, past history, colon preparation, colonoscopy finding and pathology were retrospective evaluated. 670 patients with colorectal adenocarcinoma from Jan. 2005 to Nov. 2014 and who underwent colonoscopy before the diagnosis were recruited.

Results: 22 (3.28%) patients (65.7 ± 9.2 years old; 9 male) were diagnosed as interval colon cancer. The interval colorectal cancer were predominant located at rectum and cecum (rectum 50%, cecum 18.2%, transverse colon 13.6%, sigmoid colon 13.6%, descending colon 4.5%), presented with earlier tumor stage (stage I and stage II 86.4%, stage III and stage IV 13.6%). The associated factors of interval cancer include end-stage renal disease (HR:10.494, 95% CI: 2.131-51.681), and shorter withdraw time from cecum to hepatic flexure (interval cancer: non-interval cancer 2.00 ± 0.82:4.91 ± 3.74 min) (HR: 0.561, 95% CI:0.345-0.913). Prior polypectomy and tumor size showed a tendency to develop interval colorectal cancer.

Conclusion: The prevalence of interval colorectal cancer in present study is 3.28%. Comorbidity with end-stage renal disease and shorter withdraw time from cecum to hepatic flexure could be associated factors of interval colorectal cancer.

Disclosure of Interest: None declared

P0773 THE PROSPECTIVE STUDY OF THE RELATIONSHIP BETWEEN COLONOSCOPY AND INTESTINAL ADHESION

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Introduction: When we feel scope decreased mobility at the colonoscopy, we often think that intestinal adhesion may be the reason for difficulty. But it is doubtful whether intestinal adhesion cause difficulties for endoscopy actually. We therefore sought to verify whether the scope decreased mobility is the findings as a result of intestinal adhesion prospectively.
Aims & Methods: 53 patients were performed colonoscopy and underwent laparoscopic surgery for colorectal cancer at Showa University Northern Yokohama Hospital from April 2012 to August 2012. All colonoscopist recorded the findings about colonoscopy such as time for total colonoscopy and degree of difficulty for colonoscopy (insertion grade1,2,3). And surgeon checked the location of intestinal adhesion at the laparoscopic surgery.
Results: 34 male and 19 female were included in this study. 18 cases have the abdominal surgical history and in all cases, intestinal adhesion was observed. On the other hand, intestinal adhesion was also observed in 28 cases have no surgical history. Five of 28 cases have the history of endoscopic treatment and adhesion was observed around the lesion of endoscopic treatment had been performed. There was no significant difference in the average time for reaching at cecum from anal between intestinal adhesion cases and no intestinal adhesion cases.
There were 27 cases that were evaluated as grade 2 or 3 in degree of difficulty for colonoscopy, and intestinal adhesion were observed in fifteen cases of them. We thought that insertion grade2 or 3 may be the bellwether of intestinal adhesion but result showed that insertion grade would not reflect the intestinal adhesion (sensitivity 56.4%, specificity 61.5%, PPV 81.4%, PPV 81.4%, NPV 32.0%).
Conclusion: Difficulties of colonoscopy do not always reflect the intestinal adhesion. But in case of additional intestinal resection for the lesion endoscopic treatment has been performed for colorectal cancer, we should be consider the possibility of intestinal adhesion around the target lesion.
Disclosure of Interest: None declared

P0774 SUBMUCOSAL FIBROSIS AFFECTS THE OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR COLORECTAL TUMORS ACCOMPANIED BY FIBROSIS

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Introduction: Endoscopic submucosal dissection (ESD) has recently become a standard treatment for colorectal epithelial neoplasms. Despite the success of ESD, incomplete resection has resulted when it has been applied to laterally spreading tumor (LST) of the colon with submucosal fibrosis which could complicate the separation of the submucosa from the muscular layer. Therefore, ESD for LSTs with submucosal fibrosis might cause high frequencies of incomplete en bloc resection of the tumor and intestinal perforation during ESD. In this study, we aimed to assess the relationship between the outcome of ESD for LSTs and the degree of submucosal fibrosis beneath the tumors. We also evaluated the relationship between the degree of submucosal fibrosis beneath the tumors and the features of LSTs.
Aims & Methods: We evaluated 114 colorectal LSTs larger than 20 mm in diameter between January 2010 and March 2015. LSTs were divided into granular (LST-G) (n = 78) and non-granular (LST-NG) (n = 36) tumors. LST-Gs were subdivided into homogenous-type tumors (LST-G-homo) (n = 34) and nodular-mixed-type tumors (LST-G-mix) (n = 44).The degree of submucosal fibrosis beneath the LSTs was determined on the basis of the following original classification system, which was based on the findings obtained at the time of injection of sodium hyaluronate with indigo carmine: F0, no fibrosis, which manifested as a blue transparent layer; F1, mild fibrosis, which appears as a white web-like structure in the blue submucosal layers; and F2, severe fibrosis, which appears as a white muscular like structure without a blue transparent layer in the submucosal layers. The relationship among characteristics of the LSTs, the degree of submucosal fibrosis beneath the LSTs and outcome of ESD for the LSTs were analyzed.
Results: The incidence of F2 fibrosis in LST-G-mix and LSTs-NG was significantly higher than that in LST-G-homo ($p < 0.05$, compared with F0/1). The tumor locations and sizes did not significantly differ between F2 and F0/F1 fibrosis beneath LSTs regardless of tumor growth patterns. There were no significant differences in the rate of complete en bloc resection and complications such as perforation or delayed bleeding between F2 and F0/1. However, severe bleeding during ESD strongly tended to be related to F2 fibrosis ($p = 0.06$, F2 vs. F0/F1), and the mean duration of the ESD procedure significantly differed between LSTs with severe fibrosis (F2) and LSTs with no or mild fibrosis (F0/ F1) regardless of tumor growth patterns (F2, 269.3 ± 114.4 vs. F0/1, 137.5 ± 80.2 min, $p < 0.0001$).
Conclusion: The LST-G-mix and LSTs-NG might harbor severe submucosal fibrosis which would predict outcome of ESD for colorectal LSTs. The more advanced the endoscopic submucosal fibrosis, the longer the time required for ESD and the higher the frequency of immediate bleeding during ESD. Further development of endoscopic devices are needed for safe and complete resection of colorectal tumors with severe fibrosis.
Disclosure of Interest: None declared

P0775 NOVEL BIO-MARKER FOR COLORECTAL NEOPLASIA: WHITE OPAQUE SUBSTANCE WITHIN COLORECTAL NEOPLASTIC EPITHELIUM AS VISUALIZED BY MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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Introduction: We previously reported the presence of a white opaque substance (WOS), opaque to the endoscope light, inside the epithelium when we use magnifying endoscopy (ME) to examine gastric epithelial neoplasia (adenomas and carcinomas) and chronic gastritis (intestinal metaplasia). Through further pathohistological study we elucidated that this substance is comprised of minute lipid droplets (LDs) accumulated within the mucosal epithelium of gastric epithelial neoplasia or intestinal metaplasia[1]. These minute LDs strongly backscatter the projected light, and are visualized as a white substance. When we examined colorectal neoplastic lesions (adenomas and carcinomas) using ME, we observed WOS as in the stomach. However, it is unclear whether WOS in colorectal epithelial tumors is in fact an accumulation of LDs as in the stomach.
Aims & Methods: Aims: To elucidate whether WOS observed in colorectal epithelial tumors (adenomas and carcinomas) is composed of LDs. We analyzed a continuous series of both 40 WOS-positive and 40 WOS-negative colorectal epithelial tumors. We examined colorectal neoplastic lesions (adenomas and carcinomas), prior to planned treatment, using ME with narrow-band imaging (NBI), determining whether WOS was present in the surface layers of the most anal part of the colorectal epithelial tumor. We took targeted biopsies from this part of the tumor. Biopsy specimens were immediately frozen, slices taken, and the slides were stained for lipids using oil-red O. Slides were examined using light microscopy immediately after staining for the presence of LDs within the neoplastic epithelium. Subsequently, we stained microdroplets of LDs using imunostaining by anti-adiphophilin antibody in formalin-fixed specimen. We investigated the correlation between the presence of WOS as visualized by ME with NBI and the presence of LDs in the histological specimens. And, we compared WOS-positive and WOS-negative about the density of adiphopilin.
Results: We analyzed a continuous series of both 40 WOS-positive and 40 WOS-negative colorectal epithelial tumors. Prevalence of LD as stained by oil red O staining in WOS-positive versus WOS-negative lesions was 47.5% (19/40) and 5% (2/40), respectively ($P < 0.001$, Fisher's exact test). Furthermore, WOS coincided with the expression of adipophilin. Namely, prevalence of LD as stained by anti-adiphophilin antiboy in WOS-positive versus WOS-negative lesions was 100% (40/40) and 62.5% (25/40), respectively ($P < 0.001$, Fisher's exact test). Mean density of adiphopilin was significantly greater in WOS-positive (10.8 ± 8.7 %) than in WOS-negative lesions (4.1 ± 4.1 %; $P < 0.001$).
Conclusion: LDs do not accumulate in the normal colorectal epithelium. However, this study elucidated for the first time that endoscopically visualized WOS may be composed of LDs accumulated in colorectal epithelium. This phenomenon has the potential to be a new biomarker for the pathology and diagnosis of colorectal neoplasia.

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Disclosure of Interest: None declared

P0776 TRANSLATION AND CULTURAL ADAPTATION OF THE NATIONAL SURVEY OF MEDICAL DECISIONS QUESTIONNAIRE FOR COLORECTAL CANCER SCREENING FOR USE IN THE SCREENING OF SWEDISH COLON STUDY (SCREESCO)

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Introduction: Colorectal cancer (CRC) is one of the most common cancers in Sweden and CRC screening is a preventive action. At present, Sweden is running a national randomized study Screening of Swedish Colons (SCREESCO) to understand the decision to participate in CRC screening.
Aims & Methods: The questionnaire National Survey of Medical Decisions (DECISIONS) was developed for a US population and the aim was to translate and culturally adapt the DECISIONS questionnaire to the Swedish context. A qualitative design inspired by guidelines based on methods for cross-cultural

adaptation of questionnaires in the field of psychology and sociology were used. The guideline includes focus group discussions, individual and telephone interviews and Thinking Aloud (TA) sessions to culturally adapt questionnaires.
Results: The questionnaire: National Survey of Medical Decisions (DECISIONS) was translated and culturally adapted. The translation and adaptation process resulted in reformulation and rewording of 29 items, 11 items changed due to wording and two new items were added as a result of the qualitative interviews and group discussions. The present version of the DECISION questionnaire consists of 24 items concerning decision making.
Conclusion: Our study demonstrates the importance of implementing cultural adaptation to ensure the quality of a translated questionnaire and thereby its results. The major cause for removal and changing of items can be explained by different traditions in communicating with the health care system in Sweden and the US, communication about decision-making and how risk for cancer is communicated in general. The results have hopefully produced a questionnaire that can be used to evaluate decision-making in participation in CRC screening in a Swedish population.

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P0777 SHOULD WE CHANGE THE INTERVAL OF SURVEILLANCE COLONOSCOPY AFTER REMOVAL OF ADENOMATOUS POLYPS IN PATIENTS WITH FAMILY HISTORY OF COLORECTAL CANCER? - RESULTS FROM THE JAPAN POLYP STUDY

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Introduction: The recommended interval of surveillance colonoscopy for patients with adenomatous polyps is based on adenoma histology, size, and number; however, prospective studies on the impact of family history (FH) of colorectal cancer (CRC) are limited.
Aims & Methods: The aim of this study was to assess whether the interval of surveillance colonoscopy after removal of adenomatous polyps for patients with FH of CRC should be changed compared with patients without FH. The Japan Polyp Study (JPS) is a multicenter randomized control trial conducted at 11 participating centers to evaluate follow-up interval after polypectomy. Patients were eligible if they have had two complete colonoscopies (1st- and 2nd-CS: interval; 1 year) as baseline examination with removal of all neoplastic lesions. Following this they were randomly assigned to have follow-up colonoscopy at 1 and 3 yrs or at 3 yrs only. Main outcome measurements in this subanalysis were prevalence of advanced neoplasia (AN: $\geq$1 cm, villous histology, high-grade dysplasia, or invasive cancer), high-risk adenoma (HRA: AN or $\geq$3 non-advanced neoplasia) and low-risk adenoma (LRA: 1 or 2 non-advanced neoplasia) detected during 3 yrs after randomization in patients with first degree relatives with CRC.
Results: Among 3,926 patients with no history of FAP, HNPCC, IBD or colectomy, 1,847 patients (Aged 40-49 yrs: 252, 50-59 yrs: 677, 60-69 yrs: 918, mean age 56.0 yrs, 61.4% male) who underwent two-round complete colonoscopy before randomization and follow-up colonoscopy as scheduled were included. Among patients aged 40-49 yrs who had FH of CRC in first degree relatives or not, the prevalence of AN, HRA and LRA were as follows; AN (0%, 0/43: FH+ vs. 1.0%, 2/209: FH-) ($P=0.76$), HRA (4.7%, 2/43: FH+ vs. 2.9%, 6/209: FH-) ($P=0.90$), LRA (25.6%, 11/43: FH+ vs. 21.5%, 45/209: FH-) ($P=0.56$). Among patients aged 50-69 yrs, prevalence of them were; AN (4.1%, 9/220: FH+ vs. 1.5%, 20/1,375: FH-) ($P<0.001$), HRA (14.5%, 32/220: FH+ vs. 7.9%, 109/1,375: FH-) ($P<0.001$), LRA (25.9%, 57/220: FH+ vs. 32.3%, 444/1,375: FH-) ($P=0.06$).
Conclusion: Prevalence of AN and HRA of patients aged 40-49 yrs and 50-69 yrs without FH of CRC was significantly lower than that of 50-69 yrs patients with FH of CRC during 3 yrs follow-up period. Intensive surveillance colonoscopy namely 3-yrs interval after polypectomy should be recommended only for patients aged 50 yrs or older with FH of CRC; in contrast, there was no novel evidence of changing surveillance interval in patients younger than 50 yrs. Whether these results may affect the current surveillance programs remains uncertain and longer follow-up data might be necessary.

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P0778 FACTORS AFFECTING THE POST COAGULATION SYNDROME AFTER SUBMUCOSAL DISSECTION FOR COLORECTAL TUMORS

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Introduction: Postplolypectomy coagulation syndrome (PPCS) has symptoms such as localized abdominal pain, fever, leukocytosis, and peritoneal inflammation without perforation, which occur less than 0.1%. However, post coagulation syndrome (PCS) after colorectal endoscopic submucosal dissection (ESD) is not known well. Here, we aimed to assess the clinical outcomes and factors associated with PCS after colorectal ESD.
Aims & Methods: Between January 2010 and July 2014, we performed ESD on 211 consecutive colorectal tumors in 207 patients. We investigated the incidence of PCS after colorectal ESD and conducted multiple logistic regression analysis of the following factors related to PCS after colorectal ESD: age, gender, location, tumor size (<40 mm vs. ≥ 40 mm), operation time (<120 min vs. ≥ 120 min), morphology (granular type laterally spreading tumor [LST-G], non-granular type laterally spreading tumor [LST-NG], or protruded type), fibrosis, and paradoxical movement during the procedure. PCS after colorectal ESD was defined as fever ($\geq 37.8^{\circ}$C) and abdominal pain or regional rebound tenderness in the absence of perforation during or after ESD.
Results: After exclusion of 4 of 211 cases with perforation, 207 patients were analyzed. In the treated epithelial lesions, 36 cases were located in the rectum (17.4%), 41 cases in sigmoid colon (19.8%), 44 cases in transverse colon (21.3%) and 51 cases in ascending colon (24.6%). PCS after ESD occurred in fifteen cases (7.2%). Of the fifteen cases of PCS, six cases (2.9%) occurred in cecum, four

cases (1.9%) in ascending, three cases (1.4%) in transverse and two cases (0.97%) in rectum.
Average tumor size was 30.9 ± 10.5 mm, and the average procedure length was 66.8 ± 45.1 min. The rate of en bloc resection was 96.6%, while that of en bloc curative resection was 87.4%.
Univariate analysis showed that tumor site in the cecum ($p = 0.0014$), tumor size (≥ 40 mm, $p < 0.001$), loner procedure time (≥ 120 min, $p < 0.001$) during the procedure and severe fibrosis ($p = 0.0161$) were significantly associated with PCS of colorectal ESD.
Multivariate logistic regression analysis revealed that tumor location in the cecum (odds ratio [OR] 17.58; 95% confidence interval [CI] 2.32–210.9, $p = 0.0043$), a tumor size exceeding 40 mm (OR 6.43 [95% CI 1.37-34.02], $p = 0.019$) contributed to PCS after colorectal ESD. A trend for PCS after the ESD procedure in the group which experienced longer procedure time during the procedure was also noted ($p = 0.0619$).
Conclusion: Tumors located in cecum, larger tumor size more than 40mm were independent factors contributing to the PCS of colorectal ESD.
Disclosure of Interest: None declared

P0779 DOES COLORECTAL ADENOMA INCREASE THE RISK OF GALL BLADDER POLYP?

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Introduction: Colorectal adenoma and gallbladder (GB) polyp share many risk factors. However studies concerning the association between colorectal adenoma and GB polyp has been rare.
Aims & Methods: The aims of this study were to evaluate whether colorectal adenoma increases the risk of GB polyp and analyze the risk factors associated with GB polyp. Health examinees who underwent both hepatobiliary sonography and colonoscopy in Yeungnam University Hospital health promotion center from January 2010 to December 2013 were included. Subjects with previous history of cholecystectomy and without pathologic report of colorectal polyp were excluded. To eliminating the confounding factors of GB polyp, age, gender and BMI was matched using propensity score. The clinical characteristics, colonoscopy and ultrasonographic findings of the subjects were reviewed and compared between colorectal adenoma and non-adenma group retrospectively.
Results: Among 4373 subjects, colorectal adenoma was detected in 1453 (33.2%) and colorectal cancer in 11 (0.3%). There were significant differences in age, gender and presence of fatty liver between subjects with or without colorectal adenoma. GB polyp was noted in 362 (8.3%) cases. After using propensity score matching, number of subjects in each groups with or without colorectal adenoma was 1453. Subjects with colorectal adenoma only or with concomitant colorectal cancer had tendency of more GB polyps than those without (145 (10.0%) vs 116 (8.0%), (p = 0.060)). Although mean age of the subjects was not significantly different depending on the presence of GB polyp, male was more common in subjects with GB polyp (218 (83.5%) vs 1976 (74.7%), p = 0.002). There was no significant difference in presence of GB stone and fatty liver and level of BMI and total cholesterol between two groups. Five (0.1%) subjects underwent operation of GB polyp and diagnosed as cholesterol polyp and/or adenoma. By multivariate analysis, the risk of GB polyp was higher in subjects with colorectal adenoma, however, it failed to show clinical significance (OR 1.28, 95% CI 0.99-1.65, p = 0.06) and the only significant risk factor of GB polyp was male gender (OR 1.72, 95% CI 1.22-2.40, $p = 0.002$).
Conclusion: Presence of colorectal adenoma was associated with higher tendency for GB polyp although it could not show statistical significance. Meticulous examination with ultrasonography of GB should be considered especially in male subjects with colorectal adenoma not to miss the GB polyps. Further studies concerning the common pathogenesis associated with both colorectal adenoma and GB polyp are warranted.
Disclosure of Interest: None declared

P0780 DIAGNOSTIC VALUE OF FUJINON INTELLIGENT COLOR ENHANCEMENT (FICE) TECHNOLOGY WITH AND WITHOUT MAGNIFICANTION TO DIFFERENTIATE BETWEEN HYPERPLASTIC AND ADENOMATOUS LESIONS ACCORDING TO THE NICE CLASSIFICATION - A PROSPECTIVE, RANDOMIZED, CONTROLLED STUDY

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Introduction: According to the resect-and-discard strategy the histological type of the colonic polyps (adenomatous vs. non-neoplastic or hyperplastic) is predicted in vivo by an appropriate endoscopic method, and based on this decision certain postpolypectomy pathologic specimens can be discarded rather than sent for histological assessment. The purpose of this prospective, non-interventional study was to validate the Narrow Band Imaging International Colorectal Endoscopic (NICE) classification for differentiating hyperplastic and adenomatous polyps by using Fuji Intelligent Color Enhancement (FICE) technology with high-definition with and without optical magnification.
Aims & Methods: 117 patients referred for outpatient colonoscopy were prospectively enrolled. All endoscopies were performed by experienced endoscopists. 61 patients were randomized to investigate with the Fujinon EC-600WM and 56 patients to investigate with the EC-600ZW/L series. In order to create a video-library of endoscopic cases, patients with at least one histologically verified polyp were included. A short HD video-clip (around 15-20 seconds) of each polyp and a HD DICOM still picture both at white-light and at FICE-virtual chromoendoscopy were recorded and stored in an anonymized video database. Histopathology of the lesions were confirmed by the blinded pathological evaluation of endoscopic resection, polypectomy or biopsy specimens. Finally NICE classification with FICE and histopathological results were compared.
Results: In the 117 patients we detected 247 polyps, all of them were endoscopically removed and sent to histological assessment. The average size of the polyps were 4,1 mm. According to the histopathological results, six early adenocarcinomas, 148 adenomas and 93 hyperplastic polyps were detected. There was a complete agreement between the NICE classification with FICE technology and histological results in 217 polyps (87,9%). 17 polyps classified as NICE type II despite non-neoplastic histology (6,9% false positive), whereas 14 polyps were classified as NICE type I despite adenomatous histology (5,7% false negative). No significant differences in the accuracy of NICE classification between standard and zoom HD colonoscopy compared to histology were detected.
Conclusion: FICE virtual chromoendoscopy in combination with HD colonoscopy with or without magnification is a promising tool for the differentiation of neoplastic from non-neoplastic colorectal polyps. High confidence predictions for adenomas such as NICE classification may provide precise diagnostic tool for real-time endoscopic diagnosis of neoplastic polyps.
Disclosure of Interest: None declared

P0781 LONG-TERM FOLLOW-UP AFTER ENDOMUCOSAL RESECTION FOR COLORECTAL POLYPS: A RETROSPECTIVE AUDIT OF EXPERIENCE AT A LARGE DISTRICT GENERAL HOSPITAL

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Introduction: Endomucosal resection (EMR) of colorectal polyps at lower GI endoscopy is becoming increasingly important, offering an effective means of removing large, obstinate polyps without resorting to surgery[1]. There is ample evidence on short-term recurrence post EMR but longer term data is missing[1,2]. We analysed our experience to fill this gap and provide follow-up data at 3 and 5 years post EMR.
Aims & Methods: Retrospective analysis was performed on endoscopy reports for all EMRs performed at lower GI endoscopies during a one year period in 2010 at a non-tertiary GI endoscopy unit. Reports were accessed from the hospital endoscopy reporting system (HICSS) and analysed for details of the EMR performed and follow up endoscopies for recurrence at the site of initial EMR. The location, size and morphology of polyp was recorded along with EMR details including completeness and need for APC. Polyp recurrence at subsequent endoscopies up to 5 years was also recorded.
Results: 188 lower GI endoscopies with EMR were performed. After exclusion for malignancy requiring surgery, incomplete follow up, polyp size < 1cm, 111 were analysed. Duration of follow up ranged from 3 to 60 months with a mean follow up of 32 months (median 35 months). Of the 111 polyps, 59% were 1-2cm, 36% 2-5cm, 5% > 5cm. Location was in the left colon in 59% of polyps and right-sided in 41%. The majority of polyps regardless of size were sessile (75%) with the remainder being flat (19%) or sub-pedunculated (6%).

Follow up endoscopy	6 months	1 year	3 years	5 years
No. performed	53	68	49	24
Recurrence (%)	7/53 (13)	5/68 (7)	5/51 (10)	0/25 (0)

Conclusion: This study confirms EMR is an effective alternative to surgery in the management of difficult colonic polyps. Our short-term recurrence rates are lower than those previously documented[2] and these low rates are maintained at long-term follow-up with a mean follow up duration of 32 months. Our results favour the confident use of EMR in the eradication of large and/or complex colonic polyps to achieve low long-term recurrence rates.

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Disclosure of Interest: None declared

Abstract number: P0782

Centre	Uptake (%)		Procedures (n)	Endoscopists (n)	Entonox (n(%))	ADR (%)	Cancer (n)	Colonoscopy Required (n(%))	Complications (n)
Male	Female								
1	51.6	48.4	2381	11	254 (10.7)	9.4	0	67 (2.8)	1
2	40.9	35.1	901	8	149 (16.5)	11.1	0	53 (5.9)	4
3	43.2	41.7	2062	15	110 (5.3)	10.2	0	126 (6.1)	2
4	52.3	50.2	712	5	22 (3.1)	9.0	0	26 (3.7)	0
5	49.3	45.9	1437	11	56 (3.9)	7.6	0	56 (3.9)	0
6	39.7	35.7	1326	11	57 (4.3)	7.6	1	46 (3.5)	1
Total	**45.6**	**42.4**	**8819**	**61**	**648 (7.3)**	**9.2**	**1**	**374 (4.2)**	**8 (0.1%)**

P0782 BOWELSCOPE SCREENING- RESULTS FROM THE PILOT SITES

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Introduction: A large UK study of single flexible sigmoidoscopy with adenoma clearance in patients aged 55-64, demonstrated a reduction in CRC incidence by 23% and mortality by 31% in intention-to-treat analyses.[1] This provided the rationale for provision of a new arm of the Bowel Cancer Screening Programme (BCSP), offering a single flexible sigmoidoscopy (FS) to all 55 year olds in England, known as BowelScope screening. BowelScope was introduced to 6 pilot sites, beginning in May 2013. It is to be rolled out across the country by 2016.

Aims & Methods: We aim to describe the findings, in terms of procedural data, from the first year of BowelScope screening at the pilot sites.

Data were obtained from the Bowel Cancer Screening System database for all participants who underwent FS between May 2013-May 2014. Procedural data were recorded, including entonox use, adenoma detection rate (ADR), cancer detection, complications and colonoscopy conversion rates.

Results: Overall uptake was 44.1%. 1 cancer was detected. Mean ADR was 9.2%. The mean number of patients requiring colonoscopy conversion was 4.2%. Mean complication rate was 0.1%, including bleeding, discomfort, difficult polyp excision and unwell patient. There was wide variation in entonox use. (Table 1)

Conclusion: Uptake has improved since the six month data were presented but remains lower than for the FOB arm of the BCSP, and varies between sites. The ADR is 9.2% (range 7.6% - 11.1%). This is lower than reported in the UK FS screening trial (12.1%[1]), however ADR calculations in BowelScope do not include adenomas not removed at FS but removed later at colonoscopy, whereas the FS trial did. The ADR is comparable to the BowelScope pathfinder project (9.6%[2]).

Further work is necessary to explore the variation in uptake rates. Variation in ADR exists between centres. Further analysis of endoscopist factors and patient groups may explain this. Entonox use varies widely but does not appear to correlate with ADR- further work may be required to investigate this.

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Disclosure of Interest: None declared

P0783 HIGH PREVALENCE OF SYNCHRONOUS AND METACHRONOUS COLONIC NEOPLASIA AND OTHER MALIGNANT NEOPLASM AMONG PATIENTS WITH TRADITIONAL SERRATED ADENOMAS

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Introduction: The traditional serrated adenoma (TSA) is the least frequent colorectal serrated polyp.

The prevalence of high-grade dysplasia (HGD) and adenocarcinoma in these polyps as well as association with colorectal neoplasia and malignant neoplasia has not been established.

Aims & Methods

Aim: To determine the prevalence of HGD and adenocarcinoma and to establish the association with synchronous (SNL) and metachronous neoplastic lesions (MNL) and other malignant neoplasm among patients with traditional serrated adenomas (TSA).

Methods: Reports from patients undergoing colonoscopy and polypectomy from January 2003 to September 2014, were retrospectively obtained from the electronic database of a teaching hospital. Personal and family history of colorectal cancer (CRC) and malignant neoplasm were consigned from medical records. TSA diagnosis was based on the presence of luminal serration, cytoplasmic eosinophilia and the presence of ectopic crypt foci. SNL were defined by adenomas, sessile serrated adenomas (SSA), cancer or advanced neoplastic lesions (ANL) (>1cm, HGD or >75% of villous component) in the same colonoscopy. Those lesions appearing after 12 months of index colonoscopy during surveillance were considered MNL. A multivariate analysis was performed, looking for independent predictors of HGD, cancer, SNL and MNL in patients with TSA.

Results: During the analyzed period a total of 101 STA were diagnosed in 89 patients. The prevalence of STA was 0.45% (101/ 22000 colonoscopies). The mean age was 62 years old (range: 32-90) and 55% of patients were men. A personal and family history of CRC was present in 4/89(4.5%) and 12/89 (13%) respectively. Personal history of malignant neoplasm was present in 8/89 (9%) patients (4/8 lung cancer and 4/8 skin cancer).

Familial adenomatous polyposis had been diagnosed in 1/89(2%) patients and 7/89 (9%) met the WHO diagnostic criteria for serrated polyposis syndrome. Regarding TSA characteristics, average polyp size was 9.61 mm (range 5-45) and the most frequent location was left-colon 89/101(88%). Polyps more frequent morphology were sessile 63/101(62 %) and pedunculated 33/101(33%). HGD was present in 6/101(6%). Regarding SNL 39% presented adenomas, 35% SSA, 19% ANL, and 4.5% adenocarcinoma on index colonoscopy. During surveillance colonoscopy 25% presented SSA, 31% adenomas, 44% ANL and 0% adenocarcinoma. Multivariate analysis revealed that polyp size >20mm was the only independent predictor of HGD (OR 25.14 CI 3.10-249, p 0.0001). We didńt find independent predictors for synchronous or metachronous neoplastic lesions.

Conclusion: We found low prevalence of TSA similar to reported. The frequent association of these lesions with synchronous and metachronous colonic neoplasia, intestinal polyposis syndromes and other malignant neoplasm, highlights the importance of detecting these lesions during routine colonoscopy.

Disclosure of Interest: None declared

P0784 A SECOND LOOK COLONOSCOPY INCREASES THE DIAGNOSTIC YIELD FOR SERRATED POLYPOSIS SYNDROME IN SCREENING POPULATION

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Introduction: Serrated polyposis syndrome (SPS) is often under-diagnosed in a single colonoscopy. The low sensitivity of diagnostic criteria for SPS could impair the follow-up approach in high-risk patients who have not yet met them. Current surveillance recommendations concerning serrated polyps (SP) are insufficient.

Aims & Methods: We aimed to assess the yield of a second look colonoscopy (SLC) to diagnose SPS after a screening colonoscopy and to determine the optimal SP-threshold to indicate it.

From January 2010 to July 2013, individuals with ≥1 SP ≥5 mm proximal to splenic-flexure or ≥10 mm along the colon after a screening colonoscopy were retrospectively evaluated. Despite the standard surveillance recommendations based on adenomas, an early SLC was empirically scheduled to patients with concomitant SP to rule out SPS. SLC was performed with a special aim at detecting SP.

Results: 196/3444 patients fulfilled selection criteria. At screening colonoscopy, 11 were already diagnosed of SPS. Amongst the 185 remaining patients, 71 underwent SLC in 11.9 ± 1.7 months. According to SLC findings, individuals were grouped into: 1) SPS: 20 (28%) representing a 182% increase compared to baseline-colonoscopy diagnosis, 2) SPS-like (those with a high burden of SP and almost fulfilling SPS criteria): 15 (21%) and 3) Sporadic-SP: 36 (51%). SPS and SPS-like were considered High-Risk group. Independent colonoscopy baseline and individual predictive characteristics of High-Risk were: presence of ≥5 proximal-SP (OR 4.04 [1.2-13.5], p = 0.023), ≥2 sessile serrated polyps ≥10mm (OR 12.42 [1.39-110.72], p = 0.024) and high-definition endoscopy and/or conventional/virtual chromoendoscopy use at SLC (OR 7.43 [2.01-27.49], p = 0.003).

Conclusion: A SLC within one-year doubles the number of patients diagnosed with SPS after a screening colonoscopy. The presence of ≥5 proximal-SP or ≥2 sessile serrated polyps ≥10mm at baseline-colonoscopy is an optimal threshold to indicate a SLC. SLC has to be performed preferably using advanced endoscopic techniques. These findings provide rationale to adjust surveillance recommendations in individuals with concomitant SP.
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P0785 THE NBI TECHNOLOGY COULD INCREASE THE OPTICAL DIAGNOSIS OF THE GASTROINTESTINAL GRAFT-VERSUS-HOST DISEASE

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Introduction: Athough graft versus host disease (GVHD) is a complication relatively common after allogenic hematopoietic stem cell transplantation (HSCT), it infrequently evolves in severe gastrointestinal (GI) complications. The diagnosis of GI-GVHD is often elusive, due to variability of the clinical presentation and it is based upon histologic findings. The endoscopic intestinal lesions are macroscopically pleomorphic (i.e. mucosal erytema, aphthous ulcerations) and can be patchy or absent in early phases of the disease. The Narrow Band Imaging (NBI) is a simple "push-on-a button" technique that enhances mucosal and vascular details without the use of dyes, and has proven to be superior to only High-Resolution Endoscopy (HRE).
Aims & Methods: The aims of this pragmatic trial were to explore the role of NBI system in the diagnosis of GI-GVHD. Seventeen of 51 patients (33%) which received allogenic HSCT at Bone Marrow Transplant Unit of Pesaro, presented unexplained diarrhoea at risk for acute GI-GVHD. The median time from transplantation was 40 days and the diagnosis work-up for infection causes resulted negative. These patients underwent to colonoscopy using the Evis Exera II system (Olympus Medical Systems, Tokyo, Japan) and a High-Resolution endoscope (CF-H180AI/L), integrating NBI system by only pushing a button. The multiple biopsies of the ileum, right, transverse, left and rectosigmoid colon were performed by the same operator during each procedure. The histological diagnosis was carried by a skilled pathologist
Results: The histological diagnosis of intestinal GVHD was confirmed in 7/17 patients (41%). HRE have shown macroscopic findings in 2 patients, characterized by extensive mucosal hyperemia, nodularity, hemorragic spots, patchy erosions and multiple shallow ulcers. The NBI system identified minute changes of the mucosal surface as pattern thinning and microvascular network irregularities in 5 patients (M/F 3:2, mean age 39), in whom HRE was normal (Table 1).

Table 1: The relationship between histological evaluation and endoscopic findings of HRE and NBI technologies for GI-GVHD diagnosis.

Histological Diagnosis N. Patients		Endoscopic Findings HRE	NBI
GVHD	7	2	7
Normal	10	15	10

Conclusion: The NBI system could help to identify minute abnormalities suspicious for GI-GVHD, such as alteration of vascular pattern and mucosal micronodularity, not detected by HRE. This tool could increase the yield of endoscopic diagnosis of GI-GVHD by targeted biopsy compared to random biopsies at HRE. Further evaluation may be need to establish the correlation between endoscopic and histological findings.
Disclosure of Interest: None declared

P0786 BLUE LASER IMAGING: A NOVEL ENDOSCOPIC TOOL FOR PRECISE EVALUATION OF VASCULAR PATTERN OF COLORECTAL LESIONS

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Introduction: A new system using a laser light source, Blue Laser Imaging (BLI-Lasereo by Fujifilm), has been developed allowing an *in vivo* endoscopic observation of the surface and microvascular pattern of lesions. Colonoscopy with BLI-Lasereo and magnifying zoom enable the characterization of the fine superficial capillary pattern of normal mucosa and of colorectal lesions. The endoscopic distinction between the different capillary pattern can contribute to the differential diagnosis among normal, hyperplastic, serrated and other neoplastic lesions.
Aims & Methods: Applying this latest technology, the objective of this study is to evaluate the accuracy of the capillary-vessel pattern classification of colorectal lesions diagnosed during routine colonoscopy using BLI and magnifying zoom imaging.
A total of 91 colorectal lesions in 42 patients (23 men) were prospectively examined using Kudo's pit pattern classification and capillary-vessel pattern according to our previous published classification [1]. All lesions were endoscopically or surgically resected In summary, the capillary pattern was divided into 5 subtypes according to the number, morphology and architecture of the fine blood vessels. The presumptive endoscopic diagnosis of the lesions were correlated with the histopathologic findings, determining the sensitivity, specificity and accuracy of this method.
Results: The overall accuracy of the fine blood vessel classification by BLI and magnification in differentiating neoplastic and non-neoplastic colorectal lesions was 95.6% (87/91 lesions). The sensitivity, specificity, positive predict value and negative predict value of the capillary pattern classification for distinguishing neoplasia from non-neoplasia were, respectively, 98.5%, 90.9%, 97.1% and 90.9%
Conclusion: The endoscopic classification of the superficial capillary-vessel pattern of colorectal lesions using BLI - Lasereo technology is an accurate method to predict the histopathologic diagnosis. BLI - Lasereo system is a very promising technology for precise evaluation of fine blood vessel pattern.

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P0787 ENDOSCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL POLYPS: LONG-TERM PROSPECTIVE EVALUATION OF EFFECTIVENESS AND COMPLICATIONS

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Introduction: Endoscopic mucosal resection (EMR) is a very important therapeutic procedure for large sessile and flat colorectal polyps. The aim of the study was to prospectively evaluate the success, complications and recurrence with EMR.
Aims & Methods: Prospective cohort study of patients referred for EMR of colorectal polyps ≥20mm at our gastroenterology department, between June of 2008 and February of 2015. Inject and cut technique was used and argon-plasma coagulation was applied in resection margin if any remnant tissue was suspected. Patients' and lesions' characteristics were collected, as well as complications and recurrence at 3, 12, 36 and 60 months. Statistical analysis was performed by logistic regression.
Results: A total of 155 colorectal polyps were removed in 148 patients (56% males; mean age 70 ± 10 years). Median polyp size was 30mm (20; 40) and 65% were sessile while 35% were flat polyps. Almost half of the lesions (47%) were located in rectum or sigmoid colon.
Median follow-up time was 24 months (12;41). Piecemeal resection was performed in 86%.
Recurrence rate was 19% (26/136) at 3 months, 6.3% (8/127) at 12 months and 2.7% (2/73) at 36 months. There was no recurrence after 60 months (0/36). Three polyps (1.9%) required surgery after non-complete resection/recurrence. The complication rate was 8.4% (13/155) and all complications were managed without surgery: bleeding – 10 (2 immediate and 8 delayed); perforation – 1 (0.6%); post-polypectomy electrocoagulation syndrome – 1; rectal ulcer – 1. Logistic regression identified distal rectal location of the polyp as the only risk factor for recurrence (OR 3.8, IC 95%: 1.5-10.2).
Conclusion: In our experience, EMR is a safe procedure for removing large colorectal polyp and all procedure-related complications were managed without surgical intervention. The possibility of recurrence implies an endoscopic long-term follow-up and, after 5 years, 98% of our patients were cured only with endoscopic therapy.
Disclosure of Interest: None declared

P0788 IMPACT OF PERSONALIZED PATIENT EDUCATION ON BOWEL PREPARATION FOR COLONOSCOPY – PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: An adequate bowel preparation is one of the most important quality factors of colonoscopy.
Aims & Methods: Our goal was to analyze the impact of personalized patient education on bowel preparation cleansing for colonoscopy.

We performed a single-blinded, single-center, prospective randomized controlled trial, where patients were allocated to "control" group, which received predefined oral and written information on bowel preparation from the gastroenterologist, or "intervention" group, that also had a 20-minute appointment with a nurse, receiving personalized education on all preparation steps. Primary outcome was the quality of bowel preparation (Aronchick Scale).

Results: A total of 229 patients were randomized, 113 to "control" group and 116 to "intervention" group. In intention-to-treat analysis, bowel preparation was "adequate" in 63% of colonoscopies of "intervention" group and in 40% of "control" group ($p = 0.001$). Subgroup analysis showed a significant impact of personalized education in patients under 65 years (67% vs. 35%; $p < 0.001$), males (60% vs. 33%; $p = 0.003$), those with higher educational levels (68% vs. 37%; $p = 0.002$), living in urban areas (68% vs. 40%; $p = 0.004$) and with previous colonoscopy (68% vs. 40%; $p = 0.001$). Risk factors for "inadequate" preparation were: male gender (OR = 2.1; 95% CI 1.1-4.1), diabetes mellitus (OR = 3.8; 1.2-11.6), chronic constipation (OR = 3.7; 1.7-8.2), absence of prior abdominal surgery (OR = 2.2; 1.2-4.1) and absence of personalized patient education (OR = 2.5; 1.4-4.4).

Conclusion: Personalized patient education on bowel preparation for colonoscopy significantly improved the quality of bowel preparation. We believe it should be applied in every gastroenterology department as it could improve the quality of colonoscopy.

Disclosure of Interest: None declared

P0789 ENDOSCOPIC POLYPECTOMY OF COLONIC POLYPS – PROSPECTIVE ANALYSIS OF COMPLICATIONS

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Introduction: Endoscopic polypectomy of colonic polyps decreases morbidity and mortality of colorectal cancer. Bleeding and colonic perforation are the most common complications of this technique.

Aims & Methods: Our aim was to evaluate the complication rate of endoscopic polypectomy.

We conducted a prospective registry, from 2009 to 2015, of polypectomy procedures performed at our endoscopy unit and its complications. An appointment was scheduled around 1 month after the procedure so that every patient could report any delayed complications. Complication rate and risk factors were analyzed. Statistical analysis was performed with chi-square test and logistic regression.

Results: We included 2416 polypectomies (6.4% endoscopic mucosal resections) in 1052 patients (63% males; mean age 63 ± 11 years). Mean time for the post-polypectomy appointment with gastroenterologist: 44 ± 24 days. Polyp characteristics: mean size – 8.8 ± 7.0mm; left-sided – 61%; sessile type – 71%. Complication rate per-polyp was 1.4%: bleeding – 1%; perfuration – <0.1%; other complications – 0.3%. All complications were managed without surgery. Nineteen patients (0.8%) required in-hospital stay. Delayed complications occurred 4.1 ± 3.7 days after polypectomy. From the 23 cases of bleeding, 11 needed endoscopic hemostasis treatment and 4 required red cell transfusion. Delayed bleeding probability increased with polyp size ≥20mm (3.4% *vs.* 0.7%, $p < 0.001$), was higher in sessile versus pedunculated polyps (1.1% *vs.* 0.6%, $p = 0.21$) and in patients under 65 years-old (1.2% *vs.* 0.7%, $p = 0.19$). In multivariate logistic regression only polyp size reached statistical significance, OR 4.9 (IC 95%: 2-12).

Conclusion: Complication rate of our series is similar to published data. We point out that there were no deaths and all complications were managed without surgery.

Disclosure of Interest: None declared

P0790 DISTANCE FROM RECTAL AND SIGMOID TUMORS TO ANAL VERGE – EVERY CENTIMETRE COUNTS!

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Introduction: An exact characterization of the distance from distal end of rectal and sigmoid tumours to anal verge is essential for an adequate staging and treatment decision, concerning neoadjuvant therapies and different types of surgery.

Aims & Methods: Our aim was to compare the measures from colonoscopies performed in ambulatory centre outside our hospital against a flexible sigmoidoscopy performed at our gastroenterology department.

We performed a prospective comparative study of patients with rectal and distal sigmoid malignant neoplasia, who were submitted to colonoscopy examination outside our institution and to flexible sigmoidoscopy at our endoscopy unit, to determine the distance from distal end of the lesion to the anal verge. The distance measured in pelvic magnetic resonance imaging (MRI) was used as reference. Statistical analysis performed with Mann-Whitney and Chi-square tests and Spearman correlation coefficient.

Results: We included 32 lesions from 32 patients (53% female; mean age 67 ± 12 years). In 5 (16%) of the ambulatory colonoscopies the distal end of the lesion was not reported. The median value of the difference between measured distances outside and inside our hospital department was 3.0cm (1;6). MRI and both endoscopic procedures were available in 22 of the 32 patients. Spearman correlation coefficient between endoscopic procedures and MRI was 0.68 for ambulatory and 0.93 for in-hospital flexible sigmoidoscopy. Comparing each procedure with MRI, there were statistically significant differences (ambulatory *vs.* MRI – 3.0cm; in-hospital *vs.* MRI – 0.0cm; $p = 0.007$). When using MRI as reference, the differences between distance to the anal verge would change the staging or treatment of a lesion in 5% of in-hospital exams *vs.* 37% of ambulatory colonoscopies ($p = 0.03$). In the latter, 7 out of 22 (32%) rectal tumours were wrongly classified as sigmoid (above 15cm from anal verge), which could change the staging and neoadjuvant therapeutic options, and 1 (5%) distal rectal tumour reported as proximal, which could be immediately directed to a centre with expertise in minimally invasive rectal surgical interventions.

Conclusion: Reporting the exact distance from distal end of rectal and sigmoid tumours to anal verge is important but it is endoscopist-dependent. A precise measure of these distances allows better staging options and adequate treatment decision.

Disclosure of Interest: None declared

P0791 CAN WATER EXCHANGE IMPROVE COMFORT DURING COLONOSCOPY WITHOUT SEDATION IN ELDERLY PATIENTS?

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Introduction: Previous studies have shown that colonoscopy with water exchange technique is superior to air insufflation in attenuating insertion pain and that it is difficult for trainee colonoscopists to perform colonoscopy in elderly patients.

Aims & Methods: To assess comparative effectiveness in elderly patients, we conducted a randomized controlled trial with head-to-head comparison of these two methods. We did not enroll the following cases in this study: (1) patients received endoscopy for treatment, (2) patients were diagnosed with ileus, (3) patients wished to use a sedative agent before colonoscopy. A total of 447 patients in two centers were randomized to either water exchange (WE) or the standard air (CO_2) insufflation technique (AI). In WE, warm water was infused through the forceps channel of the colonoscopy using a foot-switch-controlled water pump. Water used to aid insertion was removed predominantly during the insertion phase. Suspended fecal matter and residual air pockets were removed by suction, followed by infusion of water to improve the view. The

Abstract number: P0792 Table 1: Optical diagnosis according to level of experience and level of confidence for diagnosis.

	No. of high confidence predictions (% of total)	Sensitivity, %(range)	Specificity, %(range)	Positive predictive value, %(range)	Negative predictive value, %(range)
All endoscopists (n = 28)		60 (26-90)	95 (79-100)	91 (72-100)	75 (62-92)
Experts (n = 7)		67 (42-90)	95 (79-100)	92 (72-100)	78 (67-92)
General gastroenterologists (n = 7)		53 (32-74)	96 (83-100)	91 (78-100)	72 (64-80)
Fellows (n = 14)		59 (26-90)	95 (88-100)	90 (73-100)	75 (62-92)
-1st year training (n = 2)		37 (26-47)	94 (92-96)	82 (82-83)	65 (62-69)
-2nd year training (n = 3)		58 (42-68)	93 (88-100)	87 (73-100)	74 (66-79)
-3th year training (n = 3)		60 (47-74)	93 (88-100)	87 (75-100)	74 (68-81)
-4th year training (n = 6)		67 (42-90)	97 (92-100)	94 (82-100)	79 (69-92)
HIGH CONFIDENCE ONLY					
All endoscopists (n = 28)	645 (54)	65 (0-100)	98 (80-100)	97 (94-100)	80 (50-100)
Experts (n = 7)	229 (76)	66 (38-92)	99 (94-100)	97 (90-100)	80 (68-95)
General gastroenterologists (n = 7)	143 (48)	58 (38-100)	99 (94-100)	97 (86-100)	77 (67-100)
Fellows (n = 14)	273 (45)	68 (0-100)	98 (80-100)	96 (67-100)	82 (50-100)
-1st year training (n = 2)	20 (23)	40 (0-100)	100 (100)	100 (100)	63 (50-100)
-2nd year training (n = 3)	33 (26)	92 (86-100)	100 (100)	100 (100)	95 (92-100)
-3th year training (n = 3)	76 (59)	63 (40-75)	98 (93-100)	94 (86-100)	83 (78-86)
-4th year training (n = 6)	144 (56)	69 (33-100)	98 (80-100)	95 (67-100)	82 (66-100)

primary outcome was patient intraprocedural pain and the secondary outcome was doctor comfort and satisfaction. These outcomes were evaluated using a questionnaire (Score 1 to 5). Clinical trial registry number is UMIN000009706. All authors declare that there are no conflicts of interest.
Results: Forty four patients were excluded for further analysis. As a result, 403 patients without sedation were analyzed. The number of elderly patients aged 75 years and over was 83 (20.6%). There were no differences in patient age (65.6 ± 12.0 vs. 63.1 ± 12.6 years) and body mass index (22.9 ± 3.8 vs 23.3 ± 4.2 kg/m^2) between WE and AI groups. Patients in WE group reported less intraprocedural pain than those in AI group (2.18 ± 1.15 vs. 2.42 ± 1.03; unpaired t-test, $p = 0.024$). In contrast, there was no statistically significant difference in elderly patients between WE and AI groups (2.10 ± 1.12 vs.2.21 ± 0.98). Colonoscopy by trainee colonoscopists (T group) who performed less than 500 colonoscopy was more painful than that by non-trainee (NT group) (2.44 ± 1.08 vs.1.59 ± 0.78; $p < 0.01$). In T group, there was no significant difference in pain during colonoscopy in elderly patients between WE and AI groups (2.18 ± 1.15 vs. 2.45 ± 1.11). On the contrary, in NT group, WE could reduce pain in elderly patients compared to AI (1.88 ± 1.04 vs. 2.25 ± 1.06; $p = 0.033$).
Conclusion: Although WE is superior to AI in attenuating real-time insertion pain during colonoscopy, the efficacy of WE is limited in elderly patients. Unlike trainees, colonoscopy experts can attenuate insertion pain of elderly patients by utilizing WE technique.
Disclosure of Interest: None declared

P0792 OPTICAL DIAGNOSIS OF T1 COLORECTAL CARCINOMA BY COLONOSCOPY EXPERTS, GENERAL GASTROENTEROLOGISTS AND GI-FELLOWS: IS IT FEASIBLE?

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Introduction: An increasing number of T1 colorectal cancers are diagnosed. It is important to endoscopically recognize these cancers correctly to establish an optimal treatment strategy. Asian studies show that colonoscopy experts can reliably recognize early cancers. In daily practice however, accurate optical diagnosis of T1 carcinomas still seems challenging.
Aims & Methods: To evaluate the performance of optical diagnosis of T1 cancers by colonoscopy experts, general gastroenterologists and GI-fellows. We selected good quality endoscopic images (white light and NBI images) without magnification of 43 lesions: 19 T1 carcinomas and 24 benign polyps (7 sessile serrated adenomas and 17 adenomas with low-grade dysplasia) ranging from 8-30 mm in size. Seven international colonoscopy experts, 7 general gastroenterologists and 14 GI-fellows assessed all images for an optical diagnosis and level of confidence (high/low). We calculated sensitivity, specificity, negative and positive predictive value (NPV,PPV) for optical diagnosis of T1 carcinomas using 2x2 tables. For fellows, this was also described according to years of training.
Results: Sensitivity was 60% for all endoscopists. Sensitivity was best for experts (67%) compared to general gastroenterologists and fellows (53% and 59% resp.). NPV was lowest for general gastroenterologists. Of all endoscopists, only two (1 expert and 1 fellow) reached a NPV of $\geq 90\%$. 645 (54%) optical diagnoses were made with high confidence. High confidence diagnoses correlated with higher overall sensitivity, specificity, PPV and NPV, especially for fellows.
Conclusion: Sensitivity for predicting a T1 carcinoma and NPV for excluding a T1 cancer was insufficient. Experts did best with sensitivity of 67% and NPV 78%, and the performance of fellows in their last year of training is comparable to that of experts. This indicates that training for optical diagnosis for malignant polyps is needed.
Disclosure of Interest: None declared

P0793 RESECTION OF LARGE COLONIC PEDUNCULATED POLYPS (PARIS IP)

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Introduction: There are some techniques to resect large colonic pedunculated polyps.
Aims & Methods: To compare the safety of the techniques commonly used to resect large colonic pedunculated polyps ≥ 20mm according to the stalk measures. Descriptive - prospective study (2010-2014) regarding the safety of the techniques to resect large colonic pedunculated polyps, usually used by four endoscopists. We registered: location and polyp features, resection techniques and complications. The polyps were classified in 4 groups according to the stalk measures. The immediate postpolypectomy bleeding (IPPB) was defined as the bleeding during the resection procedure in which was necessary an additional haemostatic technique. **Resection techniques**: **A)** Hot snare, **B)** Adrenaline (0,005-0,01%) injection in the stalk, cutting snare and close of the wound/remnant stalk with clips and, **C)** Clip (Quick Clip® Olympus and Resolution clip® Boston Scientific) or detachable snare placement (Endoloop MAJ-339 Olympus®) and cutting snare.
Results: There were resected 180 pedunculated polyps ≥ 20mm (Longest diameter $= 25.34 \pm 6.54$; 20–60mm) among 168 patients, women: 49(29.16%). Age: 63.53 ± 10.96 y. There were excluded 20 polyps by incomplete data. In the Group 1 ($n = 38$, stalk: Length < 15mm/Diameter ≤ 10mm) were resected with hot snare: 57.89%, while in the Group 2 ($n = 28$, Length ≥ 15mm/Diameter ≤ 10mm) with clip: 57.15%. In the Group 3 ($n = 30$, Length < 15mm/Diameter > 10mm) were resected with Adrenaline injection: 93.33% and in the Group 4 ($n = 64$, Length ≥ 15mm/Diameter > 10mm) with Endoloop®: 75%; $p = 0.001$. The IPPB was the most frequent global complication: 31.10%(56/180), highest in the Group 3: 63.3%, $p = 0.001$; and was resolved with clips with an effectiveness $= 91.10\%(41/45)$. In the Groups 1 & 2 (stalk diameter ≤ 10mm), the IPPB rate was 18.75%(6/32) in the resected polyps with only snare vs. 31.8%(7/22) in those with clip, $p = 0.270$. In the Groups 3 & 4 (stalk diameter > 10mm), the IPPB rate was higher in the resection with adrenaline injection than Endoloop®: 64.70%(22/34) vs. 10.20%(5/49), $p = 0.001$. In these groups the IPPB rate was not different between clips and adrenaline injection: 50%(3/6) vs. 64.7%(22/34), $p = 0.65$. In the polyps with stalk diameter > 10mm, in the multivariate analysis, the adrenaline injection was significantly associated to IPPB: $p = 0.0001$; OR = 15.23(IC95% 4.43–52.34). In the Group 4, the IPPB was higher with clips than with Endoloop®: 50%(3/6) vs. 10.4%(5/48), $p = 0.036$.
Conclusion: In large colonic pedunculated polyps ≥ 20mm with thinner stalk ≤ 10mm the resection with hot snare was acceptably safe. In thicker stalk > 10mm, the polypectomy with Endoloop® was significantly safer when the stalk length was enough to place it; and the adrenaline injection has shown a high risk to IPPB. Some clips type might not have been superior to prevent the IPPB although they are effective to resolve it.
Disclosure of Interest: None declared

P0794 IN VIVO DETECTION OF EARLY COLORECTAL CANCER BY FLUORESCENCE ENDOSCOPY TARGETING THE ENDOTHELIN-A-RECEPTOR

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Introduction: Patients suffering from ulcerative colitis are at an increased risk of developing colorectal cancer. Current guidelines recommend surveillance colonoscopy with chromoendoscopy or random biopsies to further improve detection rates of dyplastic lesions. ET-A receptor (ET_AR) expression is known to be significantly increased in various malignancies including colorectal cancer (1). The objective of this study was to evaluate ET_AR-guided fluorescence endoscopy (FE) *in vivo* and fluorescence reflectance imaging (FRI) *ex vivo* for detection and characterization of early dysplastic lesions in mice.
Aims & Methods: Colorectal cancer was induced in C57Bl/6 WT mice ($n = 15$) by single injection of azoxymethane (AOM) i.p. and cyclic administration of dextran sodiumsulfate (DSS) in drinking water. A Cy5.5-labeled nonpeptidic ET_AR imaging probe was intravenously injected 24 hrs before endoscopic examination. Tumor development was assessed *in vivo* by white light endoscopy and FE. Then colons were explanted and examined by fluorescence reflectance imaging using an MS-FX PRO optical imaging system to measure tracer uptake *ex vivo*. At the end of the experiment tumors were graded after HE staining and evaluated by an expert pathologist. Tumor biology was assessed utilizing the proliferation marker Ki-67 and ET_AR expression was visualized by immunohistochemistry and western blot analysis. Additionally, binding specificity of the tracer was evaluated by simultaneous injection of an equimolar amount of an unspecific fluorochrome (Cy3.5-glycin) and the specific ET_AR tracer.
Results: In 15 mice, 77 adenomas were confirmed up to high-grade dysplasia in standard histology. FE was able to detect ET_AR expression easily applying the fluorescent ET_AR imaging probe. A significant higher fluorescent contrast was observed in colonic adenomas as compared to adjacent non-malignant mucosa (63.4 ± 7.9 vs. 56.6 ± 7.0; $P < 0.001$). Correspondingly, *ex vivo* conventional molecular imaging showed significantly increased tracer uptake in colorectal adenoma as compared to healthy mucosa (1211.0 ± 557.4 vs. 509.7 ± 137.0; $P < 0.001$). Immunochemistry revealed an increased Ki67 and ET_AR expression in colonic dysplasia. Moreover, western blot analysis verified the detected ET_AR expression. No significant difference in tracer uptake between low and high-grade adenoma was found (tumor-to-background ratio: 2.3 ± 0.8 vs. 2.4 ± 0.7, $P = 0.589$). The tumor-to-background ratio of lesions imaged for Cy3.5 was significantly reduced as compared to Cy5.5 indicating the high binding-specificity of the utilized ET_AR tracer (1.4 ± 0.3 vs. 2.5 ± 0.7, $P < 0.001$).
Conclusion: In murine colorectal dysplasia ET_AR expression was significantly increased as compared to healthy mucosa. By detection of ET_AR via FE in live mice, a prognostic biomarker for colorectal cancer development is directly visualized during colonoscopy, thus facilitating *in vivo* tumor characterization on a molecular level.

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P0795 SHOULD POLYP RESECTION BE PRIORITIZED ACCORDING TO LOCATION?

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Introduction: Prediction of histology of colon polyps according to location and other macroscopic features is particularly relevant as colonographic techniques are becoming more widespread. Advanced polyps are smaller in the right colon[1] and right-sided lesions carry increased risk of recurrence of advanced adenomas.[2] Nevertheless, differences in histologies between right- vs left-sided colon polyps are not well characterized.[2] When available, such information may be used for prioritizing colonoscopies recommended after colonography (ie, when at least one polyp ≥6mm is observed).[3]
Aims & Methods: We aimed at characterizing colonic polyp histology according to patient and polyp macroscopic characteristics.
We reviewed all polyps observed in colonoscopies performed during 2013 in an Gastroenterology Department, whose location and histology (from biopsy or complete removal) are unequivocally known. We considered high risk traditional adenomas all those with ≥10mm at colonoscopy or with advanced histology (villous histology or high grade dysplasia).
We reviewed all polyps observed in colonoscopies performed during 2013 in an Gastroenterology Department, whose location and histology (from biopsy or complete removal) are unequivocally known. We considered high risk traditional adenomas all those with ≥10mm at colonoscopy or with advanced histology (villous histology or high grade dysplasia). Patient demographics, as well as polyp macroscopic and microscopic features, were analyzed with STATA® 12.1.
Results: In total, 1960 polyps were analyzed.In the rectum, the most frequent polyps were hyperplastic (53.3%; 218/409); while in the other segments the most common polyp type was tubular adenoma with low grade dysplasia: 48.3% (236/489) in sigmoid colon, 64.5% (158/245) in descending colon, 68.3% (293/429) in transverse colon, 70.6% (202/286) in ascending colon and 69.6% (71/102) in cecum.High risk traditional adenomas were more common in the sigmoid colon (33.5% of polyps; 164/489) and descending colon (26.9%; 66/245) than in other segments.Among polyps ≥6mm (N = 878), advanced histology in traditional adenoma was more prevalent in rectal polyps (33.3%; 42/126), followed by polyps in the sigmoid colon (23.8%; 62/260), descending colon (19.7%; 27/137), cecum (18.9%; 7/37), transverse colon (15.2%; 31/204) and ascending colon (14.0%; 16/114). Advanced histology was significant more frequent in distal compared to proximal polyps, both when comparing all polyps (11.9% vs 7.2%, $p = 0.001$) or only those ≥6mm (25.0% vs 15.2%, $p < 0.001$).
Conclusion: In this series, distal polyps carried a higher risk of advanced histology. Priorization for colonoscopic removal may consider polyp location.

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P0796 EFFICACY, ACCEPTABILITY, TOLERABILITY AND SAFETY OF LOW-VOLUME POLYETHYLENE GLYCOL SOLUTION PLUS ASCORBIC ACID VERSUS STANDARD POLYETHYLENE GLYCOL SOLUTION IN BOWEL PREPARATION FOR COLONOSCOPY

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Introduction: According to an ageing population, and increasing burden of colorectal cancer at an advanced age, colonoscopies are increasingly needed in the elderly. Polyethylene glycol electrolyte lavage solution containing ascorbic acid (PEG-ASC) has recently become available in Japan, as a low-volume lavage solution. However, in view of concerns of hypertonicity for PEG-ASC, we compared it to standard PEG electrolyte solution (PEG-ELS) and evaluated the hematological and biochemical change before and after taking PEG solution.
Aims & Methods: The aim of this study is to compare the efficacy, acceptability, tolerability, and safety of PEG + ASC and standard PEG-ELS, not only in the general population, but also in patients of advanced age. This was a single-blinded, non-inferiority, randomized, controlled trial including adult inpatients. Although 3–4 L of PEG-ELS is used in Western countries, approximately 2 L of PEG-ELS, along with a laxative, is usually considered adequate for bowel preparation in Japan. Subjects were randomized to receive 1.5 L PEG-ASC or 2 L PEG-ELS, and completed a questionnaire on the acceptability and tolerability of the bowel preparation process. Hematological and biochemical parameters were assessed at baseline, 3 hours, and 7 hours after beginning the preparation solution. The Boston Bowel Preparation Scale was used to evaluate bowel cleansing, and a 3-point scale was used to assess mucosal visibility.
Results: One hundred patients were randomized to either the 1.5-L PEG-ASC group (n = 50, males 66%, mean age 66.4 years) or the 2-L PEG-ELS group (n = 50, males 64%, mean age 67.9 years). Patients in 1.5-L PEG-ASC group were more willing to repeat the procedure than the 2-L PEG-ELS group (72% 1.5-L PEG-ASC group vs. 52% 2-L PEG-ELS group (95% lower confidence limit, for a difference of 1.4%)). No significant differences were found in bowel cleansing ($P = 0.889$) or mucosal visibility ($P = 0.063$) between the groups. Except for sodium bicarbonate in the 1.5-L PEG-ASC group, all hematological and biochemical parameter variations were within the normal range. However, we demonstrated significant statistical changes in the hematological and biochemical parameters such as sodium, chloride, albumin, hematocrit, and acid-base balance parameters after both type of preparation, regardless of patient age, which were not clinically significant.
Conclusion: The 1.5-L PEG-ASC regimen had higher patient acceptability than the 2-L PEG-ELS regimen. Tolerability, bowel cleansing, and safety were similar between regimens. No significant differences in the safety profile were found between subjects aged less than 70 years and those aged 70 years or more; nevertheless, regardless of age, proper hydration is needed throughout the bowel preparation process.
Disclosure of Interest: None declared

P0797 CLINICAL IMPACT OF NEAR-FOCUS NARROW BAND IMAGING IN DIFFERENTIATING NEOPLASTIC AND NON-NEOPLASTIC COLORECTAL SMALL POLYPS FOR TRAINEES

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Introduction: Neoplastic colorectal polyps are precursor lesions recommended to remove. Both Narrow band imaging (NBI) and optical magnification have contributed to an accurate endoscopic diagnosis of the colorectal tumors. Recently, a simplified 45 times optical magnification (near-focus NBI) that is activated by only a switch has become commercially available. This near-focus NBI might help trainees to differentiate between neoplastic and non-neoplastic polyps.
Aims & Methods: The aim of this retrospective image evaluation study is to elucidate diagnostic accuracy of near-focus NBI for differential diagnosis of colorectal small polyp in trainees using western setting.
In the pre-study, education according to NICE classification was performed to 7 reviewers [6 trainees and 1 experienced endoscopists (control)] using 15 typical polyps. In Study 1, endoscopic images obtained by high-resolution white-light (WLI), NBI and near-focus NBI of 20 consecutive polyps removed between July and August 2014, were systematically assessed by the 7 reviewers. In study 2, two weeks after the study, endoscopic images of other consecutive 40 polyps removed between August and September 2014, were evaluated by the 7 reviewers after repeating the same lecture and verifying the pathological diagnosis of the 20 polyps in study 1. Diagnostic accuracy and rate of high confidence were analyzed. Trainees had performed < 100 colonoscopies and < 3 years' experience. All reviewers were blinded to clinicopathological data and evaluated the images in a random order. All images used in the study 1 and 2 were obtained by Exera III system (Olympus). All polyps were smaller than 10mm.
Results: Before the education, diagnostic accuracy for differentiating adenomas from hyperplastic polyps (HPs) of the trainees and rate of high confidence were 78% (47~87) and 67% (60~80).
Study 1) Overall diagnostic accuracy of WLI, NBI, and near-focus NBI for differentiating adenomas from HPs in trainees were 61% (55~65), 75% (65~85) and 80% (75~90), respectively. Overall rate of high confidence in WLI, NBI and near-focus NBI were 73% (35~90), 65% (45~95) and 68% (60~80). In the experienced endoscopist, diagnostic accuracies were high as 65%, 75% and 85%, and high confidence rate was 85%, 95% and 95%, respectively.
Study 2) Overall diagnostic accuracy of WLI, NBI, and near-focus NBI for differentiating adenomas from HPs in trainees were 50% (40~63), 65% (48~78) and 71% (53~83), respectively. Overall rate of high confidence in WLI, NBI and near-focus NBI were 68% (23~90), 80% (68~88) and 80% (60~80). In the experienced endoscopist, diagnostic accuracies were low as 45%, 45% and 60%, and high confidence rate was 83%, 88% and 88%, respectively.

Table: Diagnostic accuracies of the trainees.

	WLI (%)	NBI (%)	Near-focus NBI (%)
Study 1	61 (55~65)	75 (65~85)	80 (75~90)
Study 2	50 (40~63)	65 (48~78)	71 (58~83)

Conclusion: The present study clearly demonstrated that near-focus NBI was superior to WLI and NBI in differentiating neoplastic and non-neoplastic small lesions for the trainees. Near-focus NBI may help trainees to precisely manage colorectal polyps.
Disclosure of Interest: None declared

P0798 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION AS A RESCUE ENDOSCOPIC TREATMENT AFTER PREVIOUS INCOMPLETE ENDOSCOPIC MUCOSAL RESECTION: A SINGLE-CENTRE EXPERIENCE

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Introduction: Indications for colorectal endoscopic submucosal dissection (CR-ESD) include treatment of mucosal tumors with submucosal fibrosis i.e. after previous biopsy or after incomplete endoscopic mucosal resection, EMR. Little is known on the clinical outcomes of this procedure in a western setting.
Aims & Methods: The aim of our study was to evaluate feasibility of CR-ESD as a salvage endoscopic treatment for residual colorectal lesions after incomplete EMR. A retrospective study on a prospectively collected database of endoscopic procedures during period 2013-2015 was done. Data regarding lesion location, the ESD accessories used, procedure time, pathology, margin involvement (R0) and post-procedure complications, were collected.
Results: We identified 9 patients (6 male, 3 female, median age 71 years, range 39-79 years) with this clinical scenario. 8 lessions were located in rectum and 1 in sygmoid colon (median size 25 mm, range 15-80 mm). Lesions included residual adenomas (Paris Is, 7/9pts; Paris Is + IIc, 1/9 pts) and LST-NG (Paris Is + IIa, 1/9 pts). All procedures were done with Dual and Hook knife. Median procedure time was 240 min (range 60-600 min). Pathohistology specimens were: tubular adenoma with low-grade dysplasia (7/9) and villotubular adenoma with high-grade dysplasia (2/9). R0 resection was confirmed in 7/9 pts (78%). Endoscopic treatment of the intraoperative events included closure of perforation (2/9), and hemostasis (3/9). Two-step procedure was needed in 3 patients to complete the resection and post-procedural fever was observed in one patient. During median follow-up of 7 months (range 1-17 months) no delayed complications were observed.
Conclusion: CR-ESD after incomplete EMR is technically demanding and time-consuming procedure. However, in the hands of experienced endoscopist, it is a 'surgeon sparing' procedure that can achieve an acceptable rate of R0.
Disclosure of Interest: None declared

P0799 RANDOMIZED COMPARATIVE EVALUATION OF AN ESD SELF-LEARNING SOFTWARE IN FRANCE AND JAPAN

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Introduction: Endoscopic submucosal dissection is the reference method to achieve *en bloc* resections for large lesions of the digestive tract. Nevertheless, it is a difficult and risky technique with a long learning curve. To reduce first procedures morbidity, animal models like bovine colon were developed to teach the initial skills. Self-teaching program could be helpful in the western world but also in Asia even if the technique is more spread out. A self-learning software to assist students in the first steps of ESD has been developed by N. Yahagi jointly with Olympus®. We designed this study to evaluate the impact of such a tool on ESD learning curve using a bovine colon model developed previously(1).
Aims & Methods: A prospective randomized comparative study enrolled 37 students (29 in France and 8 in Japan) experienced in interventional endoscopy but not in ESD. Each student was randomized in one of the two groups and performed 30 ESD for a 30 mm simulated rectal lesion in retroflexed position. Group A used the self-learning software whereas group B only observed an ESD procedure movie. No other technical explanation was given to both groups. Procedure duration, resection completeness, perforation rate and the specimen size and surface were assessed. If the procedure exceeded 75 min, the trainee had to stop and we considered it as a failure.
Results: 39 students performed 1170 ESD (group A: 19 students, 570 ESD) (group B: 20 students, 600 ESD) with 57 failures (time out over 75 min) (group A : 26, 4.6%, group B: 31, 5.2%, $p = 0.26$). Among the 1113 resection of a specimen in less than 75 min, the complete resection rate was 76.2% in group A versus 67.4% in group B ($p = 0.001$). The rate of success defined by a complete procedure in less than 75 min without perforation was significantly superior with respectively 70.9% and 61.2% in group A and B ($p < 0.001$). The perforation rate and the procedure duration were not different with 6.0 vs 6.4 % ($p = 0.796$) and 35.7 vs 34.9 min ($p = 0.391$) respectively. Regarding only the 30th procedure of each student, the rate of complete resection was superior in group A with 84.2 versus 70% ($p = 0.292$). Other analyses (learning curve, french vs japanese trainees) are ongoing.
Conclusion: The use of an ESD self-learning software is effective to improve the quality of resection compared to a standard teaching with procedure movies. The main advantage is to save some supervision time. This result suggests to incorporate such a self-learning software in the ESD teaching program.

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Disclosure of Interest: None declared

P0800 SKIPPING ONE PRODUCT GENERATION OF COLONOSCOPES RESULTS IN DIFFERENCES IN POLYP MISS RATES: RESULTS FROM A PROSPECTIVE RANDOMIZED TANDEM STUDY

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Introduction: Multiple randomized studies have shown that changing certain features in imaging of colonoscopes (structure enhancement, wide angle view, HDTV) do not consistently improve adenoma detection rate. Similarly, change from one endoscope generation to the next one, implementing one or even several new features were not successful in achieving a rise in ADR either. There is however indirect evidence that it might need to skip one colonoscope generation (i.e. change from one generation to the next but one) may have this effect.
Aims & Methods: We therefore compared the latest generation Olympus colonoscopes (Exera III, CF- or PCF-190) with the next to last one (CF- or PCF 165) in a prospective randomized multicenter tandem study. Patients with increased risk for colorectal neoplasia (FOBT positive, personal or familial history of colorectal cancer or adenoma, rectal bleeding, recent change in frequency and consistency of stools) were included. Primary outcome was the adenoma miss rate with 190 colonoscopy in comparison to 165 colonoscopy.
Results: 848 patients (48% male, mean age 58.3 years, range 19-87) with personal (41%) or familial (38%) history of colorectal neoplasia, rectal bleeding (19%) and other indications were included. A total of 304 missed adenomas were found in 197 patients. Of the 425 patients in the intervention group (PC or PCF 190 first), 68 patients (16.0%; 95% CI: 12.5 % - 19.5%) had at least one adenoma missing during the 1st procedure, as compared with 129 of the 423 (30.5%; 95% CI: 26.1% - 34.9%) patients in the control group (PC or PCF 165 first). This difference was significantly different between the 2 study groups ($p < 10\text{-}3$). Adenoma detection rate (percentage of patients with at least one adenoma) during the first colonoscopy was 43.3% (184/425) in the intervention group (190 series) and 36.6% in the control group (165 series) ($p < 0.05$).
Conclusion: Also based on negative results of previous trials, this randomized tandem study shows that it may take two instrument generation improvements before an increase of adenoma miss rate can be observed.
Disclosure of Interest: None declared

P0801 NEW ISOLATED BOVINE COLON MODEL DEDICATED TO COLONIC ESD HANDS-ON TRAINING: DEFINITION AND PRELIMINARY EVALUATION

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Introduction: Endoscopic submucosal dissection is the reference method to achieve en bloc resections for large lesions of the digestive tract. Nevertheless, it is a difficult technique with long learning curve and relatively high risk of perforation. To reduce the risk of first procedures, animal models have been developed to teach the initial skills. In Japan, stomach ESD is the first step for students and pig stomach is a dedicated model to learn ESD in gastric conditions. In Europe, since the number of gastric lesions is low compared to colonic ones, we have to develop different strategies of teaching with dedicated models. Pig colon is a good model but thinner and more difficult than human and the caliber of the bowel is sometimes too narrow to work in retroflexed position. In this present work, we evaluated a bovine colon model to perform rectal ESD in retroflexed position.
Aims & Methods: In a first step we prepared 6 bowels to perform ESD using Dual Knife® and Nestis Enki II® in order to precise the preparation protocol. Using this protocol, two endoscopists unexperienced in ESD performed 62 procedures of 30 mm on 8 colon models. In parallel, we compared the ellipse

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Parameter		Excellent / Good Bowel Preperation	Fair / Poor / Inadequate Bowel Preperation	OR / t	CI	p
Sex	Male	370	212	1.16	0.92-1.46	0.2
	Female	406	270	0.86	0.68-1.08	0.2
Polyp Detection	PDR	0.322	0.368	0.87	0.69-1.11	0.28
	ADR	0.166	0.191	0.87	0.64-1.20	0.4
Parameter		Excellent / Good / Fair Bowel Preperation	Poor / Inad equate Bowel Preperation	OR / t	CI	p
Sex	Male	500	42	0.79	0.50-1.26	0.33
	Female	540	36	1.26	0.79-2.0	0.33
Polyp Detection	PDR	0.337	0.342	0.98	0.61-1.59	0.94
	ADR	0.178	0.165	1.1	0.6-2.04	0.76

formula evaluation of specimen area with measured area using a picture size software.
Results: A precise protocol to defrost and to prepare the colon was defined. The lesions were marked with a plastic circle of 28 mm diameter after inversion and swallowing of the bowel. The two students achieved complete en bloc resection in 89.1% of cases with 6.2% of perforations. A large heterogeneity appeared between the speed and the success rate depending on the age of the animal bowel. Using veal colon (animal under 8 months), the rate of failure was significantly higher ($p = 0.002$) and the speed of dissection was significantly lower ($p < 0.001$) than using adult bovine colon (aged between 12 and 24 months). The progression of dissection speed was significant between the first and the second half of the cases with respectively 0.49 and 0.59 cm^2/min using only the cases on adult bovine colon. No significant difference appeared between measured and calculated areas of the specimen.
Conclusion: Bovine colon model is a suitable model to teach ESD in the rectum. Nevertheless, adult bovine colon model is more homogeneous than veal ones and has to be used for comparative works. Calculated area using ellipse formula is a good way to evaluate the size of the specimen with no difference with measured areas using picture measurement software.
Disclosure of Interest: None declared

P0802 ENDOSCOPIC DIAGNOSIS OF COLORECTAL POLYPS USING BLUE LASER IMAGING AND MAGNIFICATION: IMPACT OF A SHORT TEACHING PROGRAM

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Introduction: Blue Laser Imaging (BLI) is a new image-enhanced endoscopy technique, proven highly effective, in addition to magnification endoscopy, to differentiate between neoplastic and non-neoplastic colorectal polyps. We sought do determine if these results could be reproduced in a group of non expert western endoscopists after a short teaching program.
Aims & Methods: 120 endoscopic images, including white light endoscopic images, standard BLI, BLI-bright and magnified images of 62 small colorectal polyps were used for the study. These pictures were shown to a group of 138 gastroenterologists who were asked to score each polyp as an adenoma or an hyperplastic polyp. After a one hour teaching lesson dedicated to the diagnostic criteria of hyperplastic and adenomatous lesions under BLI or narrow-band imaging and magnification, a posttest was conducted with the same images arranged in a different order.
Results: 61 gastroenterologists, among which 29 residents and 32 seniors, filled the pre and posttest questionnaires. Only 31.7% had previously received a formalized teaching in any kind of virtual chromoendoscopy. The overall sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy of BLI with magnification for the endoscopic diagnostic of small colorectal adenomas were 0.64 (95% CI = 0.63-0.66), 0.58 (95% CI = 0.55-0.6), 0.81, 0.37, and 0.63, respectively. These numbers were not significantly different in residents and senior endoscopists, and did not significantly improve after the teaching lesson. The proportion of diagnostic certainty improved from 31.5% to 41.9% ($p < 0.0001$) after training.
Conclusion: For non expert Western endoscopists, a one hour teaching lesson is insufficient to acquire basic knowledge in BLI and magnification endoscopy. Longer training programs might be required before such advanced endoscopic imaging techniques can be implemented in France.
Disclosure of Interest**:** None declared

P0803 EFFECTIVENESS OF A TRAINING SYSTEM FOR THE IDENTIFICATION OF DIMINUTIVE COLORECTAL POLYP HISTOLOGY USING NARROW BAND IMAGING

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Introduction: Patel et al developed a system that effectively trained gastroenterology fellows to identify diminutive colorectal polyp histology using Narrow Band Imaging (NBI).[1] It, however, requires the presence of an expert to provide active feedback during the training session, limiting its applicability. A modified version of the training system was thus developed and tested, which utilised a computer-based testing module, which provided automated feedback on participant performance.
Aims & Methods: A single-center, prospective, educational evaluation study was conducted among 16 gastroenterology consultants and fellows to assess if the modified training system is effective, and if its effects are durable for at least 3 months. Participants initially watched a teaching presentation that described the NBI findings that distinguish polyp histology. They then used a computer-based testing module, operable using a web browser, that showed 80 videos of diminutive colorectal polyps. Predictions of polyp histology and degrees of confidence were recorded. After each video, the module provided feedback by showing a representative picture of the polyp and providing the actual polyp histology and the NBI findings that support the prediction. Performance was evaluated by comparing predicted histology with actual histology. To evaluate durability of learning, after 3 months, the same videos were shown to the participants, and they were again asked to predict polyp histology.
Results: Participant performance and percentage of high-confidence predictions improved significantly as they progressed through video blocks. Predictions made with high confidence were statistically superior to those made with low confidence. All participants performed well during both study sessions, achieving > 90% accuracy, sensitivity, specificity, PPV, and NPV for high confidence predictions. The participants' experience in endoscopy did not affect performance or percentage of high-confidence predictions.
Conclusion: The modified training system effectively trained participants to identify diminutive colorectal polyp histology using NBI. Learning acquired from this system is durable for at least 3 months. This system is noteworthy in its ability to provide automated feedback and its potential to be used online, making it more applicable in a wider spectrum of clinical settings. Further studies that evaluate the long-term durability of learning from this system, as well as the *in vivo* real-time performance of trained endoscopists are recommended.

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Disclosure of Interest: None declared

P0804 THE ADEQUACY OF BOWEL PREPARATION HAS NO IMPACT ON ADENOMA DETECTION RATES

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Introduction: Bowel preparation is recognised as an important factor for the completion of colonoscopy. However, due to heterogenous methodologies of published literature, consensus agreement on the effect of bowel preparation on adenoma detection rate is unclear. There has been an unclear impact of the degree of colonic preparation in the literature, in part because of the differences in methodology between studies. The degree of bowel preparation is used as a marker of colonoscopic adequacy, with current guidelines suggesting shorter interval surveillance for those patients with inadequate bowel preparation at index colonoscopy.
Aims & Methods: To compare the polyp and adenoma detection rates of the adequacy of bowel preparation.
A retrospective study was performed from prospectively collected data from three day endoscopy centers involving 4 experienced gastroenterologists. Twelve hundred procedures were identified. Exclusion criteria included a previously performed partial or total colectomy or in the case of multiple

endoscopies, having a previous colonoscopy within the study period, or in the case where inadequate description of the degree of colonic preparation was found.
Results: A total of 1122 procedures were analyzed. Participants had an average age of 59.95 years, with 51.4% being female. There was no difference between the two groups in terms of demographics, indication or colonic insufflation method used. Results demonstrated there was no statistically significant difference in the adenoma detection rates dependent on the degree of bowel preparation, even when excellent, good and fair preparation were grouped together for subsequent analysis.
Conclusion: The degree of bowel preparation appears to have little bearing on the adenoma detection rate. This finding supports that the adenoma detection rate is independent of bowel preparation, and other factors affecting bowel preparation should be the subject of further study.
Disclosure of Interest: None declared

P0805 THE COLONOSCOPIC ADENOMA DETECTION RATE INCREASES DEPENDING UPON THE METHOD OF INSUFFLATION

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Introduction: There has been an increasing use of carbon dioxide insufflation recently for colonoscopy as this has been shown to improve patient comfort, shorten procedure duration and decrease the use of post procedural analgesia. There have been no studies to date comparing the difference between adenoma detection rates of carbon dioxide or air insufflation.
Aims & Methods: To compare the polyp and adenoma detection rates of carbon dioxide compared to air insufflation for colonoscopy.
A retrospective study was performed from prospectively collected data from three day endoscopy centers involving 4 experienced gastroenterologists. Twelve hundred procedures were identified. Exclusion criteria included a previously performed partial or total colectomy or in the case of multiple endoscopies, having a previous colonoscopy within the study period.
Results: A total of 1163 procedures were analyzed. Participants had an average age of 59.9 years, with 51.4% being female. There was no difference between the two groups in terms of demographics, time of day of the procedure, and indication. Results demonstrated there was a statistically significant difference in the adenoma detection rates between the two groups. The carbon dioxide group had a significant positive advantage in the detection of adenomas. Other procedural parameters were not statistically different.

Parameter		CO2 Group	Air Group	OR / t	CI	p
Sex						
	Male	316	245	1.04	0.82-1.31	0.75
	Female	332	267	0.96	0.77-1.22	0.76
Age		60.3	59.5	0.978		0.33
Withdrawl Time		7.47	7.32	0.55		0.58
Bowel Preperation						
	Excellent	31	17	1.47	0.80-2.69	0.21
	Good	370	321	0.79	0.62-1.01	0.06
	Fair	180	124	1.21	0.92-1.57	0.17
	Poor	40	22	1.47	0.86-2.50	0.16
	Inadequate	13	4	2.6	0.84-8.03	0.10
Polyp Detection						
	PDR	0.36	0.33	1.13	0.84-1.51	0.41
	ADR	0.22	0.16	1.39	1.02-1.89	0.03

Conclusion: Carbon dioxide insufflation was shown to have better adenoma detection rates when compared with air insufflation. This finding further enhances the case for carbon dioxide insufflation in addition to already established procedural benefits.
Disclosure of Interest: None declared

P0806 CLINICOPATHOLOGICAL STUDY OF SERRATED LESIONS OF THE COLORECTUM

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Introduction: Serrated lesions of the colorectum are the precursors of microsatellite unstable carcinomas. However, their clinical and pathologic features are still unclear and need further exploration.
Aims & Methods: The aims of this study was to clarify the clinicopathological features of colorectal serrated lesions. We reviewed clinical charts and pathological files of 3591 endoscopically resected specimens during January 2007 and December 2014 in our hospital. A total of 282 serrated lesions resected were classified into three categories : HP (hyperplastic polyp), SSA/P (sessile serrated adenomas/ polyps), and TSA (traditional serrated adenoma), according to the WHO criteria. We examined the clinical features of these cases. Then we studied the expressions of Ki-67 and MUCs (MUC2, MUC5AC and MUC6) immunohistochemically to evaluate the differences of the distribution of proliferation and the profile of mucins in these serrated lesions.
Results: Of these 282 lesions, a total of 151 (53.6%) were HP, 63 (22.3%) SSA/P, and 68 (24.1%) TSA. Male to female ratio (M/F) was 2.60 for HP, 1.17 for SSA/P, and 2.40 for TSA. Mean size of SSA/Ps (11.3mm) and TSAs (9.5mm) were significantly larger than that of HP (7.9mm). SSA/Ps were located predominantly in the proximal colon, whereas HP and TSA were mainly located in the sigmoid colon and rectum. 85% of SSA/Ps were flat in macroscopic appearance. SSA/Ps and HPs were whitish or almost the same as adjacent mucosa in color, whereas TSAs had a tendency to be reddish. Magnified colonoscopy showed Type II open pit pattern as characteristic of SSA/Ps, whereas pine-cone-shaped pit pattern as that of TSAs. Incidences of concomitant carcinomas in HP, SSA/P, and TSA were 0% (0 out of 151), 3.2% (2 out of 63), and 2.9% (2 out of 68), respectively. Ki-67 positive cells in HP showed regular, symmetric distribution, and those in SSA/P did irregular asymmetrical pattern, whereas most of those in TSA were distributed in "ectopic crypts". Expression levels of MUC2, MUC5AC and MUC6 were significantly different between the serrated lesions ; SSA/Ps and HPs were positive for MUC5AC in comparison with TSAs.
Conclusion: Our studies showed the three types of serrated lesions have their own distinct features and could be helpful to distinguish between them. SSA/P and TSA are premalignant lesions of colorectum and we should detect these lesions and completely remove endoscopically.
Disclosure of Interest: None declared

P0807 FLEXIBLE ENDOSCOPY FOR DIAGNOSIS OF TUBERCULOSIS OF A LARGE BOWEL IN PATIENTS WITH HIV/TB CO-INFECTION

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Introduction: In patients with HIV/TB co-infection TB-process is characterized by development of generalized and complicated forms with multiple localizations – in lungs, intrathoracic lymph nodes, in inraabdominal, mezenterial lymph nodes, bowel, peritoneum, spleen. Most of the patients of HIV/TB co-infection complain of the abdominal pain, alvine flux, which may be caused by any inflammatory process – both specific or nonspecific, adverse effects of TB-drugs and HIV-therapy. This problem demands attention and diagnostics. Diagnosis of large bowel tuberculosis and inflammatory bowel diseases can be difficult with patients HIV/TB co-infection. Flexible endoscopy and biopsy are necessary for revealing the pathology.
Aims & Methods: Data of 39 patients observed in the surgical department of Moscow Research and Clinical Center for Tuberculosis Control of the Moscow Government Health Department in the period from 2010 to 2014 with the suspecting on TB-process in bowel are examined. 32 (82,1%) patients had lung forms of tuberculosis, 7 (17,9%) patients were hospitalized with the suspecting on TB-process in bowel, these patients had no lung TB. Complex examination of all the patients included ultrasonography of abdominal cavity organs, oesophagogastroduodenoscopy, irrigoscopy, computer tomography of abdominal cavity organs and examination of fecal masses on Mycobacterium tuberculosis by the luminescent microscopy and cultural method. Colonoscopy was performed with biopsy for histological examination, microscopy, cultural method and PCR.
Results: Visual signs of large bowel tuberculosis were observed in 29 (74.4%) of patients. Types of tuberculosis lesions of large bowel are described: military form, infiltrative and infiltrative-ulcerous. They were described as erosion, infiltrative and infiltrative-ulcerous. Epithelioid-cellular granuloma was revealed in the material of biopsy in 19 (48.7%) cases. In 11 (28.2%) cases Mycobacterium tuberculosis was detected. In 2 patients (5,1%) adenocarcinoma of the large bowel was diagnosed, in 3 (7.7%) citomegaloviral ulcerative colitis was observed, in 15 (38.7%) nonspecific colitis was revealed. All the patient were treated with TB drugs, in 22 patients (56.4%) improvements, such as pain and alvine flux elimination were observed, defecation was normalized. 7 patient (17.9%) needed in the correction of TB drug therapy.
Conclusion: To sum up, colonoscopy is a rapid and valuable method of abdominal cavity organs tuberculosis diagnostic.
Disclosure of Interest: None declared

P0808 SYSTEMIC REVIEWS AND META-ANALYSIS: THE EFFECT OF PATIENT EDUCATION ON BOWEL PREPARATION FOR COLONOSCOPY

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Introduction: Colonoscopy is a useful and widely available tool for diagnosing and managing colorectal diseases. [1] According to the US National Polyp Study, colonoscopy can reduce the incidence and associated mortality of colorectal cancer (CRC) and polypectomy can lower colorectal cancer death rates if polyps are detected during colonoscopy.
Aims & Methods: Effectiveness of bowel preparation is closely linked to patient compliance and the subsequent result of colorectal cancer screening.[2] Poor bowel preparation can result in missed colonic neoplasms, a difficult and time-consuming procedure, and an increased risk of complications. This meta-

analysis aimed to determine the effect of educational intervention on the quality of bowel preparation before colonoscopy.
A comprehensive literature review identified randomized controlled trials measuring the effect of educational intervention on the quality of bowel preparation. Two reviewers independently screened relevant articles, extracted data, and assessed the risk of bias. The primary outcome was the quality of each bowel preparation before colonoscopy using a particular assessment scale. The secondary outcomes were polyp detection rates during the procedure and the need for a repeat colonoscopy due to incomplete examination. The quality of all studies was assessed with the 5-point Jadad scale for assessing RCTs. Studies with 3 or more points were considered high quality.
Results: Nine randomized controlled trials were included in this meta-analysis. In all, 2885 patients were enrolled, with 1458 receiving education and 1427 assigned to the control group. Education before colonoscopy can lead adequate bowel preparation. A significant difference was observed in adequate bowel preparation between the education and control groups (OR = 1.97, 95% CI 1.63-2.38). However, no significant differences were identified in polyp detection rates (OR = 1.24, 95% CI 0.79-1.94) and the need for repeat colonoscopy (OR = 0.47, 95% CI 0.21-1.04) between both groups. The subgroup analyses in this meta-analysis based on education delivery methods, use of educational tools, and geographical differences in education delivery indicated that bowel preparation significantly improved after patient education.
Conclusion: Concerning the bowel preparation in all studies the intervention leads to better outcome, the consistency is an important indication to establish the causality. However, there is insufficient evidence to assess improvements in polyp detection rate and avoidance of a repeat colonoscopy.

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Disclosure of Interest: None declared

P0809 CLINICAL OUTCOME OF ULCERATIVE COLITIS WITH MUCOSAL HEALING DEMONSTRATED BY WHITE LIGHT ENDOSCOPY BUT WITH SUBTLE ABNORMALITIES DETECTED BY HIGH DEFINITION ISCAN ENDOSCOPY

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Introduction: Current practice is to assess mucosal inflammation in patients with ulcerative colitis (UC) with white light endoscopy (WLE). However, high definition (HD) iSCAN endoscopy can characterize in details the mucosal and vascular pattern to assess mucosal healing (MH) and inflammation. Subtle endoscopic and histologic abnormalities can still be detected in the apparently healed mucosa and the clinical significance of this is still uncertain
Aims & Methods: We aimed to monitor the clinical outcome of patients with Mayo subscore of 0 and to determine if abnormal mucosal and vascular pattern detected on HD iSCAN endoscopy are associated with worse prognosis of the disease.
79 patients (34 female, median age 48, range 19-72) with quiescent UC Mayo subscore of 0 were followed for a median period of 19 months. All of these patients were previously endoscopically assessed by WLE and HD iSCAN (Pentax EPKi processor (EC-3490Fi; Pentax Tokyo) and Mayo endoscopic subscore was assigned to patients according to WLE findings. Mucosal pattern on iSCAN was graded as 1 = normal, 2 = mosaic pattern, 3 = tubular-gyrus, 4 = nodular rosette. The vascular pattern was graded as 1 = normal, 2 = spiral isolated vessels, 3 = crowded tortuous vessels, 4 = irregular vessels. The histologic grading system New York Mount Sinai score was used to assess the grading of inflammation on histology. The clinical outcome was assessed by monitoring Mayo clinical score, CRP levels, further endoscopic evaluation, changes in treatment, use of steroids, introduction of new medication, admission to hospital and colectomy rate. Statistical analysis was performed with Chi Square test and compared the endoscopic findings between patients that flared and patients that remained stable.
Results: Eleven patients (13.9%) out of 79 developed a relapse of UC. The initial endoscopic assessment of these eleven patients showed an abnormal mucosal pattern in 2 patients (18.2%) and an abnormal vascular pattern in 7 patients (63.6%). Amongst the 68 patients that remained stable, 35 (51.5%) presented an abnormal vascular pattern and 10 (14.7%) had an abnormal mucosal pattern on HD iSCAN colonoscopy. Histologic assessment showed quiescent colitis in all patients. There was no statistical significance between patients that relapsed and those that remained stable when comparing the distribution of normal and abnormal iSCAN scoring.
Conclusion: A high proportion of patients with mucosal healing presented subtle residual changes detected by HD iSCAN endoscopy. However, this was not associated with increased frequency of relapse or worse outcome of the disease. A more precise endoscopic score is needed to better describe the endoscopic features of mucosal healing in those patients that relapse after initial Mayo endoscopic score of 0.
Disclosure of Interest: None declared

P0810 QUALITY OF COLONOSCOPY IN NATIONAL COLORECTAL CANCER SCREENING PROGRAME IN CROATIA

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Introduction: The Croatian National Colorectal Cancer Screening Program was established by the Ministry of Health, and started at September 2007.
Aims & Methods: The Croatian National Colorectal Cancer Screening Program was established by the Ministry of Health, and started at September 2007. The aim of this study is to assess the quality of screening colonoscopy based on the fecal occult blood test (FOBT- guaiac Hemognost card-test).From 1.419.639 individuals invited to CRC screening till the end of first cicle, 288.935 (21%) persons returned correctly applied stool specimen on FOBT cards, and among them there were 15.578 (6.3%) positive. Colonoscopies were performed in 10.428 cases (67%), by 62 endoscopists in 24 centers. The quality of colonoscopies were analyzed for sample of 1003 colonoscopies, using caecal intubation rate (CIR), the adenoma and carcinoma detection rate (ADR, CDR), percentage of polypectomy during the first colonoscopy, and quality of colon cleaning. All parameters were assessed for the whole population, and the individual centers.
Results: In this sample, CIR for whole population was 82%, for individual centres 18–100%. We found 1028 polyps in 391 colonoscopied persons (ADR-39%, for centres 0–51%), and 47 cancers (CDR–4,7%). 428 (42%) polyps were immediate removed during the screening colonoscopy (for centres 0–92%). Remaining polyps, mostly larger than 1.5 cm, were scheduled for second colonoscopy. Colon cleaning was satisfactory for good and complete examination in 690 (68%), inadequate in 248 (25%), and very bad in 65 (7%) persons.
Conclusion: Caecal intubation rate was generally satisfactory in most of endoscopic centres. Numbers of polyps and cancers were very high, but proportion of polypectomies during the first screening colonoscopies was rather low. The poor colon preparation and cleansing was the main reason for inadequate examination and should be improved. On the other hand, it is very important to achieve standardized skills of endoscopists, or even, if needed, temporary exclude inadequatelly trained endoscopists from program. It is also required to assure satisfying endoscopic equipment or exclude centres where it is uncomplete or inadequate.
Disclosure of Interest: None declared

P0811 IMPACT OF NEW-GENERATION ENDOSCOPES ON COLONOSCOPY RESULTS

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Introduction: Colonoscopy remains the most accurate method for detecting pathologic lesions within large intestine. It can reveal colorectal neoplasm at asymptomatic preinvasive stage allowing for its simultaneous treatment. In recent years the amount and quality of endoscopic examinations have systematically risen. Examination technique and endoscopic equipment have evolved. Electronic video endoscopes offer now a wide field of view with high resolution imaging and electronic colorization of mucosa. Mechanical construction of the endoscope has been redesigned to improve coecal intubation.
Aims & Methods: The aim of this study was to compare colonoscopy results of asymptomatic patients from the same endoscopic center across two date ranges separated by 12 year interval. Retrospective analysis enrolled 3905 colonoscopies performed in one endoscopic center in 2000 – 2001 and 2013 respectively. All examinations were financed by the Ministry of Health as a national screening program for early colorectal cancer detection. Patients aged 40-65 without symptoms suggesting colorectal cancer were included. Analysis concerned frequency of pathological lesions detection, cecal intubation and adenoma detection rates.
Results: Patients were divided into two different groups according to the year in which the colonoscopy was performed. Group I involved 1505 patients examined in 2000-2001 and group II - 2400 examined in 2013. Incidence rate of pathological lesions was 18.4% in group I vs. 30.7% in group II regarding polyps, 20% vs. 24% regarding diverticula, 1% vs. 1.3% regarding hemangiomas and 8% vs. 2.2% for inflammatory lesions, respectively. Colorectal detection rate was 1.2% in both groups. Adenoma detection rate increased from 11.2% in group I to 18.12% in group II.
Conclusion: New-generation endoscopes and physicians who constantly improve their skills contributed to improvement of the detection rate of all polyps, adenomas and diverticula. However, colorectal cancer detection rate still remains the same. The inflammatory lesions incidence was less frequently observed in group II, what undoubtedly results from more restrictive qualification of individuals for screening endoscopy.
Disclosure of Interest: None declared

P0812 COMPARISON AMONG CONVENTIONAL 4L POLYETHYLENE GLYCOL, SODIUM PICOSULFATE AND MAGNESIUM CITRATE, AND LOW-VOLUME PEG PLUS ASCORBIC ACID AS BOWEL PREPARATIONS FOR COLONOSCOPY: A PROSPECTIVE SINGLE-BLINDED RANDOMIZED CONTROLLED TRIAL

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Introduction: There are few data that compare among the three widely used bowel preparations: conventional 4L polyethylene glycol (4L PEG); sodium picosulfate and magnesium citrate(SPMC); and low-volume PEG plus Ascorbic acid(2L PEG + Asc).
Aims & Methods: The aim of this study is to compare among the three bowel preparations in the efficacy, tolerability, and safety.
228 patients undergoing outpatient elective colonoscopy were randomly assigned to one of the three bowel preparations by computerized randomization in a single-blinded prospective study. The three bowel preparations were as follows: Group A (n = 78), 4L PEG solution; Group B (n = 74), 3 sachets of SPMC as a split dose; or Group C (n = 76), 2L PEG + Asc as a split dose. Additional stimulant laxative (Bisacodyl 10mg) was taken at the night before colonoscopy in all groups. All colonoscopy images were recorded into computed video files. One endoscopist blinded to the type of preparation gave a bowel cleansing score using recorded video files according to the Aronchick bowel preparation scale and Boston bowel preparation scale. And tolerability and safety were evaluated by a questionnaire immediately before the procedure.
Results: Age, gender distribution, history of DM, previous abdominal surgery, constipation in the three groups were not different significantly from each other. Data analysis showed that efficacy by Aronchick bowel preparation scale and Boston bowel preparation scale was not different significantly among three groups. There were no significant differences among the three groups in tolerability such as overall satisfaction by visual analogue score, consumed volume, willingness to repeat the same preparation. But, taste in SPMC group was significantly better than that in other two groups. The factors associated with safety such as abdominal distension, nausea, vomiting, general weakness were not significantly different among the three groups.
Conclusion: There were no significant differences among three bowel preparations in colonic cleansing efficacy. But, taste in SPMC group was significantly better than that in other two groups.
Disclosure of Interest: None declared

P0813 EVALUATION OF THE USEFULNESS OF BALLOON-ASSISTED ENDOSCOPY IN ERCP-RELATED PROCEDURES FOR PATIENTS WITH SURGICALLY ALTERED GASTROINTESTINAL ANATOMY

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Introduction: The endoscopic approach to pancreatobiliary disease with surgically altered gastrointestinal anatomy has conventionally involved very difficult procedures, but balloon-assisted endoscopy(BAE) has made them practical. In this study, we divided endoscopic retrograde cholangiopancreatography (ERCP)-related procedures performed in our hospital for patients with postoperative gastrointestinal reconstruction into 2 groups, a group using BAE and a group without BAE to retrospectively investigate the usefulness of BAE.
Aims & Methods: The study involved 198 cases (125 patients, including 101 males and 23 females) who underwent ERCP-related procedures performed in our hospital for patients with postoperative gastrointestinal reconstruction (excluding Billroth I reconstruction) between February 2002 and December 2014. Reconstructive procedures included 137 cases of Billroth II (B2), 39 cases of Roux-en-Y (R-Y), and 22 cases of post-pancreatoduodenectomy (or post-choledochojejunostomy). 64 patients had bile duct stones, 22 had malignant biliary strictures, 11 had bilioenteric anastomotic strictures, and 27 had other diseases (such as those who underwent detailed examination for pancreatic tumor). The cases were divided into group A, consisting of 149 cases of normal endoscopy (conventional direct-view endoscopy, colonoscopy, forward oblique viewing endoscopy, and backward oblique-viewing endoscopy), and group B, consisting of 49 cases of balloon endoscopy (single and double balloon endoscopy), to compare the rate of reaching the blind end, cannulation success rate, procedure completion rate, and complications between the groups.
Results: The rates of reaching the blind end were 85.2% (127/149) and 98.0% (48/49) in groups A and B. The cannulation success rates were 92.9% (118/127) and 75.0% (36/48) in groups A and B. The procedure completion rates were 76.5% (114/149) and 65.3% (32/49) in groups A and B. The rate of reaching the blind end was significantly higher in group B ($P = 0.0159$), whereas the cannulation success rate was significantly higher in group A ($P = 0.0011$). There was no difference in the procedure completion rate between the two groups. Complications included 4 cases of mild acute pancreatitis (3 cases in group A and one in group B), two cases of hyperamylasemia (both in group A), and 3 cases of intestinal perforation (two cases in group A and one in group B) (including two cases of emergency laparotomy [one case in group A and one in group B]).
Conclusion: The use of balloon endoscopy improved the rate of reaching the blind end in ERCP-related procedures for patients with postoperative gastrointestinal reconstruction. On the other hand, it is desired to develop not only the technology but also the devices for balloon-assisted ERCP to improve the cannulation success rate and procedure completion rate.
Disclosure of Interest: None declared

P0814 RISK FACTORS OF POST ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS AND EFFECTIVENESS OF PROPHYLAXIS IN JAPAN: A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY BY OSAKA PANCREAS FORUM (OPF)

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is an important procedure for diagnosis and management of pancreato-biliary disease. However, occurrence of complications, especially post-ERCP pancreatitis (PEP) is a huge problem. Rectal administration of 100 mg dose of non-steroidal anti-inflammatory drugs (NSAIDs) was reported to prevent PEP. However, only 25 or 50 mg of NSAIDs can be available and usable in Japan.
Aims & Methods: The aim of this study was to investigate the rate and risk factors of PEP and to assess effectiveness of prophylaxis in Japan. This was a prospective multicenter observational study. We created a common database of ERCP and each endoscopist entered data prospectively. Nineteen centers of Osaka Pancreas Forum joined this study. Study period was from October 2012 to February 2014. This protocol was approved by ethics committee at all participating centers. The definition of PEP was based on consensus criteria.
Results: A total of 2681 patients received ERCP during the study period. Patients who had undergone gastric or biliary surgery (166 patients) and who were unable to reach papilla because of perforation (3 patients), stenosis (6 patients), complications during ERCP (1 patient), or unable to attempt cannulation because of tumor invasion (2 patients) were excluded from analysis. In 2503 patients, the rate of PEP was 6.4%. Multivariate analysis revealed native papilla (odds ratio [OR] 2.96), female (OR 1.78), younger age (35-70) (OR 1.50 compared to age over 70), longer procedure time (more than 60 minutes) (OR 1.96 compared to time less than 30 minutes), pancreatogram (OR 2.57), double-guidewire cannulation (OR 1.87), endoscopic papillary balloon dilation (EPBD) (OR 2.91), biopsy or brush cytology on common bile duct (OR 1.74), transpapillary self-expandable metallic stent insertion (OR 4.71), bleeding after ERCP (OR 4.59), 25 mg administration of rectal diclofenac (OR 2.85 compared to no administration) were the significant risk factors of PEP, and history of acute pancreatitis (OR 0.33), pancreatic cancer (OR 0.53) were the significant protective factor of PEP.
Although 25 mg administration of rectal diclofenac was a significant risk factor, 50 mg administration of that was not a significant risk factor. Taking into account the bias that rectal diclofenac was selectively administered to patients who were considered vulnerable to PEP, 50 mg administration of rectal diclofenac was presumably effective to prevent PEP.
The frequency of PEP in the patients with pancreatic stent placement was significantly decreased compared to those without stent, when they were administered pancreatogram, EPBD, double-guidewire cannulation or biopsy or brush cytology on common bile duct.
Conclusion: We reported the rate and risk factors of PEP in Japan. Pancreatic stent may be effective to prevent PEP in patients with pancreatogram or procedures traumatic for papilla. Twenty-five mg rectal administration of NSAIDs may insufficient to prevent PEP. We need further investigation about administration dose of NSAIDs and its safety.
Disclosure of Interest: None declared

P0816 LEARNING CURVE OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) in patients with surgically altered anatomy is still challenging. In order to attain competence in performing this procedure, intensive training is necessary.
Aims & Methods: The study aim was to express development in ERCP in patients with surgically altered anatomy as a learning curve. We evaluate ERCP procedures by using single-balloon enteroscopy (SBE) at Yokohama City University Hospital (YCUH) in Japan between 2011 and 2014. In our facility, the same endoscopist performed the insertion into the target site, and ERCP procedures.
Results: 4 endoscopists were included in this study who have experienced more than 400 cases of the ERCP in normal anatomy. A total of 211 ERCP procedures were carried out in patients with surgically altered anatomy. The breakdown of surgical procedures was as follows: Roux-en-Y (R-Y) reconstruction (n = 55 [26.1%]), pancreaticoduodenectomy (PD) (n = 46 [21.8%]), hepaticojejunostomy (n = 80 [37.9%]), and Billroth II reconstruction (n = 30 [14.2%]). The overall success rate of reaching the target site was 94.3% (199 of 211 ERCP procedures). The overall mean time required to reach the target site was 22.8 min. The overall ERCP procedural success rate was 88.1% (186 of 211 ERCP

procedures). When the data for all the individual endoscopist assessment periods were combined, the overall insertion rate and ERCP procedural success rate were seen to gradually increase with the total of ERCPs performed in patients with surgically altered anatomy. According to learning curve per block of 10 ERCPs, in the ERCP number of less than 20, insertion rate was 82.0%, ERCP success rate was 75.4%, in 20-30 ERCPs, insertion rate was 93.3%, ERCP success rate was 83.3%, in more than 30 ERCPs, insertion rate was 96.9%, ERCP success rate was 94.0%.

Conclusion: Our findings suggest that more than 30 cases were required for competence development in ERCP with surgically altered anatomy.

Disclosure of Interest: None declared

P0817 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN ACUTE BILLIARY PANCREATITIS: SAFETY, EFFICACY AND IMPACT ON THE OUTCOME

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Introduction: The role of endoscopic retrograde cholangiopancreatography (ERCP) in the setting of acute billiary pancreatitis (ABP) is still a matter of debate.

Aims & Methods: To evaluate the safety and efficacy of ERCP in ABP and its impact on the outcome. We conducted a retrospective evaluation of ERCP performed in the setting of ABP, over a period of 11 years. Data from ERCP reports and clinical files was analyzed.

Results: Ninety-four cases were observed [Male sex 40 (42.6%); medium age 74.6+/- 12.8 years]. Seventy-three patients (77.7%) presented with severe ABP and 10 patients (10.6%) had associated cholangitis. ERCP was performed in a median of 3 days after ABP onset (range: 0-93), with 58 patients (61.7%) being submitted to early ERCP (<72 hours). Successful canullation was obtained in 92.6% of the cases. Coledocolithiasis was confirmed in 37 cases (39.4%). Spinctherotomy was performed in 83 patitens (91.5%). There were complications related to the procedure in 10 patients (10.6%): 8 post-sphincterotomy bleeding (controlled with endoscopic treatment) and 2 sedation related complications (reverted). Medium in-patient time was 11 days (range: 1-79). Early ERCP did not affect in-patient time. Thirty days mortality was 9.6%. Patients submitted to early ERCP didn't have a significant lower mortality rate. Local complications (pancreatic necrosis, collections, pseudocysts and gastrointestinal bleegind) were seen in 44.7% of cases. There was no significant association between early ERCP and the development of local complications.

Conclusion: ERCP is safe in the setting of ABP. Performance of early ERCP did not affect in-patient time, mortality or the development of local complications.

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P0818 ENDOSCOPIC PAPILLARY BALLOON DILATION WITH BILIARY SPHINCTEROTOMY : THE IDEAL TECHNIQUE FOR LARGE COMMON BILE DUCT STONES?

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Introduction: Endoscopic papillary balloon dilation (EPBD) with biliary sphincterotomy (BS) has been widely adopted when performing endoscopic retrograde cholangio-pancreatography (ERCP) for removing common bile duct stones larger than 10 mm.

Aims & Methods: The aim of this study was to compare results from EPBD with BS and BS alone (control group, CG) when treating large common bile duct stones.

We performed a rectrospective cohort study involving all cases of large common bile duct stones treated endoscopically in a single institution. The inclusion period was from 2011-2014 (4 years). EPBD was performed using a hydrostatic balloon ranging from 10 to 15 mm. We analysed efficacy (complete extraction, number of sessions needed, need for biliary stenting and lithotripsy), safety (complication rate) and recurrence.

Results: 110 patients were included. EPBD with EST was performed in 73 (66.3%), 61.6% were female and median age was 76 ± 9.4 years. GC comprised 37 patients (33.7%) 54.1% were female and median age was 77 ± 8.2 (p = ns). In EPBD with EST group, 70.6% presented multiple common bile duct stones versus 48.9% in CG ($p < 0.01$). Mean diameter of the largest stone was 15.3 ± 4.2 mm (10-30 mm) versus 16.1 ± 6.3 mm (10-35 mm) in CG (p = ns). The stones were totally removed in a single session in 73.9% versus 40.5% ic CG ($p < 0,01$). Complication (8.2% vs 8.1%, p = ns) and recurrence (5.4% vs 5.4%) rates were comparable between the two groups.

Conclusion: EPBD with BS was safe and effective in removing large common bile duct stones. When compared with BS alone, this method allowed to remove all stones more frequently in a single session, with less need for biliary stenting and no increase in complications.

Disclosure of Interest: None declared

P0819 ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION FOR TREATMENT OF LARGE BILE DUCT STONES ASSOCIATED WITH POST-PROCEDURE PANCREATITIS – MYTH OR REALITY?

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Introduction: Endoscopic papillary large balloon dilation (EPLBD) is a well-known procedure for the treatment of common duct stones larger than 10 mm. However, it is classified as an independent risk factor for post-procedure pancreatitits (PPP) and is still not recommended as an alternative to sphincterotomy in routine ERCP.[1]

Aims & Methods: The aim of this study was to acess cases of PPP associated with EPLBD in our institution and correlate them patient and procedure related risks factors.

A rectrospective single-center cohort study was performed, including all cases of large common bile ducts (diameter more than 10 mm) treated using EPLBD with biliary sphincterotomy. Inclusion period was four years (2011-2014). To perform EPLBD, a hydrostatic baloon was used (10-15mm) during at least one minute. We defined PPP as a clinical syndrome consistent with acute pancreatitis with hyperamylasemia (level of amylase > 3 times the upper limit of normal) and increased epigastric pain persisting for ≥24 hours after the procedure. We analysed the risk factors for PPP (patient and procedure-related). Incidence and severity of PPP were studied.

Results: 73 patients were included in this study. 61.6% were female. Mean age was 76 ± 9.4 years; 5.4%(n = 4) were younger than 50 years. 4.1%(n = 3) had a previous acute pancreatitis episode. None of the patients had normal bilirrubin levels or was suspected to have of Oddi sphincter disfunction. As for procedure-related risks factors, infundibulotomy was performed in 3 cases; pancreatography and pancreatic sphincterotomy were not performed. PPP prophylaxis was performed in a total of 3 patients (with administration of rectal indometacine in two and pancreatic stent in one). There was not a single case of PPP.

Conclusion: EPLBD with biliary sphincterotomy did not increase the incidence of PPP in patients with large bile duct stones. Its role as an independent risk factor probably deserves a more detailed analysis.

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Disclosure of Interest: None declared

P0820 ERCP-GUIDED CHOLANGIO-PANCREATICOSCOPY USING A SINGLE-OPERATOR SYSTEM. AN APPRAISAL OF ITS CLINICAL VALUE BASED ON A UNIQUE EXPERIENCE

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Introduction: The single-operator peroral cholangio-pancreaticoscopy enables direct visualization of duct lesions, biopsy, and therapeutic interventions in the biliary and pancreatic ductal systems. This device was introduced into clinical practice in 2007 under the trade name Spyglass (Spyglass direct visualization system, Boston Corp.). Ever since, it has been met with divergent reactions from being a valuable tool for use in diagnosis and therapy to basically offering no relevant information for the ensuing management of the patient. At Karolinska University Hospital the Spyglass technology was introduced early and has since then frequently been utilized according to a standardized protocol. Accordingly we have collected a unique experience and hereby we have critically analyzed the clinical usefulness of the technology in the diagnosis and treatment of biliary-pancreatic diseases.

Aims & Methods: All Spyglass procedures performed between March 1, 2007, and December 31, 2014, were retrospectively reviewed. Each procedure's diagnostic yield and therapeutic value was evaluated using a 4 grade scale; where 1 = No diagnostic or therapeutic value. 2 = Information gained but did not affect clinical decision-making, if a therapeutic intervention was performed it did not alter the clinical course of the patient. 3 = Information gained which had an impact on the clinical decision-making. Therapeutic intervention completed which had a subsequent impact on the course of the disease management. 4 = Essential and critically important information was gained for the clinical decision-making. Therapy performed which solved the clinical problem leading to no further requirements for diagnostic or therapeutic modalities.

Results: Over approximately 8 years, 365 Spyglass procedures were performed. The overall post-procedural morbidity was 13%, where one case of severe pancreatitis was seen. The main indications for the procedure were; indeterminate stricture (28%), primary sclerosing cholangitis (20%), IPMN (17%), complex cholelithiasis (19%), chronic pancreatitis- including lithotripsy (8%) and miscellaneous in 7% of the cases. In 70% of our patients, the bile ducts were the main target whereas the pancreatic duct was aimed for in 22%. When the clinical usefulness was assessed according to the 4 grade scale, we found the Spyglass procedure of pivotal importance in 20% of the cases and grade 3 was scored in

36%. Information gained from, or therapy performed during the procedures did not affect clinical decision-making in 44% (grade 1+2).
Conclusion: The single-operator peroral cholangio-pancreaticoscopy technique is an advanced technique for intraluminal visual inspection, and for therapeutic intervention of the biliary and pancreatic ducts associated with an increased risk of intra- and post-procedural adverse events, which shall be balanced against the information and options offered by the technique. We scored the value of the procedure as clinically significant in 56% of the cases, which signifies an important clinical role, mandating further investigation.
Disclosure of Interest: None declared

P0821 EVALUATION OF THE SHORT TYPE SINGLE- AND DOUBLE-BALLOON ENDOSCOPY ASSISTED ERCP IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY

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Introduction: Background: The pancreatobiliary disease in patients with altered GI anatomy is difficult to be intervened by endoscopic diagnosis and therapies. The development of the balloon assisted endoscope (BAE) radically made the endoscopic approaches feasible. The BAE enabled the deep insertion to the blind end, and the short type BAE made ERCP-related interventions easier to accomplish due to its applicability to almost all the devices that are used for conventional ERCP.
Aims & Methods: Objective: We evaluated utility of ERCP using short DBE (DB-ERCP) and SBE (SB-ERCP).
Patients and Methods: Between February 2006 and February 2015, we performed DB-ERCP in total of 734 patients with surgical anatomic variations (734 procedures (pro.); 400 pro. (220 patients (pts.)) for Roux-en-Y reconstruction (R&Y), 112 pro. (79 pts.) for Billroth II gastrectomy (BII), 110 pro. (44 pts.) for pancreatoduoderectomy (PD), 79 pro (39 pts.) for pylorus preserving pancreaticoduodenectomy (PpPD), and 33 pro. (21 pts.) for others) and SB-ERCP in 26 patients with surgical anatomic variations (26 pro.; 12 pro. (12 pts.) for R&Y, 3 pro. (3 pts.) for BII, 4 pro. (4 pts.) for PD, 5 pro. (5 patients) for PpPD, and 2 pro. (2 pts.) for others). We retrospectively evaluated the success rate of reaching the blind end, the therapeutic success rate, and occurrence of complications.
Results: Result: Deep insertion of the short DBE to the blind end was successful in 665 of the 677 procedures (98.2%). The success rates by type of surgical anatomic variations were; 98.3%for R&Y, 99.1% for BII, 98.2% for PD, 97.5% for PpPD, and 100% for others. Whereas, deep insertion of the short SBE to the blind end was successful in 24 of the 26 procedures (92.3%). The success rate by type of surgical anatomic variations were; 98.1% for R&Y, 100% for BII, 100% for PD, 100% for PpPD, and 100% for others. As for 2 patients in whom short type SBE failed to reach the blind end, the procedure was successfully accomplished after switching the scope to short type DBE. Deep biliary cannulation in DB-ERCP was successful in 702 of the 772 procedures (97.2%). The success rates by type of surgical anatomic variations were; 98.0% for R&Y, 94.6% for BII, 99.1% for PD, 96.1% for PpPD and 93.5% for others. Therapeutic intervention was achieved in all of the 772 procedures in which deep cannulation was successful (100%). Whereas, deep biliary cannulation in SB-ERCP was successful in 22 of the 24 procedures (91.7%). The success rates by type of surgical anatomic variations were; 90.0% for R&Y, 100% for BII, 100% for PD, 100% for PpPD and 50% for others. The therapeutic success rate was 100%. Complications for all the DBE-applied procedures were observed in 40 of the 734 procedures (5.4%). The rates of occurrence by type of surgical anatomic variations were; 5.5% for R&Y, 11.6% for BII, 2.7% for PD, 2.5% for PpPD and 0% for others. For all the SBE-applied procedures, only 1 case of laceration was observed in patients with R&Y (3.8%).
Conclusion: Conclusions: ERCP by BAE is highly effective and safe for pancreatobiliary disease in patients with altered GI anatomy. Especially the short type BAE has proved its high performance, however further improvement is yet to be expected.
Disclosure of Interest: None declared

P0822 THE PRECUT RATE: IS THERE A CORRELATION WITH INCREASED COMPLICATION RISK? RESULTS-FROM THE GERMAN SPHINCTEROTOMY REGISTRY

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Introduction: Precut sphincterotomy seems to be associated with an increased complication rate. Whether this increased risk is caused by the procedure itself or by unfavourable circumstances under which it is used, is not yet clear. Early application of precut techniques might even reduce complications. Nevertheless, in 2006, the ASGE proposed a target precut rate below 15% as a possible quality indicator for ERCP. Data that show a clear correlation between precut rate and complication risk are missing, especially in a community setting. Here, we report results obtained by the German Sphincterotomy Registry.
Aims & Methods: Data obtained by the German Sphincterotomy Registry were analysed. 44 hospitals in Germany reported all patients that had undergone sphincterotomy during a one-year time frame between 2004 and 2007. Procedural variables concerning sphincterotomy setting and technique were collected prospectively and complication rates assessed before hospital discharge.
Results: 812 precut sphincterotomies and 4529 bile-duct sphincterotomies were included in the analysis. Participating hospitals reported between 26 and 247 sphincterotomies and 0 to 80 precut sphincterotomies during a given one-year period. The median precut rate between hospitals was 15.7% and ranged from 0.0 to 43.5%. Precut sphincterotomy was associated with a significantly increased complication rate of 17.6% vs. 9,0% of patients undergoing standard bile-duct sphincterotomy. An increased complication rate was observed for all subgroups of complications. However, a higher institutional precut rate was not associated with an increased complication risk (Spearman's rank correlation coefficient: 0.04, $p = 0.8$)
Conclusion: In our Registry, which largely represents the common sphincterotomy practice in Germany in community settings, the institutional precut rates varied widely. This seems to reflect differences in the timing and indication for precuts. Although precuts are associated with a higher complication rate, there is no correlation between high institutional precut rate and the higher number of complications, which indicates that a precut itself is no risk factor. We therefore conclude that the precut rate should not be used as a quality indicator for the quality of intraprocedural ERCP.

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Disclosure of Interest: None declared

P0823 THE COMBINED USE OF THE EUS-FNA AND BILIARY BRUSHING INCREASES ACCURACY OF CYTOLOGICAL DIAGNOSIS IN PANCREATOBILIARY MALIGNANCES

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Introduction: Fifteen percent of patients with suspected pancreatobiliary malignancy that undergo surgery without a cytological assessment have a benign lesion. Cytological or histological diagnosis of pancreatobiliary malignancies before surgery is desirable in order to avoid unnecessary interventions.
Aims & Methods: We conducted a study in order to assess whether the combined use of biliary brushing and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) has greater accuracy than the individual procedures in diagnosing pancreatobiliary malignancies before surgery. We recruited 25 patients with probable pancreatobiliary malignancy who underwent both biliary brushing and EUS-FNA at the Gastroenterology Unit of Azienda Ospedaliero-Universitaria Santa Maria della Misercordia, Udine (Italy). After brushing procedure, both collected material and cytology brush were sent for cytological analysis. The results of cytology were compared to the results of histology from surgical specimen, in order to evaluate the diagnostic accuracy of the two procedures.
Results: Histology of surgical specimen confirmed the diagnosis of pancreatobiliary malignancy in 24 of 25 patients, benign lesion caused by chronic pancreatitis was identified in one patient. Cytology from biliary brushing provided a correct diagnosis in 9 patients, with diagnostic accuracy of 36%, including the patient with a benign lesion. For the remaining 16 patients (54%), cytological diagnoses were as follows: indeterminate because of poor quantity or quality of the specimen in 15 patients, negative in one case (1 false negative). EUS-FNA provided a correct diagnosis in 18 patients with diagnostic accuracy of 72%, including the patient with a benign lesion. In 7 patients (28%) EUS-FNA didn't provide any result because of the poor quality of the specimen. The combined diagnostic accuracy of both methods was 80% as they together provided a correct diagnosis in 20 patients. The additional diagnostic gain derived from the joint use of biliary brushing and EUS-FNA was 11 cases, compared to biliary brushing alone (+44%) and 2 cases compared to EUS-FNA alone (+8%).
Conclusion: The combined use of the EUS-FNA and biliary brushing results in increased accuracy of cytological diagnosing in pancreatobiliary malignancies. The biliary brushing as an addition to EUS-FNA should be considered in patients undergoing the endoscopic retrograde cholangiopancreatography (ERCP) in therapeutic purposes.
Disclosure of Interest: None declared

P0824 A NEW PROTOTYPE OF SHORT SBE FOR ERCP IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: The recent advent of balloon enteroscopy has achieved to perform ERCP in patients with surgically altered anatomy. However we have to use special long devices because of the long length of endoscope and can't use wire-guided devices because of smaller channel. Then we have designed newly developed short-type prototype of single balloon enteroscope (SBE) and investigated its usefulness.
Aims & Methods: Then we have designed newly developed short-type prototype of single balloon enteroscope (SBE) and investigated its usefulness. From 2009 up to now, we have performed 233 ERCP in 160 patients (R-Y: 110, B- II: 50) with a new prototype of short enteroscope, which is 152 cm in length, 9.2 mm in diameter, and with 3.2 mm working channel. And we historically compared with a standard enteroscope which is used in 26 patients (R-Y: 18, B- II: 8) from 2007 to 2009, 200 cm, 9.2 mm, and with 2.8 mm working channel.
Results: Among the all sessions of ERCP, the rate of prototype and standard one of reaching the blind end was 88% (136/155), 84% (16/19) in R-Y, and 95 % (74/78), 100% (9/9) in B-II. The diagnostic success rates were 81%(80/99), 68% (11/16) in R-Y, and 84% (27/31), 89% (8/9) in B- II. The therapeutic success rates were 94% (75/80), 90% (9/10) in R-Y, and 96% (64/67), 100% (8/8) in B-II. The mean procedure time were 44.0 min., 50.6 min. in R-Y and 41.0 min., 38.4 min. in B-II. Because of the short length of endoscope, most conventional devices of ERCP could be used. And because the channel diameter was 3.2 mm, we could perform with wire guided devices. Hyperamylasemia and post-ERCP pancreatitis occurred 15.5% (24/155), 18.8% (3/16) and 5.2% (8/155), 12.5% (2/16) in R-Y, and 7.7% (6/78), 11.1% (1/9) and 0% (0/78), 0% (0/9) in B- II. Perforation occurred 2.6% (4/155), 0% (0/18) in R-Y, and 1.3% (1/78), 0% (0/9) in B- II.
Conclusion: Short-type SBE is effective for ERCP in patients with surgically altered anatomy and allows most conventional ERCP devices to be used.
Disclosure of Interest: None declared

P0825 USEFULNESS OF CONTRAST-ENHANCED EUS FOR INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM (IPMN) PATIENTS WITH MURAL NODULES

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Introduction: Endoscopic ultrasonography (EUS) is a modality with high resolution. Recently, EUS has made it possible to use new diagnostic imaging techniques, such as contrast-enhanced EUS (CE-EUS). Furthermore, CE-EUS has been reported to be useful in evaluating for Intraductal papillary mucinous neoplasm (IPMN) with mural nodules.
Aims & Methods: The aim of this study is to evaluate the usefulness of CE-EUS relative to other imaging methods for diagnosing mural nodules of IPMN. 17 patients of IPMN who underwent CE-EUS were enrolled. EUS device system was HI VISION900 or HI VISION Avius (Hitachi Aloka Medical, Inc.) and, EG3870UTK endoscope (Pentax Co., Ltd.), or using ProSound SSDα-10 (Hitachi Aloka Medical, Inc.) and GF-UE260-AL5 endoscope (Olympus medical systems).The contrast agent used was Sonazoid® (DAIICHI SANKYO COMPANY). CE-EUS was performed after the B-mode EUS observation.
Results: The male/female ratio was 11:6, mean age was 61.8(38-78) years old, and mean cyst diameter was 20.5(8.2-50) mm, and mean diameter mural nodule was 7.3(2-16)mm . The modality by which mural nodules were detected was EUS for 5 patients, US for 5, CT for 4 and MRI for 3. Of the 17 patients, mural nodules were detected by EUS B-mode in 12 patients. B-mode imaging showed slightly high echo in 3, and low echo in 9 patients. The mural nodules in 5 of 12 patients was enhanced by CE-EUS. Seven mural nodules was not enhanced to diagnose as mucus lump or debris. Three of 7 patients with enhanced mural nodules were operated. The pathological diagnosis was Intraductal papillary mucinous carcinoma (IPMC) in 1 and Intraductal papillary mucinous adenoma(IPMA) in 2 patients.
Conclusion: CE-EUS is useful in evaluating whether mural nodule of IPMN or tumor.
Disclosure of Interest: None declared

P0826 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN HUMANITARIAN MEDICAL CAMPAIGNS: EXPERIENCE OF A TERTIARY CARE ASSOCIATION IN REMOTE AREAS IN MOROCCO

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Introduction: In developing countries, access to medical care for populations outside the large urban centers is often difficult. Endoscopic retrograde cholangiopancreatography (ERCP) is a gold standard in the management of pancreatobiliary diseases. It is often reserved for tertiary referral hospitals and until now, it is only available in a few centers in Morocco. The aims are to study the benefits of these humanitarian actions and to determine the challenges to achieve this kind of procedure in remote areas.
Aims & Methods: This is a prospective study carried out from April 2014 to April 2015, including all the medical campaign organized by "Action Urgence" Association (AU), in partnership with the Ministry of Health, local autorithies and other various partners, in public or private hospitals in the secluded areas of Morocco. We included all the patients who underwent ERCP. The characteristics collected were: age, gender, indication, outcome, complications and the main difficulties in realizing such procedures.
Results: During our study, AU organized 11 medical campaigns on a 12-month period all over Morocco, through mobile clinics involving many specialities such general surgery, pediatric surgery, ophthalmology and general medicine. Every event lasted an average of 3 days. 44 patients underwent ERCP: 30 women (68.1%) and 14 men (31.8%). The mean age was 48 years (11-80 years). The procedure was performed for treatment of choledocholithiasis in 36 cases (81.8%) (including 8 cholangitis and 5 pancreatitis), for a traumatic stenosis of the commun biliary duct (CBD) in 3 cases (6.8%), for a tumor stenosis requiring the placement of stents in 2 cases (4.5%), for a hydatid cyst fistulizing in the CBD in 2 cases (4.5%), and for 1 suspected sphincter oddities (2.27%). 5 patients (11.3%) underwent combined treatment (cholecystectomy under coelioscopy followed by endoscopic treatment) in the same procedure. The average length of hospital stay was 24 hours. We realized 35 sphincterotomies (79.5%), 6 infundibulotomies (13,6%) and 1 sphincteroclasy (2.27%). The biggest stone extracted measured 5/3 cm. treatment success was obtained from the first session in 38 patients (86.3%): 3 patients required performing a second procedure. Treatment by ERCP failed in 3 cases (6.8%). Complications were represented by 1 case of acute pancreatitis (2.27%). 1 death (2.27%) occurred as a result of severe cholangitis. The main difficulties met in these campaigns were: availability of the X-ray image intensifier, selection of patients and the difficulty of follow-up.
Conclusion: Performing ERCP in mobile hospitals provides access to tertiary centers care for population of remote areas. Our study demonstrates the feasibility of this procedure showing a good results and an acceptable complication rate. However, the organization of this kind of mobile unit requires an experimented multidisciplinary team and a significant investment.
Disclosure of Interest: None declared

P0827 AGE-APPROPRIATE SEDATIVE STRATEGY USING DEXMEDETOMIDINE AND MIDAZOLAM FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) often requires deep sedation because it is an invasive procedure. Although propofol has been widely used and accepted for ERCP, these agents occasionally cause respiratory depression. Dexmedetomidine (DEX), a highly selective α2-adrenoreceptor agonist with sedative effects and minimal respiratory effects, has recently been widely used for patients in the intensive care unit. However, its usefulness in endoscopic procedures remains unclear, particularly for elderly patients because of its effects on cardiac depression. In this study, we retrospectively investigated the safety and efficacy of DEX sedation during ERCP.
Aims & Methods: Among the patients who underwent ERCP from January 2013, 126 patients were sedated using DEX (intravenous infusion of 3.0 μg/kg/hr over 10 min followed by continuous infusion at 0.4 μg/kg/hr) with the addition of midazolam and pentazocine. Thirty elderly patients (> 81 years) were included in the study group. Additionally, pentazocine, midazolam, and propofol were administered as required to maintain a Ramsay sedation scale level of 4. For the control group, we collected information from patients who had undergone ERCP before January 2013 and who had been sedated with midazolam and pentazocine without DEX. The outcome measures were the amounts of midazolam and pentazocine administered, any adverse events associated with sedation, and patients hemodynamics.
Results: The incidence rate of decreased SpO_2 levels (3.5% vs. 11.6%, $p = 0.04$) and the median dose of additional midazolam and pentazocine were significantly lower in the DEX group than in the control group (5.2 mg vs. 12.5 mg and 7.5 mg vs. 11.4 mg, respectively; both at $p < 0.001$). There were no cases in whom propofol was required or the procedure had to be discontinued because of respiratory depression in the DEX group. The blood pressures and pulse rates were significantly lower in the DEX group than in the control group. The lower pressures and pulse rates were more common in the elderly patients in the DEX group. However, no patients required a vasopressor or suffered cardiac failure in the study group.
Conclusion: DEX reduced the incidence of respiratory complications and the total doses of other sedative agents that are concurrently administered. DEX can be used as an alternative to conventional methods for adequate sedation during ERCP even in elderly patients.
Disclosure of Interest: None declared

P0828 FULLY COVERED METAL STENTS VS MULTIPLE PLASTIC STENTING IN THE TREATMENT OF BILIARY STRICTURE AFTER LIVER TRANSPLANTATION: COST-EFFECTIVENESS ANALYSIS

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Introduction: Multiple plastic stenting (MPS) is the traditional first-line endotherapy for anastomotic biliary stricture (ABS) after orthotopic liver transplantation (OLT). However, MPS requires multiple procedures to progressively maximize dilation of ABS, thus accounting for the high costs related to the procedures and hospital stay.
Aims & Methods: Aim was to compare, in patient with ABS, fully covered self expandable metal stent (FCSEMS) with MPS as concerns respective effectiveness, complications and costs. 25 OLT patients with clinically relevant ABS were retrospectively reviewed (#12) or prospectively collected (#13). FCSEMS and MPS groups were balanced for sex, age, etiology of cirrhosis and time from OLT. Eight or 10 mm large FCSEMS were used according to biliary duct diameter and removed after 4-6 months. Number of 10 Fr plastic stents was increased at 3 months interval up to maximal dilation. At stent removal, technical success was assessed by the easy passage of a balloon catheter through the anastomosis. During follow-up patients underwent clinical, laboratory and ultrasound abdominal examinations according to a standardized protocol. In case of technical failure or ABS recurrence, the patient was crossed-over to the other endoscopic procedure, whereas surgery was carried out when facing with endotherapy failure after cross-over. Overall costs included both procedures, stents and hospitalization.
Results:

	FCSEMSn = 10	MPSn = 15	p
ERCP, #pt (range)	2 (2-3)	4 (3-9)	**<0.01**
Technical success, n (%)	9 (90%)	14 (93%)	ns
Clinical success, n (%)	8 (80%)	14 (93%)	ns
Endoscopy costs (€) / pt,	4.432	6.509	**<0.01**
Hospitali stay costs (€) / pt,	2.400	6.720	**<0.01**
Treatment costs (€) / pt,	6.352	13.452	**<0.01**

Complications occurred in 2 (8.6%) cases after FCSEMS and in 3 (4.4%) cases after MPS (p = ns). Endotherapy duration was 4 (3-18) and 8 (4-55) months in the FCSEMS and MPS groups (p = 0.001). After cross-over, endotherapy achieved clinical success in 24/25 (94%) pts at 19 (3-84) months.
Conclusion: Technical and clinical success and complication rate of FCSEMS and MPS were comparable, but FCSEMS achieved a significant reduction in costs, because of a lower number of procedures and a shorter length of hospital stay. These preliminary data suggested the role of FCSEMS as first-line endotherapy in ABS. A larger controlled randomized trial is currently ongoing to confirm the above findings.
Disclosure of Interest: None declared

P0829 TOLERABILITY OF COVERED METAL STENTS VS MULTIPLE PLASTIC STENTS FOR TREATMENT OF ANASTOMOTIC BILIARY STRICTURE AFTER LIVER TRANSPLANTATION. INTERIM ANALYSIS OF A RANDOMIZED STUDY

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Introduction: First-line endoscopic treatment of the anastomotic biliary stricture (ABS) is under debate. After orthotopic liver transplantation (OLT), high rate of technical and clinical success may be achieved by both multiple plastic stents (MPS) or covered self-expanding metal stent (CSEMS). However tolerability of these two endotherapies has never been evaluated, deserving integration in the ongoing randomized studies on effectiveness.
Aims & Methods: This prospective series was aimed at evaluating *tolerability and effectiveness* of CSEMS vs MPS in ABS management. From June 2013, 23 OLT pts with ABS were randomized to MPS or CSEMS in two Academic Centres. Age, sex, etiology of cirrhosis, time from OLT and severity of ABS were balanced between study groups. *Tolerability* was evaluated on: intensity of abdominal pain (Numerical Rating Scale, NRS), use of analgesics, need of pethidine, length of hospital stay (LOS ≥ 1 day) and early removal of stent for persistent pain. NRS was administered 1 day before ERCP (basal value) and daily after procedure with a thirty-day diary. To overcome intrapatient variability, for each value reported after maximal MPS or CSEMS, ΔNRS(daily value – basal) was evaluated. An easy transanastomotic passage of a balloon inflated at the diameter of native bile duct was considered as technical success, whereas absence of symptoms, cholestasis and bile duct dilation at US tested for clinical success. Tolerability data were correlated with severity of ABS, maximal diameter of stenting and type of endotherapy. ΔNRS > 4 was considered as relevant abdominal pain. Data were expressed as median ± IQ range. Mann-Whitney and Chi-squared (χ^2) tests were used.
Results: Tolerability data are summarized in the Table.

Parameter		MPS(n = 10)[1]	CSEMS(n = 12)	p
Pain	Pt # (%)	2 (20)	8 (67)	**<0.05**
ΔNRS (range)	0 (-2:9)	3 (-1:8)	ns	
ΔNRS > 4	Pt # (%)	2 (20)	5 (42)	ns
Need for:				
- drugs	Pt# (%)	2 (20)	8 (67)	**<0.05**
- pethidine	Pt # (%)	0 (0)	4 (33)	**<0.05**
Prolongation of LOS	Pt # (%)	1 (10)	6 (50)	**<0.05**

[1]*One patient was excluded because of mild post-ERCP pancreatitis*

Intensity of pain and use of drugs did not differ for other scheduled recordings. No patient underwent early stent removal for persistent pain and treatment is still ongoing in two MPS and three CSEMS pts. Technical success was achieved in 7 of 8 MPS pts (87%) and in 8 of 9 CSEMS ones (89%, p = ns). In one case, MPS failed due to bleeding and cross-over to CSEMS was needed for ABS treatment and hemostasis as well; in one case CSEMS failed for early migration and cross-over to MPS was needed due to cholangitis. Clinical success was achieved in 5 of 8 MPS patients (62%) at 7 mos (3-8) and in 7 of 9 (77%) CSEMS patients at 2 mos (1-16). ABS recurred in two MPS cases at 3 and 5 mos; the first was retreated with CSEMS and the other with maximal MPS. Technical and clinical success rates were not related to characteristics of population. Use of pethidine was associated with a more severe grade of ABS (>90%) (p = 0.04) and use of CSEMS but was not correlated with maximal diameter of stenting.
Conclusion: Due to its more rapid expansion, the need for analgesics was higher with CSEMS leading to a longer hospital stay. Noteworthy, the occurrence of abdominal pain did not impact on the success rate of endotherapies.
Disclosure of Interest: None declared

P0830 BALLOON ASSISTED ERC - AN ALTERNATIVE IN BILE DUCT DISORDERS IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: Bile duct disorders in patients with surgically altered anatomy are a growing problem. ERC performed with a ballon assisted enteroscope has been reported as a way to handle these problems.
Aims & Methods: To evaluate double-ballon assisted ERC in postsurgical patients. ERC were performed with a double-balloon enteroscope with a working channel of 2.8 mm. All examinations were performed by a single investigator.
Results: Thirty-six investigations were performed in 29 patients, 15 women and 14 men. Mean age was 53 year, range 17 – 73. Surgery altering the anatomy was: Liver transplantation (n = 13), Whipple-procedure (n = 5), gastric by-pass (n = 5), Billroth II (n = 4) and Bile duct reconstruction after iatrogenic damage (n = 3). Seventeen had a biliodigestive anastomosis and 12 had an intact papilla. Mean procedure time were 86 min. 23/36 procedures were performed in full anesthesia. Overall success rate per procedure were 24/36 (67 %) and per patient 22/29 (76 %). Following procedures were successfully performed: Brush- cytology (n = 4), papillotomy + dilatation of the papilla + stone-extraction (n = 3), papillotomy + stone-extraction (n = 2), stone-extraction (n = 2), dilatation of the hepaticojejunostomy + stone-extraction (n = 2), stent-removal (n = 2), stent-insertion (n = 1). Five subjects had bile ducts without pathology, of whom two had an inconclusive MRCP and 3 had a false positive MRCP. Three patients had complications: one had a bowel perforation, one mild pancreatitis and one subject had post-procedural abdominal pain.
Conclusion: Balloon assisted enteroscopy is a feasible way to gain access to bile ducts in patients with altered anatomy. However, it is cumbersome and should probably be used in selected cases.
Disclosure of Interest: None declared

P0831 THE POLYMORPHISMS AT PRSS1-PRSS2 AND MORC4 LOCI AND THE RISK OF POST-ERCP PANCREATITIS

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Introduction: The risks of post-ERCP pancreatitis (PEP) are identified as patient- and procedure-related factors. Recent data show that the polymorphisms of *PRSS1-PRSS2 (rs10273639)* and MORC4 *(rs12688220)* are associated with recurrent acute pancreatitis and chronic pancreatitis. However, the genetic contribution for PEP is still unclear.
Aims & Methods: We aim to evaluate the association between these polymorphisms and post-ERCP pancreatitis in order to improve better prognosis and better care for these patients. This is a retrospective, case-control study includes 49 cases and 101 controls that had age-, procedure-, and risk of PEP-matched with the cases in 1:2 fashion. The PEP was diagnosed and graded for severity according to the standard consensus, and the risk factors of PEP were identified according to ESGE guideline. Polymorphisms at *rs10273639* and *rs12688220* were evaluated by TaqMan technique and were identified in 133 (40 cases & 93 controls) and 150 patients repectively.

Results: The demographic data between 2 groups are not significantly different. The genotype frequencies of *PRSS1-PRSS2* (TT, TC, CC) are 26, 13, and 1 vs 67, 25, and 1 in cases and controls, respectively (p = 0.642). The genotype frequencies of *MORC4* in female (TT, TC, CC) are 8, 23, and 5 vs 12, 27, and 21 in cases and controls, respectively (p = 0.071). The genotype frequencies of *MORC4* in male (T, and C) are 5, and 8 vs 21, and 17 in cases and controls, respectively (p = 0.468). The allelic frequency of MORC4 in combination of both genders (T, C) are 44, and 41 vs 72, and 86 in cases and control, respectively (p = 0.431). In PEP cases, the allelic frequencies of PRSS1-PRSS2 (T, and C) are 59, and 13 vs 6, and 2 in mild and moderate/severe cases, respectively (p = 0.633). The allelic frequencies of MORC4 (T, and C) are 38, and 39 vs 4, and 4 in mild and moderate/severe cases, respectively (p = 0.972).

Table 1: Baseline characteristic and results of polymorphisms of PRSS1-PRSS2 and MORC4

	Case (n = 49)	Control (n = 101)	P-value
Age, mean (SD) (years)	60.3 (14.1)	60.0 (15.4)	0.901
Gender (%female)	72%	61%	0.145
Risk group (%high risk)	67%	63%	0.632
PRSS1-PRSS2 genotype frequency* TT TC CC	26131	67251	0.642
MORC4 genotype frequency TT (female)/ T (male) TC (female) CC (female)/ C (male)	8/5235/8	12/212721/17	0.071 (female)/ 0.468 (male)
PRSS1-PRSS2 allelic frequency* T C	6515	15927	0.493RR (95%CI) = 0.81(0.52-1.28)
MORC4 allelic frequency T C	4441	7286	0.431RR (95%CI) = 1.17(0.83-1.66)

* n = 113 (40 cases and 93 controls)

Conclusion: Polymorphisms at *PRSS1-PRSS2* and *MORC4* are not associated with the risk or severity of post-ERCP pancreatitis.

Disclosure of Interest: None declared

P0832 A RANDOMIZED ASSESSMENT OF A SEMI-DISPOSABLE, FIBEROPTIC SINGLE-OPERATOR CHOLANGIOSCOPE WITH A FULLY-DISPOSABLE, DIGITAL SINGLE-OPERATOR CHOLANGIOSCOPE IN A BILIARY TRACT BENCH MODEL

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Introduction: A new four-way tip deflection digital single-operator cholangioscope (DSOC); (SpyGlass DS ™ Boston Scientific, MA) has a complementary metal-oxide semiconductor (CMOS) chip for higher resolution, magnification, and field of view; it has a thin copper cable for digital transmission and lacks a separate fiber optic probe which may improve catheter tip articulation. The processor is portable for simplified setup.
Aims & Methods: The aim was to compare maneuverability between the fiber optic SOC (FSOC) and DSOC. A biliary tract model devised after input from the authors (PULSE R&D, Southampton, PA) contained three fixed "left intrahepatic" (LIHD) tracts at varying angles with colored terminal targets and a variable "common bile duct" (CBD) and "right intrahepatic" (RIHD) tracts each with two ~4mm colored targets, respectively, and multiple configurations. Seven targets were placed on the circumference. Investigators were blinded to target locations. Runs were randomized and timed with a goal to target each colored area using forceps (Spybite™). Definitions: Visual Success – identifying targets; Targeting Success – touching a target with a forceps; Complete Run – touching all targets with a surrogate metric for futility of 20 minutes. Image quality and ease of use was recorded on a visual analog scale (VAS) of 0 to 10. Time to completion was analyzed using a t-test and a negative binomial model was used to test visual and targeting success between the groups (SAS 9.4).
Results: A total of 39 runs were completed by five expert investigators; 2 were excluded due to inadequate randomization and 37 (20 DSOC, 17 FSOC) were analyzed. DSOC was superior to FSOC in terms of Visual (96% vs. 66%, p < .001) and Targeting Success (6.6 vs. 4.5, p = .007) and Complete Runs (13/20 vs. 0/17, p < .001). Five FSOC trials terminated due to futility. For fixed LIHD, DSOC achieved higher targeting success compared to FSOC (2.6 vs. 1.1, p < .001); no difference was seen with RIHD and CBD targets (4.0 vs. 3.4, p = 0.39). DSOC run completion time (minutes) was faster than FSOC (mean 10.1 vs. 15.4, p < 0.001). By VAS (0-10), investigators reported superior image quality and ease of use with the DSOC.

TABLE 1: Comparison of Fiberoptic Single-Operator Cholangioscopy with Digital Single-Operator Cholangioscopy

	Fiberoptic SOC (n = 17)	Digital SOC (n = 20)	P-value
Percentage of Targets Visualized (n)	66% (79/119)	96% (134/140)	<0.001
Variable (n)	90% (61/68)	100% (80/80)	<0.001
Fixed (n)	35% (18/51)	90% (54/60)	<0.001
Successful Targeting per Run	4.47+/-0.72	6.55+/-0.69	0.007
Variable Targets	3.41+/-0.71	3.95+/-0.22	0.394
Fixed Targets	1.06+/-0.24	2.60+/-0.68	<0.001
Time of Run	15.35+/-4.00	10.05+/-3.72	<0.001
VASImage Quality	4.25+/-0.96	8.25+/-0.50	<0.001
VASEase of Use	4.75+/-0.96	8.50+/-0.58	<0.001

Conclusion: 1) In this benchtop biliary tract model that simulated CBD and intrahepatic ducts with variable and fixed colored targets, respectively, DSOC performed superiorly to FSOC with respect to image quality and maneuverability based on the metrics of visualization, targeting, and complete runs. 2) Whether these advantages will translate to higher clinical success or be appreciated by non-experts requires further investigation.
Disclosure of Interest: R. Shah Consultancy: Boston Scientific Endoscopy, H. Neuhaus Consultancy: Boston Scientific Endoscopy, M. Parsi: None declared, D. N. Reddy: None declared, D. Pleskow Consultancy: Boston Scientific Endoscopy

P0833 EUS-GUIDED GALLBLADDER DRAINAGE : AN ALTERNATIVE TREATMENT FOR ACUTE CHOLECYSTITIS

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Introduction: Therapeutic EUS has greatly improved since the past years. Endoscopic ultrasound-guided gallbladder drainage (EUS-GBD is one of the next challenges in the field of therapeutic EUS and may become an alternative to the conventional percutaneous transhepatic gallbladder drainage for acute cholecystitis in non-surgical candidates.
Aims & Methods: This is a single center case-study of 10 EUS-GBD. All cases were reviewed retrospectively from June 2014 to March 2015. Surgery was contraindicated for all patients, most being in a palliative situation. Primary outcomes measured were technical and clinical success. Secondary outcomes were adverse events and recurence of cholecystitis.
Results: 10 patients underwent EUS-GBD with a mean age of 79 (62-92, 3M/7F). The mean follow up time was five months (3 days - 8 months). 7 cases were performed for malignant disease (pancreatic and biliary cancers). Transmural acces was prefered, offering better stability, from duodenal bulb in 8 cases and from gastric antrum in 2 cases. EUS-GBD was achieved by placement of combined metallic and plastic stents with stent in stent technique (Boston Scientific WallFlex™ biliary fully covered metallic stent 10mm x 4cm with double pigtail plastic stent 7Fr x 5cm). Technical and clinical success occured in all cases with no early adverse event. A delayed stent migration occured in one case at 3 week and was discovered by recurrence of cholecystitis, managed conservatively.
Conclusion: EUS-GBD appears to be a feasible, effective and safe technique for the treatment of acute cholecystitis in high risk patients. Further studies are needed to confirm theses results and establish safety of this procedure. Device and technical options needs also to be specified.

References

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Disclosure of Interest: None declared

P0834 OBSERVATIONAL, MULTICENTER STUDY TO EVALUATE THE DIAGNOSTIC ACCURACY OF A NEW EUS 20-GAUGE NEEDLE FOR INTRAINTESTINAL AND EXTRAINTESTINAL LESIONS

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Introduction: Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) is an accurate technique for sampling intraintestinal and extraintestinal lesions. However, cytology possesses certain limitations, which may be overcome if histological specimens are provided to the pathologist.
Aims & Methods: The aim of the study was to evaluate the feasibility and accuracy of a newly developed 20-gauge histology needle. METHODS: Retrospective

analysis of a prospectively collected data base including patients who underwent EUS-guided biopsy with the 20-gauge ProCoreTM histology needle with reverse bevel (3-HD-20) for the evaluation of intraintestinal or extraintestinal lesions. EUS procedures were performed under sedation with linear echoendoscopes (Olympus and Pentax).
Samples recovered into cytological solution or formalin and processed for histological evaluation. Results were compared to the gold standard of surgical histopathology, or global pathological, clinical and radiological assessment, and follow-up in non-operated cases. Feasibility of the procedure and different technical aspects were recorded. Percentage of samples suitable for histological evaluation and the overall diagnostic accuracy were evaluated. Results are shown as mean and standard deviation or 95% confidence interval.
Results: 51 patients (mean age 62.2 years, range 36-83 years, 26 male) were included. A total of 52 lesions were attempted to be sampled (mean size 31.88 ± 12.4mm). Indications were pancreatic mass (n = 30), intraabdominal lymph nodes (LN) (n = 6), subepithelial lesions (n = 6), liver mass (n = 3) and 1 cases of mediastinal LN, lung cancer, rectal mass, esophageal lesion, hiliar mass, intraabdominal mass and a left suprarenal gland mass. Lesions were accessed from esophagus in 3 cases, stomach in 27 cases, bulbous in 15 cases, second part of the duodenum in 6 cases and from the rectum in 1 case.
EUS-guided biopsy was feasible in 50 cases (96.1%), with a mean of 1.7 passes (range 1-4). From 50 cases completed, sample quality was adequate for histological assessment in 46 lesions (92.0%). In the intention to treat analysis, diagnostic yield was 84.6% (95%CI: 72.5-91.9) and in per protocol analysis, diagnostic yield was 88.0% (95%CI 76.2-94.4). There were 2 (3.9%) mild complications (intraparietal hematomas at the place of FNB).
Conclusion: The EUS-guided biopsy with the 20-gauge ProcoreTM histology needle provides with a very good core sample for histological evaluation allowing a high histopathological diagnostic accuracy.
Disclosure of Interest: J. Iglesias-Garcia Conflict with: International Advisor Cook, P. van Riet Conflict with: International Advisor Cook, A. Larghi Conflict with: International Advisor Cook, M. Giovannini Conflict with: International Advisor Cook, M. Petrone: None declared, J. Lariño-Noia: None declared, J. Poley Conflict with: International Advisor Cook, E. Bories: None declared, E. Davizzi: None declared, I. Abdulkader Conflict with: International Advisor Cook, G. Monges: None declared, K. Biermman: None declared, C. Doglioni: None declared, G. Rindi: None declared, G. Costamagna: None declared, P. Arcidiacono Conflict with: International Advisor Cook, M. Bruno Conflict with: International Advisor Cook, J. E. Domínguez-Munoz: None declared

P0835 OBSERVATIONAL, PROSPECTIVE, SINGLE-CENTER COMPARATIVE STUDY BETWEEN STRAIN HISTOGRAM AND STRAIN RATIO FOR THE QUANTIFICATION OF ENDOSCOPIC ULTRASOUND (EUS)-GUIDED ELASTOGRAPHY OF SOLID PANCREATIC LESIONS

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Introduction: Quantitative EUS-elastography allows quantifying tissue stiffness during a standard EUS examination. Elastography is a very accurate technique supporting the diagnosis of malignancy in solid pancreatic lesions. Elastography result may be analyzed either by strain ratio (SR) or strain histogram (SH).
Aims & Methods: Aim of the study was to evaluate the accuracy of SR and SH for the differential diagnosis of solid pancreatic masses. METHODS: A prospective, observational, comparative study was designed. 162 consecutive patients (mean age 63 years, range 17-89, 98 male), with a solid pancreatic mass at EUS were prospectively included. Elastography was performed with linear Pentax-EUS and Hitachi-Preirus. For SH, the tumor area was selected and analyzed. The mass (area A) and a peripancreatic soft reference area (B) were selected for SR analysis (quotient B/A). Final diagnosis was based on surgical histopathology, or EUS-FNA/FNB and global clinical and radiological assessment at follow-up in non-operated cases. Data are shown as mean (95%CI) and analyzed by ANOVA. Diagnostic accuracy was calculated by drawing the corresponding ROC curves.
Results: Size of masses was 35.0 ± 17.8mm. Tumors were located in the head (n = 107), body (n = 45) and tail (n = 10) of the pancreas. Final diagnosis was pancreatic adenocarcinoma (n = 106), malignant neuroendocrine tumor (NET) (n = 9), benign NET (n = 4), pancreatic metastasis (n = 9), and inflammatory masses (n = 34). Results of SH were 84.42 (76.4-92.45) in benign masses and 26.33 (24.7-28.0) in malignant tumors ($p < 0.001$). SR was 8.73 (5.21-12.2) in benign masses and 43.90 (37.8-50.0) in malignant tumors ($p < 0.001$). Sensitivity and specificity of SR for diagnosing malignancy were 100% and 92.1% (cut-off 9.74) (AUC = 0.942; 95%CI 0.88-1), and of SH 92.1% and 100%, respectively (cut-off 62.0) (AUC = 0.961; 95%CI 0.91-1). There were no differences in terms of diagnostic yield between both methods.
Conclusion: Elastography is a very useful tool for the diagnosis of malignancy in solid pancreatic masses. SR and SH are equivalent in this setting.
Disclosure of Interest**:** None declared

P0836 A COMPARATIVE STUDY OF ENDOSCOPIC ULTRASOUND-GUIDED CHOLEDOCHODUODENOSTOMY AND TRANSPAPILLARY STENT PLACEMENT IN PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION AS THE FIRST-LINE TREATMENT

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Introduction: Endoscopic ultrasound-guided choledochoduodenostomy (EUS-CDS) has gained popularity as an alternative to percutaneous biliary drainage in patients with failed ERCP. There was no comparative study as the first-line treatment for distal malignant obstruction between EUS-CDS and endoscopic trasnpapillary stenting (ETS).
Aims & Methods: The aim of this study was to compare the clinical efficacy and safety of EUS-CDS and ETS in patients with distal malignant biliary obstruction as the first-line treatment. Before May 2012, 56 patients underwent ETS, after that, 26 patients underwent EUS-CDS as the first-line treatment for the management of distal malignant biliary obstruction. We retrospectively compared the clinical success rate, adverse event rate and reintervention rate.
Results: Clinical success rate was equivalent in both groups (EUS-CDS; 96.2, ETS; 98.2%, p = 0.54). Procedure time was significantly shorter in EUS-CDS than in ETS (19.7 vs 30.2 min, $p < 0.01$). The rate of overall adverse events was not significantly different between groups (EUS-CDS; 27%, ETS; 36%, p = 0.46). Post-procedure pancreatitis was only observed in ETS group (0% vs 16%. P = 0.03). Reintervention rate at one year was 16.6 and 13.6% in EUS-CDS and ETS, respectively (p = 0.50).
Conclusion: EUS-CDS could be considered the first-line treatment of patients with distal malignant biliary obstruction due to the short procedure time and no risk of pancreatitis.
Disclosure of Interest: None declared

P0837 ENDOSCOPIC ULTRA SOUND-GUIDED INTRAHEPATIC PORTOSYSTEMIC SHUNT (EGIPS) IN A LIVE PORCINE MODEL

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Introduction: Interventional EUS is a promising novel approach in intravascular interventions. The aim of this study was to assess the feasibility and the safety of EUS-Guided Intrahepatic Portosystemic Shunt (EGIPS) in a live porcine model.
Aims & Methods: The Left Hepatic Vein (LHV) or the Inferior Vena Cava (IVC) was punctured with a needle which was advanced into the Portal Vein (PV). A guide-wire was inserted into the PV and an intrahepatic fistula between LHV and PV was created with a needle-knife. A portal pressure was recorded. The intrahepatic fistula was dilated with a balloon and an expandable biliary metal stent was deployed between LHV and PV under sonographic and fluoroscopic observation. A final portocavography validated the permeability of the stent. Euthanasia allowed necropsies.
Results: A portosystemic stenting was technically achieved in 19/21 cases. Final portocavography confirmed the stent permeability between the PV and the LHV or the IVC in 17 cases (efficacy of 81%): 4 stents were dysfunctionning because 2 were thrombosed and 2 too proximal. Portal pressure before and after shunt was achieved in 20/21 cases. Necropsies revealed that 19/21 procedures were transesophageal, and 2 were transgastric. We observed 1 hemoperitoneum and 1 pneumothorax in pig 5, 1 hemothorax in pigs 6 and 20. The morbidity was 14.2% (3/21 animals).
Conclusion: EGIPS in a live porcine model was technically feasible in 91%, functional in 81% and with a morbidity of 14.2%. EGIPS should be assessed in portal hypertension pig models and could become an option to TIPS failure.
Disclosure of Interest: None declared

P0838 NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY (NCLE) FOR THE DIAGNOSIS OF PANCREATIC MASSES: VALIDATION OF THE DESCRIBED CRITERIA (CONTACT STUDY)

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Introduction: Needle-based Confocal Laser Endomicroscopy (nCLE) is an imaging technique, which enables microscopic observation of solid organs, *in vivo* and in real-time, during an EUSFNA procedure. The CONTACT study

Abstract number: P0838

Final diagnosis	n	Sensitivity		Specificity		PPV		NPV		Accuracy	
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Adenocarcinoma	23	86%	78%	100%	100%	100%	100%	79%	67%	91%	85%
Neuroendocine neoplasm	3	100%	100%	93%	97%	60%	75%	100%	100%	94%	97%
Chronic Calcifying Pancreatitis	5	67%	40%	100%	100%	100%	100%	93%	90%	94%	91%

(Clinical evaluation Of NCLE in The lymph nodes Along with masses and Cystic Tumors of the pancreas) aims at building an image atlas, define interpretation criteria for nCLE images in the pancreatic masses and propose a first validation of these criteria.

Aims & Methods: 3 centres in France (7 investigators) took part in this prospective study. Any pancreatic mass studied by EUSFNA could be imaged by nCLE, but if a patient had multiple masses, only one of them could be imaged.

40 patients with a pancreatic mass were included prospectively during the study (June 2012 to March 2014).Out of these 40 patients, 33 were evaluable : 23 adenocarcinomas, 3 neuroendocrine neoplasms, 1 pseudopapillary tumor and 5 chronic pancreatitis.

Based on the previously described criteria (1), two validations of these criteria have been performed : one by the physicians who described the criteria (M.G, F.C, F.P, G.M), the second one by three gastroenterologists and one pathologist (B.N, B.P, L.P, A.I.L) external to the definition of the criteria.

For this evaluation, physicians were completely blinded to the clinical history of the patient, and the EUS examination. They only had the nCLE recorded sequence.

For each of the 33 patients, they were asked to give a diagnosis based on the existing criteria (1). When agreement between investigators was not complete, a consensus was reached.

Results: For the first validation (by investigators who established the classification- Group 1): IOA was perfect (k = 1) – agreement between the observers was complete in 70 % of the cases. A consensus was obtained for the other 30 %.

For the second validation (by external investigators- Group 2) : IOA was moderate (k = 0.55) – Agreement between the observers was complete in 40 % of the cases. A final consensus was obtained for the other 60 %.

Diagnostic performances of nCLE for the characterization of pancreatic masses are presented in Table 1.

Conclusion: These two validations, even preliminary due to the small number of inclusions, show a really slight difference between experts and less trained physicians: the learning curve seems to be short.

Although the sensitivity still needs to be improved (by an additional work on the criteria), the excellent specificity of nCLE for the characterization of pancreatic masses could be very usefull tu rull out malignancy and avoid repeated diagnosis procedures.

Reference

1. Needle-based confocal laser endomicroscopy (nCLE) for the diagnosis of pancreatic masses : correlation between nCLE and histological criteria (CONTACT Study), Giovannini M., Oral Presentation UEGW 2014 (OP 063).

Disclosure of Interest: None declared

P0839 PERFORMANCE OF LINEAR-ENDOSCOPIC ULTRASONOGRAPHY FOR LOCOREGIONAL EVALUATION OF AMPULLARY LESIONS

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Introduction: Accurate preoperative staging for ampullary neoplasm is mandatory for making therapeutic decisions. Endoscopic Ultrasound (EUS) has been suggested as the modality of choice in the locoregional staging of the ampullary lesions, because the high frequency ultrasound transducer probe can be placed in close proximity to the ampullary region. To date, almost all information available on staging of ampullary tumors has been obtained with radial echoendoscope, that is considered the gold standard.

Aims & Methods: Aim of the study was to compare the accuracy of linear array echoendoscope in locoregional staging of ampullary lesions, with histology and surgical pathology as gold standard. The Endoscopy Database of a tertiary referral center was reviewed, searching for patients referred for an evaluation in known or suspected ampullary lesion between January 2010 and January 2015. Patients demographic and clinical data were collected, including the lesion size and local tissue invasion. Histology from endoscopic and surgical specimens was assumed as reference standard. All EUS were performed by 3 experienced endosonographers by using linear array echoendoscopes (Pentax EG3870UTK). Data were analyzed using descriptive statistics.

Results: We identified 89 patients who underwent EUS for ampullary lesions. Among them, 48 pts were excluded (41/48 underwent EUS, without any treatment and in 7/48 histology did not confirm the suspected diagnosis). 41 pts (22 M; mean age 70.7 years± 12.1) were included in the study (5 pts previously treated with biliary stent). The mean size of the lesions was 15.9 ±7.5 mm. 23 patients (56%) were treated with whipple resection, 15 patients (37%) underwent endoscopic papillectomy, and 3 (7%) surgical papillectomy. Pathologic type of the tumors were adenoma in 18 pts (44%), adenocarcinoma in 23 pts (56%). In those undergoing endoscopic/surgical papillectomy, 16 had adenoma (89%), and 2 had adenocarcinoma (11%). Of the patients who underwent whipple resection 2 had adenoma (9%), 21 had adenocarcinoma (91%). For the assessment of local tissue invasion, the overall accuracy of EUS was 75.6% by using histology as the reference standard. Excluding pts with biliary stent, accuracy raised up to 81.1%. The diagnostic accuracy of EUS was 85.7%, 55.6%, and 80% in identifying patients with T1, T2, T3-4 stages, respectively. Overstaging by EUS occurred in 5 patients (12%), 3 of them had biliary stent. Understaging occurred in 2 patients (5%).

Conclusion: Linear EUS accurately predicts the depth of invasion in the preoperative evaluation of ampullary lesions, providing useful information for making therapeutic decisions, especially in selection of eligible patients for endoscopic treatment.

Disclosure of Interest: None declared

P0840 FINE NEEDLE ASPIRATION OF PANCREATIC CYSTIC LESIONS: A MULTICENTER, RANDOMIZED STUDY COMPARING STANDARD AND FLEXIBLE NITINOL NEEDLES

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Abstract number: P0840 Table 1: Percent aspirated unilocular PCL volume by needle type

	19G Flex Mean ± SD(N)	19G	22G	Total	19G Flex-22G P-value	19G-22G
Overall	86.9 ± 28.7(34)	80.0 ± 39.2(24)	79.3 ± 38.4(18)	82.9 ± 34.4(76)	0.453	0.946
Location						
B/T	91.3 ± 20.1(21)	94.7 ± 18.7(14)	83.4 ± 34.5(11)	90.4 ± 23.7(46)	0.380	0.248
H/U	79.8 ± 38.8(13)	59.4 ± 51.2(10)	72.8 ± 45.9(7)	71.4 ± 44.2(30)	0.741	0.551
Viscosity						
LW/SV	83.6 ± 31.5(27)	94.0 ± 23.5(18)	92.2 ± 25.4(12)	88.7 ± 27.9(57)	0.378	0.862
VV	99.8 ± 0.5(7)	38.0 ± 48.7(6)	53.4 ± 48.8(6)	65.6 ± 45.6(19)	0.046	0.497
Location & Viscosity						
B/T & NV	88.7 ± 22.6(16)	99.8 ± 0.7(11)	99.6 ± 0.7(7)	94.5 ± 16.2(34)	0.136	0.976
H/U or VV	85.3 ± 33.9(18)	63.3 ± 47.8(13)	66.4 ± 45.1(11)	73.5 ± 41.8(42)	0.240	0.856

Location: B = body, T = tail, H = head, U = uncinate; Viscosity: LW = like water, SV = somewhat viscous, VV = very viscous, NV = non viscous

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Introduction: Endoscopic ultrasound fine needle aspiration (EUS-FNA) is the reference standard for pancreatic cystic lesions (PCLs) diagnosis. Limited fluid aspirate can restrict analysis. A new nitinol 19G flexible (19G Flex) needle may improve access and aspiration, especially for viscous and/ or difficult to reach PCLs.
Aims & Methods: Document impact of needle gauge and flexibility on success of PCL aspiration and sufficient yield for cytology and CEA. Prospective multinational trial of 250 patients (pts) with PCLs $\geq$ 13mm at largest axis. Interim report on ITT basis for 125 pts with 30 day follow up. Pts randomized in 2:1:1 ratio to 19G Flex:19G:22G needles. Salvage with another needle if no access or incomplete aspiration. Primary endpoint: percent (%) total cyst volume aspirated based on pre- and post-aspiration PCL measurements. Other endpoints: successful EUS-FNA (complete aspiration/ fluid sufficient for testing), salvage rate, 30 day adverse events.
Results: 125 pts (mean age 67, 43% male, 30% symptomatic) treated with 19G Flex(62), 19G(32), or 22G(31) needles. PCLs: mean largest diameter: 22.6 $\pm$ 13.1mm; head 43%, body 22%, tail 31%; unilocular: 61% (76). Mean # passes all procedures including salvage: 1.1 $\pm$ 0.5. Mean % aspirated volume: 78 $\pm$ 38% (124). Successful EUS-FNA: 93.5% (116/124); performance of all needles was equivalent. Primary endpoint for 76 pts with unilocular PCLs by location and viscosity (Table 1) illustrates % aspirated volume for viscous PCLs in head of pancreas of 85% (19G Flex), 63% (19G std) and 66% (22G std) with enrollment ongoing. Salvage required in 13.6% (17/125) pts including 14 (82.4%) in head or very viscous PCLs. 19G Flex required fewer rescues compared to other needles: 9.7% (6/62)-19G Flex, 18.8% (6/32)-19G, and 16.1% (5/31)-22G needles. Complications in 7pts (6%): 1 bleeding PCL that refilled with blood (22G), 1 abdominal pain (19G), 3 acute pancreatitis (2-19G Flex, 1-22G), 2 unrelated deaths from metastatic endometrial (19G Flex) and neuroendocrine (22G) cancer.
Conclusion: Results suggest that nitinol 19G flexible FNA needles may require fewer salvage procedures and show a trend of higher fractional cyst aspiration compared to standard needles for very viscous PCLs. Further data are forthcoming.
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P0841 VARIATIONS IN DIAGNOSTIC ACCURACY OF RADIAL AND LINEAR ENDOSCOPIC ULTRASOUND (EUS) FOR SUSPECTED CHOLEDOCHOLITHIASIS ARE RELATED TO CLINICAL PRESENTATION AND NOT TO TIME TO ERCP OR CHOLEDOCHOLITHIASIS RISK LEVEL

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Introduction: EUS is considered a reliable method in assessment of choledocholithiasis, but reported diagnostic accuracy rates vary, and patient numbers are not very large in the majority of reports. Given the high occurrence of suspected choledocholithiasis seen in daily practice and use of an invasive method (ERCP) in those with positive EUS findings, implications of inaccurate diagnosis are medically, financially and organizationally significant.
Aims & Methods: Our aim was to evaluate diagnostic accuracy of EUS in our setting with a large emergency department and very frequent cases of biliary lithiasis complications, and to compare the accuracy across different clinical scenarios and ASGE choledocholithiasis risk levels, as well as its dependence on time elapsed between EUS and ERCP and type of EUS probe used (radial vs. linear).
We retrospectively included 194 consecutive patients who underwent EUS for suspected choledocholithiasis in the period of two years (2011 and 2012). Mechanical radial (n = 149) and linear (n = 45) Olympus probes were used for EUS examination in all patients.
We compared the positive EUS findings with subsequently performed ERCP, and in patients with negative EUS we confirmed the lack of later biliary events at a 6-month follow-up visit and through electronic medical records revision. Comparison of accuracy was made between different clinical presentations, ASGE choledocholithiasis risk levels, time elapsed between EUS and ERCP and probe type.
Results: 106/194 (54.6%) of patients had a positive EUS finding of choledocholithiasis, and positive predictive value when compared to ERCP was 88.5% (85/96). There were no differences in accuracy with ASGE choledocholithiasis risk levels (6/11 pts with a false positive finding were ASGE high risk level) or type of EUS probe used (PPV with linear 92% vs. radial 87.3%). Time elapsed to ERCP was only slightly longer in pts with a false positive finding (mean 3.87 vs. 2.71 days).
However, significant difference was observed when comparing PPV in pts presenting with biliary colic or pancreatitis (PPV 72.0 %, n = 18/25) and pts presenting with either cholangitis, obstructive jaundice or asympthomatic biliary dilatation or elevated liver enzymes (PPV 97.1 %, n = 67/69, P = 0.0011).
In 88 patients with negative EUS findings, there were only 3 cases of biliary complications during follow-up, and neither of them underwent recommended cholecystectomy after the initial event, so negative predictive value of EUS would at worst be 96.6%.
Conclusion: Although generally high, different levels of diagnostic accuracy of EUS for choledocholithiasis reported in various studies could well be influenced by a difference in distribution of clinical presentations of patients studied. This is probably the result of a transitory nature of biliary obstruction (due to a spontaneous propulsion of the stone), which is very frequent in settings of biliary colic and biliary pancreatitis, whereas obstructive jaundice and cholangitis are related to a more persistent CBD obstruction.
Disclosure of Interest: None declared

P0842 NATURAL HISTORY OF ASYMPTOMATIC UNIQUE PANCREATIC CYSTIC TUMORS CONSIDERED OF BENIGN POTENTIAL IN ENDOSCOPIC ULTRASOUND LONG-TERM SURVEILLANCE OF 144 PATIENTS

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Introduction: A follow up (FU) can be proposed for asymptomatic pancreatic cystic tumors with benignpotential (BCT) such as serous cystadenomas (SC) or congenital cysts. However, it is often difficult to confirm the diagnosis of BCT.In 1991,we proposed the criterias of BCT in endoscopic ultrasound (EUS).
Aims & Methods
Aim: Evaluatethe natural history of asymptomatic pancreatic cystic tumors considered as BCT by EUS. Between June 1992 and November 1996, 144 asymptomatic patients with suspected single BCT by the EUS were included. The exclusion criteria: acute or chronic pancreatitis; criteria for malignant potential in the EUS (wall thickening,echogenic fluid,mass syndrome,duct communication,unilocular cyst > 3 cm); multiple cysts. 111 women with a mean age of 60 years.EUS found in 101 cases a cyst multilocular(probable SC). In 43 cases,one cyst unilocular $\leq$ 3 cm. Cysts had an average diameter of 21 mm, a localization body-tail in 49. Clinical and radiological FU was recommended. Patients and physicians were recontacted every 5 years. Thelast assessment has been in September 2014.
Results: 4 patients (3%)were lost to FU. 21 patients (15%) underwent surgery,7 immediately (5 SC,1 Brunerienne,1 inconclusive) and 14 in FU due to the appearance of symptoms (1 SC),an increase in size or appearance of suspicious signs (8 SC,5 mucinouscystadenoma with one degenerated).47 patients (33%) died during the FU (mean 7 years).2 patients died of pancreatic pathology (1 neuroendocrine tumor,1 cystadenocarcinoma),42 died for a cause independent of the pancreas,3 died of unknown cause.4 patients had other cysts appearing (IPMN probably).54 patients are alive in October 2014 asymptomatic (mean 20 years).18 were a partial FU (mean 10 years). For these 72 patients (50%) the diagnosis of IPMN was mentioned 12 times before.4 cases the signs for a MC have occurred in older patients for surgery too.The mucinous lesions accounted for 18% of patients and were distributed between lesion initially unilocular (n = 9/43:21%) or with microcysts (n = 17/101:17%).
Conclusion: In this follow-up study in the very long term (20 years) EUS criteria had an accuracy of 82% for the diagnosis of BCT.One death related to pancreatic tumour was noted.18% of patients ultimately had mucinous cysts with malignant potential to justify the creation of more specific tests for BCT diagnosis.
Disclosure of Interest: None declared

P0843 IS ASCITES A CONTRA-INDICATION TO AN ENDOSCOPIC ULTRASOUND-GUIDED BILIARY DRAINAGE IN CASE OF UNSUCCESSFUL CATHETERIZATION?: RESULTS OF A PILOT STUDY

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Introduction: In case of malignant obstruction of the bile duct with failure of endoscopic retrogradecholangiography (ERCP), a percutaneous trans-hepatic biliary drainage (PTBD) is usually done.One contra-indication of this procedure is the presence of ascites.Endoscopic ultrasound-guided biliary drainage (EUS-BD) could be a solution but it has never been evaluated in this situation.The objective of this single-center study is to determinewhether ascites is a contra-indication for EUS-BD.
Aims & Methods: Between July 2010 and July 2014 patients with choledocoduodenostomy (CD) or hepaticogastrostomy (HG) for an ERCP failure were included. Systematic bile samples for bateriology were performed at the time of puncture.October 2014 a retrospective analysis was performed comparing those with ascites (group 1) to those without ascites (group 2). The technical and clinical success, complications andfollow-up until death were compared between the two groups.
Results: 31 patients included.Group 1(5CD, 6HG) technical success in 10/11 cases.One complication (migration of the stent). Clinical success in 7/10 patients.4 patients died in the first month. One death related to the procedure. Bacteriology of the biliary fluid positive twice (22%). All patients died of disease progression (mean survival 78 days). Group 2 (8CD,12HG) technical

success in 17/20 cases. Three complications (1 perforation, 1 bile peritonitis, 1 bleeding). Clinical success in 16/17 cases. Bacteriology of the biliary fluid positive in four cases. One patient had cholangitis. 14 patients died of disease (mean 115 days, 6 alive (mean 300 days).
Conclusion: This study showsthat we can achieve a EUS-BD with good technical efficacy in patients with ascites.The risk of infection remains limited (22% of patients) and comparable to patients without ascites.These results suggest aprospective multicenter study.
Disclosure of Interest: None declared

P0844 AN ALTERNATIVE METHOD OF DRAINAGE OF PSEUDOCYSTS IN PRESENCE OF BIG VARICES IN THE FUNDUS

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Introduction: An alternative method of drainage of Pseudocysts in presence of big varices in the fundus.
Aims & Methods
Aims: A study 18 cases of draining pseudocysts complicated by portal hypertension and gastric varices with EUS guided locating the site of puncture distally on the bulge.
Methods: 18 cases from all that were referred to us from 1st January 2011 to May 30, 2014 with pseudocysts were found to be complicated with fundic and esophageal varcies secondary to splenic vein. UES revealed big varices around the GE junction and the proximal body and no window was found for EUS guided cyst drainage in the conventional manner. The bulge of the cyst was followed distally with an EUS scope and an area devoid of varices was found distally. Here the tip of the EUS scope was fully up and it was impossible to get a 19G needle out for puncture and further steps of conventional cyst drainage. Ttherefore we marked the area with biopsy forcpes taking a pinch of tissue for identification on passage of the side viewing scope subsequently. A conventional ERCP 4.2mm channel scope from Olympus was then passed, positioned in front of the marked area and the cyst punctured around the mark with a needle knife papillotome from Boston and guide wire placed under fluoroscopic control. The tract was then dilated with a 6.5Fr cystotome from Endoflex and dilated with a CRE balloon upto 12mm only to avoid bleeding. Two 10 Fr Double pig tail stents were kept. In cases with necrosis and additional naso cystic catheter was placed for lavage which was removed after 48 to 72 hours exchanging it for an additional 10Fr DPT stent. ERCP done if a leak was suspected at the time of removal of naso cystic drain and stent placed. Stents were removed after six weeks to three months and the PD stent removed or changed as needed.
Results:

Bulge Present	**18**	**100.%**
Puncture Possible around marked site	**17**	**94.4%**
Bleeding (Minor)	**3**	**16.7%**
Necrosis Present	**5**	**27.7%**
Infected Fluid	**4**	**22.2%**
Naso Cystic Drain kept	**9**	**50%**
Perforation	**0**	**0**
Sepsis	**4**	**22.2%**
ERCP Performed	**6**	**33.3%**
Cysto gastrostomy stents Removed	**12**	**63.1%**
Stents still present	**4**	**22.2%**
Lost to Follow up	**2**	**11.1%**
Procedure Related Mortality	**0**	**0**

The bleeding was minor from the wall and was treated with injection of adrenaline and balloon tamponade.
The sepsis was treated with antibiotics for 5 to 7 days and was seen in patients with necrosis and infected fluid.
4 patients had a disrupted duct and hence the stents have not been removed.
Conclusion: In difficult situations of pseudocysts complicated with varices, puncturing distally on the bulge at a site marked by EUS scope is a feasible alternative. EUS guide drainage is difficult in these situations as the scope is angled acutely and this makes the procedure very difficult. The complications rates are also reasonable.
Disclosure of Interest: None declared

P0845 GLOBAL ASSESSMENT OF EUS PERFORMANCE SKILLS (GEUSP) - A NEW TOOL AND APPROACH TO OBJECTIFY AND MEASURE THE LEARNING CURVE AND TECHNICAL SKILLS OF ENDOSONOGRAPHISTS

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Introduction: The overall learning curve of endoscopic ultrasound (EUS) is regarded long, but until now it is not very well characterized in the literature. There is also a lack of easy to use tools to assess the practical skills of endosonographists in training.
Aims & Methods: The aim of this study was to elaborate and validate a new tool for the assessment of endosonographists in training and by this elucidate the learning curve of EUS.
The study was conducted at a tertiary university endoscopy center in West Sweden. Patients undergoing EUS for clinical reasons were enrolled and examined first by an endosonographist in training (performer) and secondly by an experienced endosonographist (observer). Both doctors performed EUS-guided puncture if this procedure was indicated. The observer assessed and scored 5 different parameters of the performer's EUS-procedure, each on a 5-graded scale. A study specific assessment sheet, GEUSP, was designed for this purpose. The performer also scored him- or herself regarding the same 5 parameters including an aspect on confidence in own performance. Previous endoscopy experience including EUS and annual endoscopy volumes of the performer were registered. The overall GEUSP score was calculated regarding each case to assess the performeŕs development over time. The influence of different variables on the GEUSP score was analyzed using non-parametric tests.
Results: During May 2014 – February 2015 a total of 60 patients (38 males and 22 females) were examined and four performers were assessed according to GEUSP. Two performers performed the majority of examinations (P1 = 48, P2 = 10, P3 = 1, P2 = 1) all were assessed by one single observer. EUS-FNA/FNB was performed by the performer in 22 cases. Target organs were as followed: Pancreas (29), Submucosal lesions (22), Paraintestinal lesions (11). There was a good correlation between the overall mean GEUSP-score of the observer and that of the performer ($r = 0.68$, $p < 0.001$) supporting the robustness of the assessment sheet. Analyzing comparable lesions there was a correlation between the overall mean GEUSP-score and the previous overall EUS experience of four performers assessed so far ($r = 0.9$, $p = 0.06$). The observeŕs mean overall GEUSP Score of Performer 1 was significantly higher after initial first 25 examinations, (3.7 vs 3.1, $p < 0.01$). There was no significant difference in the overall GEUSP score comparing different target organs nor comapring solid and cystic lesions. The assessment sheet was easy to use and the registration engaged few minutes. We did not notice any negative influence on the everyday endoscopy program due to the use of GEUSP. Two patients reported brief abdominal symptoms the day after EUS, but no certain complications related to EUS were verified during follow-up.
Conclusion: A new tool for the assessment of endosonographists in training (GEUSP) has been proven feasible and simple to use in clinical practice. Further evaluation of a larger cohort of endosonographists is ongoing. We invite other centers to participate in this study.
Disclosure of Interest: None declared

P0846 DIAGNOSTIC EFFICACY OF ENDOSCOPIC ULTRASOUND-GUIDED NEEDLE SAMPLING FOR UPPER GASTROINTESTINAL SUBEPITHELIAL LESIONS: A META-ANALYSIS

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Introduction: An increasing number of studies have been conducted on the use of endoscopic ultrasound (EUS)-guided needle sampling, including fine needle aspiration, fine needle biopsy, and trucut needle biopsy, for upper gastrointestinal (GI) subepithelial lesions (SEL). However, reported diagnostic efficacy varies greatly.
Aims & Methods: We did a meta-analysis to summarize up current evidences on diagnostic efficacy of EUS-guided needle sampling for upper GI SEL. A reproducible strategy was used to search four databases. 17 studies, including a total of 978 sampling attempts, were included in the final analysis. The primary outcome was the pooled efficacy of EUS guided needle sampling in upper GI SEL. Secondary outcomes were procedure-related complications, diagnostic errors, and independent factors related to a higher success rate.
Results: The pooled diagnostic rate of EUS-guided needle sampling was 59.9%, with a heterogeneity I^2 of 55.2%. Subgroup analysis and meta-regression suggested that the cell block method might be correlated with a higher diagnostic rate. Few severe complications were reported. Diagnosis errors were rare.
Conclusion: EUS guided needle sampling is a safe, but only moderately effective method for pathological diagnosis of upper GI SEL. However, the results have inherent limitations, especially in view of the limited sample size and heterogeneity of the original studies.
Disclosure of Interest: None declared

P0847 LONG-TERM REBLEEDING RISK AFTER ENDOSCOPIC THERAPY OF SMALL-BOWEL VASCULAR LESIONS WITH DEEP ENTEROSCOPY

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Introduction: In western countries, small-bowel vascular lesions (SBVL) represent the most frequent small bowel finding in patients with obscure gastrointestinal bleeding (OGIB).[1] Recent systematic reviews raise some doubts concerning the therapeutic efficacy of Balloon-Assisted Enteroscopy (BAE) of SBVL after 2y of follow-up and there is limited data regarding the long-term outcome of these

patients.[2,3] Objective: Evaluate the short- and long-term rebleeding risk after BAE therapy of SBVL detected in capsule enteroscopy.
Aims & Methods: Between July 2007 and February 2015, all patients with SBVL who underwent BAE therapy were included. The endpoint was rebleeding, defined as the presence of overt OGIB, the need for red blood cells transfusions or a decrease in haemoglobin ≥2g/dL. Factors predictive of rebleeding were also analysed. Statistical analysis: Kaplan-Meier survival curves, Log-rank test, t-student test, X^2. Significance: $p < 0.05$.
Results: 35 patients with SBVL underwent BAE therapy, 57.1% were men with a mean age of 67.8+/-13.7 years. Findings included angioectasias in 97.1% (n = 34), classified in types 1a in 14.3% (n = 5) and 1b in 82.9% (n = 29), and Dieulafoy's lesion in 2.9% (n = 1) classified as type 2a.[4] Types 1a/1b were approached exclusively with argon plasma coagulation in 88.6% (n = 31) or combined with other technique in 11.4% (n = 3); and the type 2a lesion was treated with adrenaline and clips. Globally, rebleeding occurred in 40% (n = 14) of cases, manifested as overt OGIB in 35.7% (n = 5), need of blood transfusion in 42.9% (n = 6) and haemoglobin drop ≥2g/dL in 21.4% (n = 3). Rebleeding at 1y/2y/3y/4y/5y after BAE therapy occurred in 32.7%/38.3%/46.0%/53.7%/63.0%, respectively. Patients with aortic stenosis/chronic renal failure/cirrhosis/Osler-Weber-Rendu syndrome had a rebleeding risk at 2y/3y after BAE therapy of 51.3/67.6%, superior to those without these comorbidities (22.2/22.2%), p = 0.006.
Conclusion: Rebleeding at 2y after BAE therapy of SBVL occurred in 38.2%, consistent with two recent systematic reviews which revealed a rebleeding rate of 45% at 26 months and 42.7% at 1.5-2y.[2,3] Long-term risk of rebleeding progressively increases, reaching 63% at 5y after BAE therapy. The presence of comorbidities increases the rebleeding risk.

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P0848 SMALL-BOWEL SURVEILLANCE IN PATIENTS WITH PEUTZ-JEGHERS SYNDROME: COMPARING MAGNETIC RESONANCE ENTEROCLYSIS AND DOUBLE BALLOON ENTEROSCOPY

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Introduction: Surveillance of the small-bowel with polypectomy of significant polyps (SP, defined as polyps ≥15mm in diameter) prevents polyp-related complications in Peutz-Jeghers syndrome (PJS). However, evidence for the optimal imaging technique for these patients is lacking. Therefore, we aimed to compare the diagnostic yield and patient preference of Magnetic Resonance Enteroclysis (MRE) and Double Balloon Enteroscopy (DBE) in PJS.
Aims & Methods: Adult PJS patients recruited from two academic centers underwent MRE followed by a proximal DBE with polypectomy of SP within 20 weeks. The endoscopists were blinded for the MRE results. DBE was performed under conscious sedation with midazolam and fentanyl intravenously or under general anaesthesia with propofol. We compared the number of SP and total number of polyps detected by MRE and DBE. Patients' perception regarding shame, pain, burden and duration of both procedures were assessed through questionnaires, as well as their preference for future surveillance.
Results: Fifteen PJS patients, 67% males with a median age of 47 (IQR 39-53) years underwent both MRE and DBE. The median maximal insertion depth for DBE was 270cm (IQR 160-340cm). SP were identified by MRE and/or DBE in 12/15 (80%) patients. Agreement between MRE and DBE on the presence of SP was 87% (13/15) and both methods identified 11 patients with SP. Significantly more polyps were detected by DBE than with MRE (148 vs. 93, p = 0.03), however there was no significant difference in the detection of SP (47 by DBE vs. 38 by MRE, p = 0.37). Patients' perception regarding shame and burden at preparation and during both procedures did not differ significantly between MRE and DBE. However, patients reported significantly more pain during the preparation for MRE than for DBE (moderate vs. no pain, p = 0.02). Perception of pain during the procedures was comparable (both mild, p = 0.89). Significantly more patients perceived a longer procedure time for MRE than for DBE (38.5% vs. 8.5%, p = 0.05). For future small-bowel surveillance 10/13 (77%) patients preferred DBE over MRE (p = 0.09).
Conclusion: Our results suggest that MRE and DBE have comparable diagnostic yield of clinically relevant polyps ≥15mm in diameter. Although DBE resulted in incomplete small-bowel visualization in all patients, it allows for direct intervention and was preferred over MRE by patients in this series. Based on the MRE results, 11/15 (73%) patients had an indication for DBE with polypectomy. Larger cohorts of PJS patients are needed to fully evaluate the diagnostic yield of DBE compared with other diagnostic modalities.
Disclosure of Interest: None declared

P0849 THE ROLE OF DOUBLE-BALLOON ENTEROSCOPY IN MALIGNANT SMALL BOWEL TUMORS MAY BE DECISIVE

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Introduction: Malignant small bowel tumors (MSBT) are a heterogeneous and relatively rare group of neoplasms. Double balloon enteroscopy (DBE) role in these lesions remains controversial.
Aims & Methods: The aim of this study was to assess the DBE role in MSBT. The present retrospective study included all consecutive patients who underwent a DBE with final diagnosis of a malignant neoplasm from 2004 to 2014 in our referral center. Patient demographic and clinical pathological characteristics were reviewed. MSBT diagnosis was achieved either by DBE directed biopsy, endoscopic findings or histological analysis of surgical specimen. We have analyzed DBE impact in the outcome and clinical course of these patients.
Results: Of 627 patients, 28 (4.5%) (mean age: 60 ± 17.3 years) underwent 30 procedures (25 anterograde, 5 retrograde) and were diagnosed of a malignant tumor. Patients presented with obscure gastrointestinal bleeding (n = 19, 67.9%), occlusion syndrome (n = 7, 25%) and diarrhea (n = 1, 3.6%). They were diagnosed by DBE biopsy (n = 18, 64.3%), histological analysis of surgical specimen (n = 7, 25%) and unequivocal endoscopic findings (n = 2, 7.1%). Gastrointestinal stromal tumor (n = 8, 28.6%), adenocarcinoma (n = 7, 25%), lymphoma (n = 4, 14.3%), neuroendocrine tumor (n = 4, 14.3%), metastatic (n = 3, 10.7%) and Kaposi sarcoma (n = 1, 3.6%) were identified. In summary, DBE modified outcome in 7 cases (25%), delaying or avoiding emergency surgery (n = 3), modifying surgery approach (n = 2) and indicating emergency SB partial resection instead of elective approach (n = 2).
Conclusion: DBE may be critical in the management of MSBT providing additional information that may be decisive in the clinical course of these patients.
Disclosure of Interest: None declared

P0850 A PROSPECTIVE COMPARISON OF SAFETY AND TOLERABILITY OF PROPOFOL VERSUS STANDARD SEDATION FOR DOUBLE BALLOON ENTEROSCOPY - TIME FOR A PUSH FORWARD?

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Introduction: Double balloon enteroscopy (DBE) is routinely performed with moderate sedation in the UK. However, in comparison to standard endoscopy, DBE is complex and takes longer, therefore deep sedation with propofol could improve tolerability and feasibility of the test.
Aims & Methods: All patients undergoing DBE between March13 and October14 were prospectively enrolled. DBE was performed either with administration of sedation with fentanyl and midazolam or with anesthetist-assisted deep sedation with propofol, the decision being made on the basis of patients' clinical history and expected length of the test. Data from patients receiving propofol were compared to those from patients receiving standard sedation during the same period. Patients were asked to fill in a questionnaire regarding their expectations before the test and their satisfaction afterwards. Anxiety, pain and discomfort were assessed by means of validated numeric rating scales (NRS, range 0-10). Data on comorbidities, previous surgery and hospital anxiety and depression scores (HADS) were also collected. The procedural characteristics of DBE were assessed.
Results: Twenty-one DBE (18 oral, 3 anal, 33% male) were performed with the aid of propofol infusion and 67 (54 oral, 13 anal, 51% male) with standard sedation. Mean age was 48 ± 14.3 in the propofol group and 58.6 ± 15.9 in the sedation group (p = 0.012). There were no other differences in demographics, comorbidities or HADS scores between the groups. The indications for DBE included obscure gastrointestinal bleeding (n = 45), Peutz-Jeghers syndrome (9) and suspected Crohn's disease (20), small bowel tumor (10) or celiac complication (2). The mean dose of propofol administered was 1123 ± 483 mg. The mean doses of midazolam and fentanyl were 6 ± 3 mg and 118 ± 54 mcg respectively. No differences were observed in terms of diagnostic yield (52% vs 57%, p = ns) and therapeutic yield (33% both groups). Patients in the propofol group reported lower scores of pain (median score 0, IQR 0-0.5 vs 3, IQR 0-6, p < 0.0001), discomfort (median 0, IQR 0-0.5 vs 3, IQR 1-7, p < 0.0001) and distress (median 0, IQR 0-0 vs 1, IQR 0-5, p = 0.001) during the procedure. Whilst there were no complications in the propofol group, there was one episode of oxygen desaturation in the control group.
Conclusion: The use of propofol for DBE has a good safety profile and better patient tolerability and satisfaction in comparison with moderate sedation. It is associated with a high diagnostic and therapeutic yield. Its use should be

recommended when the procedure is expected to be longer and technically challenging.
Disclosure of Interest: None declared

P0851 DOUBLE-BALLOON ENTEROSCOPY IN PATIENTS WITH CARDIOVASCULAR COMORBIDITIES - IS IT WORTH THE 'CORONARY'?

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Introduction: Double balloon enteroscopy (DBE) is an advanced endoscopic technique for the diagnosis and treatment of small bowel diseases. It is a relatively invasive and long procedure therefore its use in patients with comorbidity can be risky.
Aims & Methods: The aim of our study was to assess the safety and feasibility of DBE in patients with cardiovascular comorbidities.
All consecutive patients referred for DBE in our trust were prospectively reviewed. Clinical and demographic data were collected and patients with cardiovascular comorbidities were included in the analysis. Patients were divided into 2 groups- elderly (Group 1: age > 70 years) and the young (Group 2: age < 70 years) Diagnostic and therapeutic yields, dose of sedation and complications rates were collected.
Results: Out of a total of 404 DBE procedures, 97 were performed in patients with one or more cardiovascular (CV) comorbidities (Group 1 = 52, group 2 = 45), including ischaemic heart disease (n = 61), valvular replacement (n = 24), atrial fibrillation (AF, n = 19), chronic cardiac failure (CCF, n = 16), arrhythmias with pacemaker implantation (n = 5), previous cerebrovascular event (n = 8). AF and CCF were commoner in the elderly compared to the young (p = 0.035 and p = 0.026 respectively). There were no significant differences in warfarin or NSAIDS use in the two groups. The indications for DBE were obscure gastrointestinal bleeding (occult, 59%, and overt, 27%), suspected Crohn's disease (7%), small bowel stricture at radiology (4%) and suspected celiac complication/malabsorption (3%). Transfusion was required in 67% patients in the elderly group and 60% in the younger group (p = ns). There were no differences in terms of procedure time between the elderly and the young (median time 70 minutes, range 35-125, vs 65, range 25-140, p = ns). Elderly patients were administered significantly lower doses of midazolam (median dose 4 mg, range 1.5-10 vs 6 mg, range 2-10, $p < 0.0001$) and fentanyl (median dose 50 mcg, range 12.5-100 vs 75, range 12.5-200, $p < 0.0001$).
DBE had high diagnostic (65% and 58%, p = ns) and therapeutic yield (54% vs 33%, p = ns) in both groups. The most common finding was angiodysplasia in both groups (48% vs 29%, p = 0.06), other findings included ulcers (6% vs 9%), small bowel polyps (0% vs 7%) or tumors (0% vs 4%), diverticula (4% vs 0%), changes of celiac disease and intestinal lymphangectasia (0% vs 6%). The complication rate was 3% overall with one non STEMI in the elderly group and one episode of cardiac failure and a respiratory arrest in the younger group.
We also made comparisons between patients with CV comorbidity compared to all others without CV comorbidity undergoing DBE in the same period. The overall diagnostic yield was higher in patients with CV, irrespective of age, as compared to all other patients without CV comorbidity (62% vs 46%, p = 0.005). Similarly, the therapeutic yield was also higher (44% vs 18%, $p < 0.0001$) in relation to the high number of vascular lesions treated in patients with CV comorbidity. The difference in complication rate between patients with and without CV comorbidities did not reach statistical significance (3% vs 1%, p = 0.15).
Conclusion: We are the first to demonstrate that DBE in patients with CV comorbidity is relatively safe and with a good diagnostic and therapeutic yield. Careful patient selection is imperative to prevent serious complications.
Disclosure of Interest: None declared

P0852 THE OVER-THE-SCOPE-CLIP (OTSC) AS A THERAPEUTIC OPTION FOR IATROGENIC PERFORATION (IP), ANASTOMOTIC LEAKAGE (AL) AND CHRONIC FISTULA (CF) IN THE GASTROINTESTINAL TRACT

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Introduction: Patients with iatrogenic perforation during endoscopy, anastomotic leakage and chronic fistula used to be transferred to the surgeon for further therapy. Since the recent development of the Over-The-Scope-Clip (OTSC), an increasing number of such lesions can be treated endoscopically which makes the closing procedure to a fast and safe method.
Aims & Methods: All applications of OTSC in our department between 12/2009 and 02/2015 were assessed prospectively and classified into three groups: 1. iatrogenic perforation (IP) during endoscopy, 2. anastomotic leakage (AL) after upper, middle or lower gastrointestinal surgery and 3. chronic gastrointestinal fistula (CF). Technical success was determined by the endoscopist subsequently to the procedure. As a second end point, we assessed the clinical success. Additionally, we added all cases of further interventional or surgical treatment All additionally required interventions (e.g. interventional radiology or surgery) were documented.
Results: n = 34 patients (m = 20, f = 14; mean age 70 years, range 30-89) underwent OTSC-treatment and were classified by indication:
1. IP (n = 10): The perforations were caused by piece-meal resection of an duodenal (4) or antral (1) adenoma, endoscopic retrograde cholangiopancreatography (2), diagnostic colonoscopy (2) and accidental perforation of an endosonographic fine-needle biopsy (1).
None of the patients needed to be transferred for surgical treatment. One patient (10 %) showed an insufficient closure but could be treated conservatively by means of a drainage of a retroperitoneal abscess. All patients survived with an excellent outcome.
2. AL (n = 15): OTSC clipping was performed due to anastomotic leakage in different surgery sides of the upper, middle and lower gastrointestinal tract: Gastric anastomosic leakage in bariatric surgery (2), duodenal leakage after pancreas- or aorta-surgery and cholecystectomy (3), leakage after esophageal (5) and colonic surgery (5). Technical success was achieved in 100% of these interventions. However, 6 patients (40 %) did not experience sufficient clinical amerlioration. The reason for these failure were additional developed leakage and persisting leakage. Further interventional and surgical treatment was needed.
3. CF (n = 9): Persisting leakage after removal of an infected percutanous endoscopic gastrostomy (1), intestinale fistulae due to acute-necrotising panceatitis (2), chronic enterocutanous fistula (1), rectovaginal fistula after radiation therapy (1), perforating nasojejunal tube (1), spontaneously perforated gastric ulcer (1) and colonic perforation of unknown reason (2). All 9 patients could be successfully treated by endoscopic closing with the OTSC primarily. However, 7 patients (77.8%) developed a relapse of fistula or new fistula were arisen. Endoscopic treatment failed in these cases.
Conclusion: All iatrogenic perforations were sufficiently closed by OTSC and showed an excellent technical and clinical outcome without any further surgical treatment required. However, anastomotic leakage and chronic fistula that are endoscopically closed by OTSC, often require additional interventional or surgical procedures.
Disclosure of Interest: None declared

P0853 HYPERAMYLASAEMIA AND ACUTE PANCREATITIS AFTER DOUBLE BALLOON ENTEROSCOPY: A PROSPECTIVE STUDY

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Introduction: Hyperamylasaemia and acute pancreatitis are potential complications following a double balloon enteroscopy (DBE) procedure. The mechanism of these complications is not fully understood. We present a prospective analysis of all patients undergoing DBE at a tertiary centre.
Aims & Methods: Single centre, prospective study involving all consecutive patients attending for DBE by either route, between 23rd Aug 2012 and 3rd October 2014. Serum amylase levels were obtained before and three hours after the procedure. Clinical evaluation for signs and symptoms of pancreatitis was performed three hours after the procedure. A record of the procedure duration, insertion depth and number of passes was also documented. Hyperamylasaemia was defined as an elevation of the serum amylase level to greater than the upper limit of normal.
Results: 115 procedures were performed on 89 patients, mean age 57.4 years (21-83 years), 46 male (51.7%). Indication for procedure is presented in Table 1. 91 procedures were performed per orally and 24 via the anal route. 88 procedures were performed on the basis of a positive small bowel capsule endoscopy (SBCE), 9 patients did not have prior SBCE due to failure to excrete the patency capsule. Indication for DBE is presented in Table 1. Overall 47 patients (61%) had an elevated serum amylase post procedure. Hyperamylasaemia post-procedure was observed in significantly more patients following per-oral DBE compared to DBE via the anal route (p = 0.03). Hyperamylasaemia in the per-oral group was associated with procedure depth (mean 147cm vs 187cm $p < 0.0009$) and number of passes (mean 10 vs 18 $p < 0.0007$), but not procedure duration (mean 64 vs 70 mins p = 0.2) or dose of fentanyl administered (mean 108mcg vs 118mcg p = 0.6). No patients developed signs or symptoms of pancreatitis post-procedure.

Table 1

INDICATION	No. of PATIENTS
Iron deficiency anaemia	46
Obscure gastrointestinal bleeding	19
Suspected Crohn's	15
Peutz Jegher's syndrome	11
Abnormal radiology	6
Small bowel stricture	6
Abdominal pain	4
Coeliac complications	3
Other	4

Conclusion: Hyperamylasaemia is common following DBE per-orally and is associated with procedure depth and number of passes. However, in the majority of cases this is of limited clinical significance and no patients in our series went on to develop pancreatitis.
Disclosure of Interest: None declared

P0854 MAGNIFYING NARROW-BAND IMAGING BY USING NEWLY DEVELOPED MAGNIFYING ENTEROSCOPY CAN BE USEFUL FOR EVALUATION OF INFLAMMATORY ACTIVITY IN SMALL INTESTINAL CROHN'S DISEASE: A PILOT STUDY

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Introduction: The development of balloon endoscopy and capsule endoscopy has made observation of the small intestine possible in clinical practice. The usefulness of magnifying endoscopy has already been reported in observing the pharynx, esophagus, stomach and colon. The prototype of a single-balloon enteroscopy (SBE) with 80x magnification has been recently developed.
Aims & Methods: The aim of this pilot study was to assess the efficacy of narrow-band imaging (NBI) magnifying findings for evaluating the severity of inflammation in small intestinal crohn's disease (CD). The study was conducted in Showa University Northern Yokohama Hospital. We included CD patients who underwent enteroscopy with magnification from September 2013 to December 2014. NBI images and a biopsy specimen were obtained from small intestinal mucosa for CD patients with use of SBE (Y-0007, Olympus, Tokyo). Magnifying NBI was performed, and the images were evaluated by assessing visibility, increased vascularization, and the increased caliber of capillaries into three grades as follows: Normal, Visible and Irregular. Normal was indicative of inactive disease, while Visible and Irregular were indicative of acute inflammation in our study. The outcome measures included the diagnostic ability of magnifying NBI findings to distinguish active CD from inactive CD on the basis of histological activity.
Results: Twenty-two patients were enrolled. There was a correlation between magnifying NBI findings and the histological assessment (Spearman's $|r| = 0.667$).The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of magnifying NBI findings for diagnosing acute inflammation were 71.4%, 95.2%, 83.3%, 90.9%, and 89.3%, respectively.
Conclusion: The NBI magnifying findings in the small intestinal mucosa had a correlation with histological inflammation and could help in distinguishing between active and inactive in CD.
Disclosure of Interest: None declared

P0855 MULTICENTRE EXPERIENCE USING A NOVEL DEEP ENTEROSCOPY PLATFORM IN SURGICALLY ALTERED GASTROINTESTINAL ANATOMY

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Introduction: Conventional deep enteroscopy platforms achieve technical success rates between 61-98% in patients with surgucally altered anatomy. However, they lack widespread availability and have limited therapeutic potential due to a smaller working channel. Through-the-scope balloon-assisted enteroscopy (TTS-BAE) marketed as NaviAid AB (Smart Medical Systems Ltd., Ra'anana, Israel) is a novel technique using a standard adult colonoscope allowing for a broader range of interventions through the larger working channel but may be hampered by a shorter depth of maximal insertion.
Aims & Methods
Aims: to determine the efficacy and safety of TTS-BAE in patients with surgically altered anatomy.
Methods: A retrospective multicentre (2 in U.S., 1 in Germany) study of consecutive patients with sugrically altered anatomy who underwent TTS-BAE between 2012 to 2014 were included. Target success was defined as ability to access the intended target. Technical success was defined as completion of the procedure as intended. Clinical success was defined as >50% reduction in abdominal pain or hepatic enzyme levels and resolution of jaundice or bleeding. Adverse events were graded according to the ASGE lexicon's severity grading system.
Results: A total of 42 patients (mean age 53yr, 18 female) underwent anterograde enteroscopies with a median procedure time of 42.5 minutes (25-250) (**Table 1**). Overall, the intended target was reached in 57.14% (n = 24), of which 95.83% (n = 23) were technically successful and 91.67% (n = 22) were clinically successful. The biliopancreatic limb and deep small bowel had the highest rates of target and technical success (**Table 1**). Success rates did not differ between patients with RY vs not RY anatomy (P = 0.78). A total of 7 metal stents and one 10Fr plastic stent were successfully deployed (5 biliary, 2 jejunal); this would not have been possible using other platforms. Adverse events occurred in 3 (7.14%) cases: aspiration pneumonia (mild), cholangitis (mild) and perforation (severe) distal to the HJ requiring surgical closure.

Continued

	N (%)	Target success (%)	Technical success (%)	Clinical success (%)
Type of anatomy				
RYGB	8 (19.05)	62.5	62.5	62.5
Transplant RYHJ	7 (16.67)	57.14	57.14	57.14
Non-transplant RYHJ	12 (28.57)	50	41.67	41.67
Whipple	10 (23.81)	60	60	60
Other	5 (11.90)	60	60	40
Indication for TTS-BAE				
ERCP	33 (78.57)	57.58	54.55	54.55
Small bowel stricture	5 (11.9)	80	80	60
GI bleeding	4 (9.52)	75	75	75
Target of TTS-BAE				
Hepaticojejunostomy/ Jejunojejunostomy	32 (76.19)	56.25	56.25	56.25
Deep bowel	5 (11.9)	75	75	50
Biliopancreatic limb	4 (9.52)	50	25	25
Excluded stomach	1 (2.38)	0	0	0

Conclusion: TTS-BAE does not reach the therapeutic target as often as conventional platforms possibly due to its shorter depth of insertion and the less flexible adult colonoscope. However, we demonstrate very high technical and clinical success rates once an intended target is reached, which can be particularly useful for metal stent deployment.
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P0856 THE SMALL BOWEL VIDEOCAPSULE ENDOSCOPY: MAY WE DELEGATE IT TO NURSES ?

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Introduction: Small bowel videocapsule endoscopy (VCE) is a non-invasive and validated technique allowing the visualization of the small intestine mucosa. It generates more than 40,000 images per examination and induces a long median time of medical reading that may exceed one hour. In a transfer of skills' program, Nurses (N) might be involved in the VCE reading. We herein present a feasibility study that evaluated two strategies of transfer skills of the VCE to N through either the pre-selection of abnormalities or the complete analysis.
Aims & Methods: Twenty VCE were selected and interpreted by two medical experts (group A). Two N with endoscopic experience were trained for the small bowel VCE reading. Pre-selection of VCEs' pathological images were performed by N. Other experts in VCE readings established the definitive VCE's report from pre-selected images (group B). Meanwhile, N produced a report of the VCE (group C). The stomach and small intestine transit times and the reading time were recorded. The accuracy of the whole VCE interpretation was compared (group A vs. B; A vs. C). Experts reviewed all discordant interpretations.
Results: The extent of transit time in the stomach and the small intestine, and the identification of a normal endoscopic examination were not statistically different between group A and group B. The accuracy of reports from group A and B was 95% (19/20). In one case, N has not selected the pathological image, corresponding to a duodenal ulcer. The VCE average reading time by the expert in the group B was significantly shorter than in the group A (9.2min +/- 0.5 vs. 34 +/- 9.9min; $p < 0.01$). Time analysis was not statistically different between the groups A vs. C (34min +/- 9.9 vs. 4.1 +/- 34.1min; $p = 0.53$). The accuracy of reports from group A and C was 80% (16/20). In 4 cases, proofreading revealed a discordant interpretation. The discrepancy was due to a lack of pathological images' selection of the selected pictures for the final report (n = 2) and a lack of interpretation (n = 2) in group B.
Conclusion: In small bowel VCE interpretation, a pre-selection of pathological images by a trained N could be integrated in a transfer of skills' program and appeared feasible. The average gain of time for the gastroenterologists is significant and up to 25 minutes per examination. Interestingly, an overall delegation of small bowel VCE interpretation from physicians to N remained not sufficient enough and deserved to be improved. Considering the medical time constrains, our study justifies evaluating in a larger study the delegation of the pre-selection images by N in a transfer of skills' program.
Disclosure of Interest: None declared

P0857 HISTORICAL ANALYSIS OF SMALL BOWEL CAPSULE ENDOSCOPY PERFORMANCE IN A SPANISH TERTIARY HOSPITAL

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Introduction: Capsule endoscopy (CE) is a widely extended technique for the diagnosis of small bowel pathology. In our hospital it has been available since 2004 with an increasing number of procedures along the time. At the beginning no more than some tens of studies were performed while up to 150 patients per year have come for CE in the last years.
Aims & Methods: Our aim is to analyze the data from our historical database of small bowel CE starting in year 2004.
We have retrospectively analyzed the data from the patients under small bowel CE in our hospital from October 2004 to April 2015, including demographic data, indications, findings and complications. Indications have been divided in: obscure occult gastrointestinal bleeding (OOcGIB), obscure overt gastrointestinal bleeding (OOvGIB), inflammatory bowel disease (IBD), and other indications (including polyposis, celiac disease, abnormal previous radiologic test, etc.). Findings in CE studies have been defined as: vascular ectasia (VE); ulcerative lesions (UL), including drug-induced lesions and Crohn's disease; other lesions, such as polyps, submucosal tumors, atrophy, etc.; normal (no findings); and inconclusive studies due to gastric o enteric retentions, technical problems, poor bowel cleansing, etc.
Results: We have included 1027 CE studies, after exclusion of those with incomplete or indefinite information. The average age of the patients is 56.45 years old (4 - 91 y-o), including 471 men (57.55 y-o) and 556 women (55.54 y-o). The most frequent indication was OOcGIB (n = 471, 214 men/257 women), followed by OOvGIB (n = 240, 126 men/114 women), IBD (n = 224, 94 men/130 women) and other indications (n = 92). In *TABLE 1* we show the distribution of the different indications according to sex and age.
The most frequent finding was VE (n = 583), alone or with secondary findings. UL were observed in 329 cases, alone or with other lesions. Other kind of lesions as polyps or small bowel submucosal tumors were observed in 159 cases, in most of them as secondary or incidental findings.
It is remarkable that the greatest rate of normal studies occur in the group of IBD, probably related to the lack of evidence referring to factors associated to the diagnostic yield of CE in these cases and over-indication of the technique. On the other hand it is also striking the number of UL seen in patients presenting with OOvGIB, probably because many of them were under nonsteroidal anti-inflammatory drugs or antiplatelets.
No major complications have been observed in our database. 3 cases of gastric and 5 small bowel retentions of the capsule have been reported. All of them were managed conservatively, with no need for urgent surgery.

	OOcGIB	OOvGIB	IBD	Other indications
MEN	n = 214	n = 126	n = 94	n = 41
	Age: 65.2	Age: 62.2	Age: 35.4	Age: 52
WOMEN	n = 257	n = 114	n = 130	n = 51
	Age: 63	Age: 62	Age: 37.8	Age: 49.3
OVERALL	n = 471	n = 240	n = 224	n = 92
	Age: 64	Age: 62	Age: 36.8	Age: 50

Conclusion: Our experience shows that CE is a safe and useful tool for the diagnosis of small bowel pathology. We have observed an increasing number of studies along the years, with a high diagnostic yield specially in cases of obscure bleeding.
Disclosure of Interest: None declared

P0858 "SUSPECTED BLOOD INDICATOR" AND "QUICK VIEW" IN SMALL BOWEL CAPSULE ENDOSCOPY FOR OBSCURE GASTROINTESTINAL BLEEDING: A COMPARATIVE STUDY

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Introduction: Small bowel capsule endoscopy (SBCE) is indicated to evaluate for obscure gastrointestinal bleeding (OGIB). As Standard view (SV) reading is time-consuming, Suspected Blood Indicator (SBI) and Quick View (QV) readings can be useful in the initial evaluation of the VCE study, as they allow for a more rapid reading.
Aims & Methods: To compare the diagnostic accuracy of SBI reading and QV reading *versus* SV reading in OGIB.
Unicentric retrospective study which included patients who underwent SBCE studies for evaluation of OGIB in a 7-year period. Exclusion criteria: incomplete SBCE and technical recording errors. SBI and QV readings were performed by two independent investigators. The presence of small bowel active bleeding, P2 lesions and QV reading time were recorded. Goldstandard: SV reading.
Results: Three-hundred patients were included: 63.3% female, mean age 62 years, 16.7% with overt OGIB. In SV, active small bowel bleeding was visualized in 31 cases (10.3%) and the bleeding origin was identified in 13 (41.9%). For SBI, the sensitivity was 93.5%, with a negative predictive value (NPV) of 99.3%; for QV, the sensitivity was 100%, with a NPV of 100%. SBI revealed the bleeding origin in 34.5% of the cases and QV in 38.7% of them. In SV, small bowel P2 lesions were visualized in 29.3% of the SBCE. The sensitivity for P2 lesions was 42.0% for SBI and 79.5% for QV, with a NPV of 80.6% and 92.2%, respectively. The mean diagnostic reading time in QV was 2min22s.
Conclusion: Although both modalities are extremely sensitive at identifying active bleeding, Quick View reading detects a higher number of P2 lesions than the Suspected Blood Indicator. In comparison to SBI reading, QV reading is a more accurate diagnostic tool at evaluating patients with OGIB, and it may prove useful as an initial screening in urgent cases.
Disclosure of Interest: None declared

P0859 ENABLING TANDEM PROCEDURE OF COLONOSCOPY FOLLOWING COLON CAPSULE ENDOSCOPY IN COLORECTAL CANCER SCREENING

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Introduction: Importance of prevention of colorectal carcinoma (CRC) is rising due to increased incidence; yet, acceptance of screening by colonoscopy remains low in Germany. Major reasons are the invasive and intimate character of the colonoscopy itself and the bowel preparation. To overcome these barriers a pilot project by AOK Bayern health insurance in north-eastern Bavaria offers patients aged 45 to 75 to choose between a colon capsule endoscopy (CCE) and screening colonoscopy. If significant findings are discovered during CCE (polyps ≥ 6mm, or ≥ 3 polyps) a so-called tandem procedure is offered: a therapeutic colonoscopy follow-up on the same day with the same bowel preparation, therefore avoiding a second appointment. Feasibility of such a tandem procedure in a non-clinical trial setting has not yet been proven.
Aims & Methods: To allow a tandem procedure, capsule excretion has to be achieved before 3 pm (about 7 hours after capsule ingestion). Following the protocol all patients receive a series of boosts of sodium phosphate to propel the capsule through small and large bowel. To avoid too fast colonic transit, a reduced first boost of 15 ml instead of 30 ml sodium phosphate was given after capsule entry into the duodenum. If CCE was not excreted after 2.5 hours, a second and eventually a third boost after further 2 hours were administered while not exceeding 55 ml of total concentration of sodium phosphate, as recommended in Spada et al. (2012). Percentages were performed to demonstrate that tandem procedure is feasible in clinical practice. Total capsule transit time not exceeding 7 hours was used as outcome criteria.
Results: In total, 260 patients received a CCE from January 2014 – March 2015. In our setting 78% (n = 203) of the CCE was below 7 hours, which allows a tandem procedure. 53 patients (20%) out of the 260 patients needed one boost to complete CCE. 207 patients (80%) received a second boost and out of them 46 (18%) even a third to achieve capsule excretion. 130 (81%) out of 161 patients who received only two boosts would have qualified for a tandem procedure. If a third boost was necessary 43% of the patients would have been able to receive a tandem procedure.
Conclusion: The analysis shows that a tandem procedure of CCE followed by a therapeutic colonoscopy within one day with only one bowel preparation is feasible in a real-world clinical setting. In most of the cases realizing a passage time under 7 hours while producing high-quality video recordings could be achieved with a first boost of 15 ml. However, the quite high percentage of a necessary third boost in our setting suggests that dosages of the first and second boost should be analysed further to potentially reduce the need of a 3rd one.

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Disclosure of Interest: None declared

P0860 REALIZATION OF COLON CAPSULE ENDOSCOPY AND COLONOSCOPY FOLLOW-UP IN TANDEM ON THE SAME DAY IN A REAL-WORLD SETTING

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Introduction: To increase prevention of colorectal carcinoma (CRC) a pilot project by AOK Bayern health insurance in north-eastern Bavaria offers patients aged 45 to 75 both traditional colonoscopy and colon capsule endoscopy (CCE) as well as a so-called tandem procedure. It enables colonoscopy follow-up on the same day in case of significant findings during CCE, thereby avoiding a second bowel preparation. Aim of this abstract is a description of processes that allow for this tandem procedure.
Aims & Methods: To realize tandem procedure, several organizational and personal requirements need to be considered (see also Krause & Riemann, 2013). At least 3 days before CCE the medical staff needs to inform the patient comprehensively about advantages and disadvantages of traditional colonoscopy, CCE and tandem procedure. Like colonoscopy, CCE preparation involves bowel cleansing including high intake of fluids two days before, a liquid diet one day before and 1.5 l of peg 3350-electrolytes-vitamin C (PEG C) and 2 l water between 6-8 pm the night before CCE. The next morning the patient again has to drink 1 l of PEG C and 2 l of water until 6:30 am, since no fluids should be taken 90 min before swallowing the capsule to ensure quick stomach passage. During CCE the patient should not eat. Optimally, the CCE should start at 8 am in the doctor's practice to realize capsule excretion before 3 pm. During CCE patients may rest in a recreational room, which allows the medical staff to supervise capsule progress every 30 minutes and to give recommended boosts according to protocol to accelerate passage time. Further, average video analysis time (90 min) needs to be reduced, which can be warranted due to intelligent image recognition software and highly trained staff. If significant findings (polyps ≥ 6mm in size, or ≥ 3 polyps) are observed, the patient may receive a

follow-up colonoscopy the same evening without further intake of bowel cleansing. This however requires availability of spatial resources and medical staff until 7 pm.
Results: Following this procedure a colonoscopy on the same day after significant findings during CCE could have been realized in 78% of all screenings. In total, 348 patients opted for a CCE from September 2013 – March 2015.
Conclusion: The pilot project shows that a follow-up colonoscopy the same day than a CCE in case of significant findings can be realized in a real-world practice setting, which avoids a second bowl preparation in case of diagnostic findings. This method however, requires a well-timed and personnel good organized practice as well as a trained doctor. Advantages of a tandem procedure are a non-invasive procedure, only one bowl cleansing, and an intensive medical support. Disadvantages are long fasting times before and during the examination day, preparation early in the morning and spending a whole day in the medical practice.

Reference

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Disclosure of Interest: None declared

P0861 PANENTERIC CAPSULE ENDOSCOPY: WHOLE GUT VISUALISATION WITHOUT INTUBATION

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Introduction: Capsule endoscopy (CE) is a well-tolerated, first-line small bowel (SB) investigative modality. A specifically adapted version is available to image the colon, thus providing an option for non-invasive, single visit imaging of the entire gastrointestinal tract. This study evaluates a novel panenteric protocol utilised to investigate patients with symptoms which could originate from the SB, large bowel or both sites.
Aims & Methods: Retrospective, single centre, involving consecutive patients attending for panenteric CE between July 2008 and December 2014. PillCam SB (Given Imaging, Israel) or MiroCam (Intromedic, Korea) and PillCam Colon 2 (Given Imaging) were used. All patients with known inflammatory bowel disease (IBD) successfully passed a PillCam Patency device prior. Patient demographics, procedural data, final diagnosis and outcomes were collected.
Results: 108 procedures were performed, mean age 41.5 years (range 16-95), 72 female, median follow up 27 months (range 2-79).
41 patients had known IBD (37 Crohn's, 4 ulcerative colitis (UC)) and were undergoing disease re-assessment after 12 months of anti-TNF therapy (12), or due to relapse in symptoms (29). The remaining 67 patients had suspected IBD with predominant symptoms of diarrhoea (33), abdominal pain (15), iron deficiency anaemia (8), weight loss (6) and gastrointestinal bleeding (5). 51 patients refused colonoscopy, 37 chose CE over colonoscopy, 17 had an incomplete colonoscopy and 3 were unfit for colonoscopy.
Panenteric capsule endoscopy completion rate (CECR) was 60.1% (65/108), SB CECR 86.1% (93/108) and colon CECR 71.3% (77/108). Colon CE bowel preparation was graded as good or excellent in 61.8%. 2 patients were excluded due to prolonged gastric retention of the colon capsule, 1 subsequently diagnosed with narcotic bowel syndrome. No complications were encountered.
In the IBD group, 25 patients (61.0%) had evidence of active disease, leading to medication alterations in 21, surgery in 1 and conservative management in 3. Of the 16 patients in whom mucosal healing had been achieved, medication regimens were downgraded in 10 patients.
In the suspected IBD group, this was identified in 13.4% (7 Crohn's, 2 UC). Clinically relevant alternative findings included colon polyps (16), diverticular disease (9 colonic, 1 SB), angioectasia (6 SB, 1 colonic) and a small bowel carcinoid (1).
The remaining 24 patients were diagnosed with functional bowel disorders and discharged.
Of all the 34 patients with IBD identified, 22 had ileitis alone, 5 had ileocolonic disease and 7 had colonic disease alone.
Conclusion: Panenteric capsule endoscopy is feasible and can be performed safely in patients known to have IBD. It can be used to guide management without resorting to conventional endoscopy and identifies pathology in all areas of the gastrointestinal tract.
Disclosure of Interest: None declared

P0862 COLON CAPSULE ENDOSCOPY: A USEFUL DIAGNOSTIC MODALITY THAT INFORMS PATIENT MANAGEMENT

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Introduction: Colon capsule endoscopy (CCE) has been demonstrated to be a feasible alternative to colonoscopy for the detection of polyps and neoplasia[1] and avoids intubation and sedation**.** This study evaluates the utility of CCE in routine clinical practice and its impact on patient outcomes.
Aims & Methods: Retrospective, single-centre, including symptomatic patients attending for CCE using PillCam Colon 2 (Given Imaging, Yoqneam, Israel). All patients with known inflammatory bowel disease (IBD) successfully passed a PillCam Patency device prior. Patient demographics, procedural data, final diagnosis and management outcomes were collected.
Results: 101 patients were included, mean age 43 years (range 16-95), 73 female, median follow-up 29 months (range 1-52). 48% refused colonoscopy, 29% had an incomplete colonoscopy, 17% chose CCE over colonoscopy and 6% were unfit for colonoscopy. Indication for the procedure: anaemia (24%), IBD assessment (16%) and suspected IBD (60%). The latter had predominant symptoms of diarrhoea (77%), abdominal pain (18%) or weight loss (5%). Procedure completion rate 69%, bowel preparation was adequate in 75%. There were no complications.
Results are summarised in Table 1.
In the anaemia group, CCE altered management in 15%: 3 further procedures (1 double balloon enteroscopy (DBE) and argon plasma coagulation, 1 catheter embolisation and 1 small bowel capsule endoscopy) and 1 altered medication. The remaining 20 were managed conservatively.
In the known IBD group, CCE altered further management in 69% (7 altered medication, 2 surgery, 2 further procedures (1 DBE, 1 colonoscopy), the remaining 5 patients were managed conservatively.
In those suspected as having IBD, this was identified in 7%. Other clinically significant diagnoses were made in 36%. The remaining 57% patients were thought to have functional bowel disorders and were discharged. 3 patients were excluded due to a non-diagnostic examination.

Abstract number: P0863

Performance characteristics in the evaluation of the study images

Randomized VC setting	Evaluator	Accuracy for the first reading	Accuracy for the second reading	Difference in accuracy (%) [95% CI]
WLI		61.7	54.3	-7.4 [-12.5, -2.3]*
	1	49.1	44.6	-4.6 [-8.8, -0.3]*
	2	49.1	52.6	3.4 [0.0, 6.8]*
	3			
	Globally§	**53.3**	**50.5**	**- 2.9 [- 9.2, 3.5]**
FICE 1	**4**	63.4	52.3	-11.1 [-16.2, -6.0]*
	5	61.4	63.4	2.0 [-3.3, 7.3]
	6	44.7	75.4	30.7 [24.3, 36.7]*
	Globally§	**56.5**	**63.7**	**7.1 [-17.0, 31.3]**
FICE 2	**7**	63.1	73.4	10.3 [5.3, 15.2]*
	8	65.4	58.9	-6.6 [-12.0, -1.1]
	9	75.7	79.4	*3.7 [-0.5, 7.9]
	Globally§	**68.1**	**70.6**	**2.5 [-7.1, 12.1]**
FICE 3	**10**	62.0	77.7	15.7 [10.1, 21.2]*
	11	58.9	50.6	-8.3 [-14.2, -2.2]*
	12	52.6	59.7	7.1 [1.3, 12.9]*
	Globally§	**57.8**	**62.7**	**4.9 [-8.9, 18.6]**
Blue Mode	**13**	36.9	62.3	25.4 [19.1, 31.4]*
	14	71.7	77.1	5.4 [1.0, 9.8]*
	15	68.0	76.3	8.3 [3.3, 13.3]*
	Globally§	**53.7**	**70.2**	**16.5 [13.6, 19.4]***

VC, virtual chromoendoscopy; *statistically significant; § stratified McNemar test; WLI, white light image; CI, confidence interval

Table 1

INDICATION	DIAGNOSIS							
		FRESH			SB			
NORMAL	POLYPS	BLOOD	AE	DD	ULCERATION	COLITIS	HAEMORRHOIDS	
ANAEMIA	10	3	3	2	2	3	1	0
KNOWN IBD	7	0	0	0	0	8	1	0
SUSPECTED IBD	33	16	0	0	4	3	1	1

Conclusion: CCE may be a useful alternative for detecting clinically relevant pathology in symptomatic patients and can help guide management. An incomplete examination (i.e. distal colon not visualised) was less relevant in the 29 patients who had already had an incomplete colonoscopy beforehand or the 24 patients whose incomplete CCE was sufficient to provide a diagnosis. Although marketed as a colonic imaging device, a third of pathology identified by CCE was in the SB, serving as a reminder that it may be difficult to distinguish symptoms arising from the small or large bowel, or both.

Reference

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Disclosure of Interest: None declared

P0863 USEFULNESS OF VIRTUAL CHROMOENDOSCOPY IN THE EVALUATION OF SUBTLE SMALL BOWEL ULCERATIVE LESIONS BY TRAINEES OR YOUNG GASTROENTEROLOGISTS WITH NO EXPERIENCE IN VIDEOCAPSULE ENDOSCOPY

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Introduction: Identification of subtle small bowel mucosal lesions by less experienced videocapsule endoscopy (VCE) readers can be challenging, as small differences in mucosal hue or pattern are difficult to detect. To improve lesions' characterization, chromoendoscopy virtual techniques based on narrowing the bandwidth of the conventional white light endoscopy image (WLI) were developed. However, data on the virtual chromoendoscopy (VC) application in VCE are limited.
Aims & Methods: This multicenter study involved 15 trainees or young endoscopists with good experience in GI endoscopy but no experience in VCE examination. In the first step, they evaluated a WLI selection of mixed de-identified images of 250 unequivocally confirmed difficult to interpret small bowel ulcerative lesions, and 100 artifacts mimicking ulcerative lesions. In the second step, they were randomized in clusters of 3 to evaluate the same images with the addition of one of the VC setting (FICE 1,2,3 and Blue Mode) or in WLI again, labeling them as real or faked. The comparison of accuracies in correctly categorizing the images was performed between the two readings (McNemar's test).
Results: The results were very heterogeneous. There was a small decrease in accuracy for the second evaluation of WLI pictures. By adding any of the chromoendoscopy settings resulted in an improvement in lesions' characterization; statistical significance was obtained only for Blue Mode (*see table*).
Conclusion: Virtual chromoendoscopy (especially Blue Mode) seems to help beginner VCE readers in correctly categorizing small bowel mucosal ulcerative lesions.
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Disclosure of Interest: M. Rimbas: None declared, D. Zahiu: None declared, A. Voiosu: None declared, T. Voiosu: None declared, A. Zlate: None declared, R. Dinu: None declared, D. Galasso: None declared, L. Minelli Grazioli: None declared, M. Campanale: None declared, F. Barbaro: None declared, B. Mateescu: None declared, B. Busuioc: None declared, T. Iordache: None declared, O. Dolofan: None declared, A. Popescu: None declared, V. Balaban: None declared, M. Raducan: None declared, C. Spada Consultancy: Given Imaging/ Coviden, C. Baicus: None declared, G. Costamagna Consultancy: Given Imaging/ Coviden

P0864 A NOVEL PREP-LESS X-RAY IMAGING CAPSULE FOR COLON CANCER SCREENING: SAFETY AND PRELIMINARY HUMAN TESTS

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Introduction: The demand for bowel cleansing hampers participation in screening colonoscopy, while poor preparation impairs adenoma detection. A screening method, which generates structure data of the colon, without any cleansing or diet restrictions, would offer an attractive modality for many of the non-compliant patients from the target population.
Aims & Methods
Aims: To evaluate feasibility, safety and outcomes of a novel prep-less X-ray imaging capsule for colon screening.
Device: The capsule is similar in dimensions to other approved capsules. Novel ultra-low dose X-ray based imaging technology (X-Ray radar) generate high-resolution 3-dimensional (3D) imagery of the colon without bowel cleansing. The radar is activated and scans the inner surface only when the capsule is propelled within the colon.
Methods: Capsules were swallowed by ~20 volunteers (aged 37-66) and tracked during the entire passage of the capsule through the alimentary tract using radio frequency telemetry and a Capsule localization system (CPS). The system performed scans upon detecting effective capsule motion in the colon and transmitted imaging data to an external recorder unit attached to the patients' lower back. Combined data from colon scans and the CPS system were used to reconstruct 3D colon segments in non-prepped colons. Total transit time and total X-ray exposure were calculated to assess the safety profile of the capsule in human subjects.
Results: All capsules were swallowed and eliminated naturally and uneventfully after an average transit time of 68 ± 31 hours. The volunteers were exposed to an ultra-low total radiation dose (average total exposure 0.03 ± 0.007 mSv). The generated traces from various participants present large variability of colon macro structure. Reconstruction of synthetic colon phantoms with and without polyps as well as data from a Bovine colon phantom with induced tissue-made polyps showed spatial resolution of 2–3 mm in colon diameter measurements.
Conclusion: A safety and preliminary efficacy study has been performed using a novel prep-less x-ray imaging capsule for colon cancer screening.
Quantitative ultra-low dose x-ray 3D imaging was achieved in the colon of human subjects. The efficacy of the tracking system and the colon 3D reconstruction will be validated in a multicenter study.
Disclosure of Interest: None declared

P0865 USEFULNESS OF NEW ALGORITHM-IMPLEMENTED READING SOFTWARE FOR SMALL-BOWEL CAPSULE ENDOSCOPY (CE)

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Introduction: Reading of tens of thousands of CE images is labor-intensive and time-consuming. Olympus Corp. has developed a new algorithm to minimize redundant images so that all the areas captured by CE can be displayed.
Aims & Methods: The co-primary endpoints in this study were (1) to demonstrate the non-inferiority of this new algorithm modality showing only selected images in reading major and minor lesions compared to the control (EC-10 normal mode modality) showing all the images in terms of the number of true positives (TP), and (2) to demonstrate the superiority of this modality to the control in reading time. Multicenter crossover study was performed at 8 hospitals in Japan. This study consisted of 7 readers and 3 adjudication committee members, 2 reading modalities, and 40 patients with various small-bowel pathology reviewed and documented by 3 judging members from 60 patients with suspected small-bowel diseases (10 patients from 6 hospitals). Each patient's images were read by randomly-allocated 2 readers, each of whom used each modality for each patient (i.e. Doctor A: the new modality followed by the control, Doctor B: the control followed by the new modality). The reading modalities were switched after a certain interval more than 2 weeks. Thereby, this amounted to a total of 4 readings per patient. The adjudication committee defined clinically relevant lesions as major lesions, and irrelevant subtle lesions as minor lesions. A priori non-inferiority margin of 0.9 was established.
Results: Estimated ratios of detection rates of total, major, and minor lesions with the new modality compared to the control were 0.87 (0.80-0.95), 0.93 (0.83-1.04), and 0.83 (0.74-0.94), respectively. Although non-inferiority was not demonstrated with the new modality, the detection rate of major lesions was not significantly different between the new modality and the control. The reading

time of the new modality and the control was 27.3 and 75.1 minutes, respectively, the difference of which was -47.7 minutes (-52.0,-43.4)($P < 0.001$).
Conclusion: The Olympus new algorithm-implemented reading software significantly shortened the reading time without declining detection rate of major lesions, although non-inferiority was not demonstrated in detecting all small-bowel lesions.
Disclosure of Interest: None declared

P0866 POLYETHYLENE GLYCOL SOLUTION PRIOR TO SMALL BOWEL CAPSULE ENDOSCOPY – DOES IT HELP?

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Introduction: The diagnostic yield of capsule endoscopy (CE) relies heavily upon obtaining clear luminal views and is often hampered by biliary secretions, small intestinal fluid and bubbles. Studies assessing the efficacy of bowel preparation in CE have been inconsistent and a general consensus on this matter has not been reached. Our department has recently moved from a pre-procedure regimen of 24 hours of clear fluids only, to 24 hours of clear fluids and the addition of a single sachet of polyethylene glycol (PEG) solution the evening prior to CE. To investigate the effect of this change, we performed a retrospective review of CE findings in patients who received PEG solution vs. clear fluids.
Aims & Methods: Patients who underwent CE from August 2013 to March 2015 were indentified using Rapid® capsule endoscopy software. This provided an even distribution of patients receiving PEG solution vs. clear fluids only. Data were collected on patient demographics, indication for CE and clinical findings. Three independent assessors then reviewed image quality of capsule footage at 20 minute intervals to examine the bowel preparation. Overall adequacy was determined as 'adequate' or 'inadequate' (views of mucosa obscured by cloudy fluid or bubbles in a high proportion of images) by consensus opinion. Lesion detection rates were then calculated for patient groups. Comparisons between groups were performed using chi-square analysis.
Results: A total of 62 patients were identified: 31 (50%) received polyethylene glycol (PEG) solution and 31 (50%) received clear fluids only (CF) prior to CE. There were no significant differences in patient demographics between PEG and CF groups (mean age 50 vs. 52, and M:F 20:11 vs. 18:13, respectively). Indications for CE included obscure gastrointestinal (GI) bleeding (18 in PEG group vs. 22 in CF) and possible small bowel Crohn's disease (13 in PEG group vs. 9 in CF). There were no significant differences in lesion detection rate between the two groups when all lesions, including those deemed clinically insignificant (e.g. minor aphthous ulceration) were analysed (90.3% PEG group vs. 83.9% CF, $p = 0.45$). When these lesions were excluded, the detection rate for clinically significant lesions in the PEG group was significantly higher than that in the CF group (58.1% vs. 32.3%, $p < 0.05$). Moreover, a significantly higher proportion of patients had 'adequate' image quality following bowel preparation in the PEG group vs. CF group following independent assessment (74.2% vs. 48.4%, $p < 0.05$).
Conclusion: We conclude that moving to a regimen of clear fluids and a single sachet of PEG solution prior to CE has significantly improved our detection rate of clinically significant lesions. This may be explained by improved image quality and adequacy of bowel preparation associated with PEG solution. Larger prospective studies comparing different bowel cleansing regimens (including a 'full' bowel preparation as taken prior to colonoscopy) are needed to firmly establish the ideal preparation for capsule endoscopy.
Disclosure of Interest: None declared

P0867 STANDARTIZATION OF VIRTUAL NAVIGATOR WORK IN ABDOMINAL RADIOLOGY

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Introduction: The essence of the virtual navigator is to synchronize the real-time data obtained by ultrasound and MSCT / MRT. There are 2 modes of synchronization: 1-manual alignment of the plane and point 2-technology automatically align with a magnetic sensor - Active Tracker. The scientific sources available to us is not given a standardized method of using the device Active Tracker, depending on the zone of interest.
Aims & Methods: In order to standardize the work of the virtual navigator LOGIQ E9 in abdominal radiology surveyed 11 people (6 male, 5 female) with different pathologies of the abdominal cavity during 2014. Algorithm examination consisted of 3 phases. The first phase was carried out ultrasound research of the abdomen, which determines the location of the pathological focus in the abdomen. The second stage was carried out MSCT of the abdomen (model Toshiba Aquilion) superimposed on the anterior abdominal wall unit Active Tracker. In the third phase image obtained by MSCT were loaded on the console LOGIQ E9, where the automatic synchronization of the image obtained by MSCT and ultrasound research in real time using the device Active Tracker. We have proposed a method of standardization Active Tracker device location on the anterior abdominal wall at pathological foci ranging in 1- the right lobe of the liver, 2 - the left lobe of the liver, 3- pancreas, 4- right kidney, 5-, left kidney. In the study of the pathological focus in the right lobe of the liver is necessary to have Active Tracker midline at a distance of 7-8 cm from the edge of the xiphoid process. In the study of the pathological focus in the left lobe of the liver is necessary to have Active Tracker midline at a distance of 10-11 cm from the edge of the xiphoid process. In the study of the pathological focus in the pancreas is necessary to have Active Tracker midline at a distance of 12-13 cm from the edge of the xiphoid process. In the study of the pathological focus in the right kidney is necessary to have Active Tracker on the right midclavicular line in the 7-8 intercostal space. In the study of the pathological focus in the left kidney is necessary to have Active Tracker on the left midclavicular line in the 7-8 intercostal space.
Results: The standardization work of the virtual navigator has led to a reduction in the time synchronization of images from 15-20 minutes to 3-7 minutes, increase the accuracy of coincidence of the two images (with 78% for the standard method to 92% with improved), reducing the number of operator errors when synchronizing images.
Conclusion: Thus, we developed a technique proved its efficiency and propose to use when working with virtual navigation.
Disclosure of Interest: None declared

P0868 ENDOSCOPIC ULTRASONOGRAPHY-GUIDED INTERSTITIAL BRACHYTHERAPY BASED ON SPECIAL TREATMENT-PLANNING SYSTEM FOR UNRESECTABLE PANCREATIC CANCER: A PILOT STUDY

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Introduction: EUS-guided interstitial brachytherapy is promising in the treatment of unresectable malignant carcinoma adjacent to the digestive tract. The feasible treatment plan is not established.
Aims & Methods: To develop a novel treatment plan and evaluate the feasibility in patients with unresectable pancreatic cancer.14 patients with unresectable pancreatic cancer.A special treatment-planning system (TPS) for EUS was designed and evaluated by comparing with the traditional TPS. (IIIstage: 6; IVstage: 8) underwent EUS-guided interstitial brachytherapy based on the new software.
Results: In the test model, there was no obvious difference of irradiation doses calculated by the two softwares (EUS TPS vs. traditional TPS) ($P > 0.05$). Under the support of EUS TPS, a novel treatment plan for EUS-guided interstitial brachytherapy was successfully established, which contained seven principles. All patients tolerated the treatment well without any serious complications. In 5 patients (stage III) that the minimal peripheral dose was larger than 90Gy, the PD rate was 80%(4/5).Four patients (4/6) in stage III were alive for more than 12 months with a median peripheral dose of 107.5 Gy. The expected median survival time of the 14 patients was 9.0 months (95%CI, 7.6–10.4 months).
Conclusion: The results demonstrated that the new EUS TPS will play an important role in EUS-guided interstitial brachytherapy in patients with unresectable malignant carcinoma.
Disclosure of Interest: None declared

P0869 TYPE OF COMBINED ENDOSCOPIC BILIARY AND GASTRODUODENAL STENTING IS A SIGNIFICANT FACTOR FOR BILIARY ROUTE MAINTENANCE

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Introduction: Some patients with malignant gastric outlet obstruction require combined biliary and gastroduodenal stenting (double stenting)[1], but there is often difficulty performing biliary re-intervention for stent dysfunction, and the optimal biliary stenting for such cases remains controversial[2].
Aims & Methods: From the perspective of biliary re-intervention, 43 consecutive patients who successfully underwent endoscopic double stenting with metallic stents were reviewed, and features of double stenting and clinical outcomes were evaluated. The present study aimed to clarify what affects for long-term maintenance of the biliary drainage route.
Results: All patients with biliary stent dysfunction were studied, and univariate analysis showed that the separate type of double stenting (two stents placed not in a crossed position) was a unique predictive factor related to successful biliary re-intervention for stent dysfunction (odds ratio 73.67, $P = 0.001$). From the comparison of clinical features between the separate and cross (two stents placed in crossed position) types, cases with biliary stenting before gastroduodenal stenting ($P = 0.008$) and transpapillary biliary drainage ($P = 0.01$) tended to become the cross type. There were no significant differences in overall survival and the biliary stent dysfunction rate, but the Kaplan-Meier method showed that the separate type was superior for biliary stent patency after double stenting ($P = 0.04$). Moreover, the initial biliary route maintenance rate was significantly higher in the separate type, with an estimated hazard ratio of 0.25 (95% confidence interval, 0.061-0.99; $P < 0.001$).
Conclusion: The separate type of double stenting might contribute to successful biliary re-intervention and maintain the drainage route longer. Technical considerations of biliary drainage should be considered in order to perform the separate type of double stenting.

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Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00–17:00
SURGERY II – HALL 7

P0870 INDICATION FOR THE PLACEMENT AND THE REMOVAL OF PROPHYLACTIC DRAINS FOLLOWING HEPATECTOMY

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Introduction: Although abdominal prophylactic drains following hepatectomy is still controversial, they have been routinely placed in most of institutions for hepato-biliary-pancreatic surgery. The present study was aimed to establish the indication to place prophylactic drains after hepatectomy and the optimal time for their removal.
Aims & Methods: From June 2011 to December 2014, consecutive 77 cases underwent hepatectomy without biliary reconstruction for benign and malignant liver tumors in JA Hiroshima General Hospital. Of them, prophylactic drains were placed in 60 cases whose Glissonean pedicles of more than 2 mm in diameter were ligated or clipped and divided. Perioperative data were prospectively collected and analysed. Bilirubin levels in drain fluid were measured on postoperative day (POD) 3 after surgery. Drains were removed on POD 3 or 4 if the drain-fluid bilirubin level was less than three times as the serum level of bilirubin according to the International Study Group of Liver Surgery (ISGLS). As postoperative complications related with placement of prophylactic drains, biliary leakage was analysed and classified into two groups: one is early biliary leakage (EBL) when diagnosed within POD 10. The other is delayed biliary leakage (DBL) when diagnosed after POD 11.
Results: Biliary leakages of Grade A and B according to ISGLS were observed in 6 cases (7.8%). The drain-fluid bilirubin level more than three times as the serum level of bilirubin was observed only in one case, treated conservatively by repeated replacement of drainage (Grade A). In the rest of 59 cases, placed with prophylactic drains, they were removed on mean POD 3.5. Of them, five cases were treated with re-drainage on mean POD 19.0 (ranging from 11 to 30) and four cases were co-treated with endoscopic nasal biliary drainage (Grade B). On multivariate analysis, the exposure of Glissonean pedicles of more than 2 cm in the major axis was the strongest predictor of biliary leakage (odds ratio 14.210, 95 per cent confidence interval 1.289 to 156.717; $p = 0.03$).
Conclusion: Prophylactic drains might be essential in hepatectomy, exposing the Glissonean pedicle. The optimal time for their removal according to the ISGLS criteria of biliary leakage was thought to be appropriate for EBL. However, the careful observation is also needed after POD 11 for DBL.
Disclosure of Interest: None declared

P0871 POSTTRANSPLANT PEAK C-REACTIVE PROTEIN CORRELATES WITH ISCHEMIA-REPERFUSION INJURY AND RECURRENCE-FREE OUTCOME IN LIVER TRANSPLANT PATIENTS WITH HCC

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Introduction: Ischemia reperfusion (I/R) injury was shown to promote intra- and extrahepatic tumor outgrowth in liver transplant patients with hepatocellular carcinoma (HCC). C-reactive protein (CRP) is a parameter of inflammatory response to surgical trauma.
Aims & Methods: The aim of this study was to determine the correlation of posttransplant peak CRP-level with I/R-induced hepatocellular damage and recurrence-free outcome following liver transplantation (LT) for HCC. 103 liver transplant patients with HCC were included. Patients were classified as Milan In and Milan Out, based on explant histopathology data. By ROC-analysis, the most optimal cut-off post-LT peak CRP-level for overall and recurrence-free outcome was determined. Peak CRP values along with other established clinicopathologic variables were correlated with early hepatocellular damage (transaminases, hepatic artery resistive index) and tumor-specific outcome.
Results: ROC-analysis defined an optimal cut-off peak CRP-level of 3.5 mg/dl for overall and recurrence-free survival. In the high CRP-group (< 3.5 mg/dl), hepatocellular damage was higher and hepatic artery perfusion more compromised than in the low CRP-group (≤ 3.5 mg/dl; $P < 0.001$). Five patients in the low CRP-group (7.8%), but 19 patients of the high CRP-subset (48.7%) developed HCC relapse post-LT ($P < 0.001$). The 1- and 5-year disease-free survival rates were 95.3% and 91.7% in the low CRP-group, but 89.5% and 48.7% in high CRP-subset ($P < 0.001$). In multivariate analysis, presence of microvascular invasion (Hazard ratio [HR] 10.9), peak CRP > 3.5 mg/dl (HR 4), AFP-level > 400 IU/ml (HR 3) and total ischemia time > 450 min (HR 3.4) were identified as independent predictors of HCC relapse. In Milan In patients, CRP level had no predictive value. In contrast, peak CRP-value (HR 5.8) together with microvascular invasion (HR 8.3) were identified as the only independent predictors of recurrence-free survival in Milan Out recipients. The 1- and 5-year recurrence-free survival rates in this special subset were 94.4% and 88% the low (n = 36), but only 87.8% and 29.3% in the high CRP-patients (n = 25; $P < 0.001$).
Conclusion: Early posttransplant peak CRP correlates with I/R-induced hepatocellular injury and risk of HCC recurrence. In particular patients with HCC exceeding the Milan criteria might benefit from targeting inflammatory mechanisms.
Disclosure of Interest: None declared

P0872 POST CHOLECYSTECTOMY BILIARY INJURIES: ONE CENTER EXPERIENCE

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Introduction: Laparoscopic cholecystectomy has lead to a rise in the incidence of BDIs from 0.1-0.2% in OC to 0.4-0.6% after LC.[1] The early and accurate diagnosis of postcholecystectomy BDIs is mandatory for surgeons and gastroenterologists, because unrecognized or badly managed BDIs lead to serious complications such as biliary cirrhosis, hepatic failure and even death.[2] The choice of the appropriate treatment for BDIs is very important, because it may avoid these serious complications and improve quality of life among these patients. Therefore, the question regarding the type of treatment for patients with BDIs is still a matter of debate. Initially, endoscopic treatment is recommended in patients with BDIs. When endoscopic techniques are not effective, surgical reconstruction is performed.[3] The management of BDIs is a surgical challenge that needs collaboration among surgeons, gastroenterologists and interventional radiologists at tertiary referral centers.[4,5]
Aims & Methods: Between 1995 and 2012, 330 patients with post-cholecystectomy bile duct injuries presented to Gastroenterology Surgical Center, Mansoura University, Egypt.
Results: Of the studied patients, 232 were females and 98 patients were males. Their mean age was 38 years $\pm$ 12. 63% of the patients were referred from private hospitals while 34.5% were referred from primary hospitals. 252 patients had open cholecystectomies while 78 patients had laparoscopic cholecystectomies. Regarding the type of injuries according to Strasberg-Bismuth classification, the most common was type E2 injury (31.2%) followed by type A injury (20.6%). According to the time of diagnosis, 10 patients were diagnosed intraoperatively, 236 patients were diagnosed early (within one month of the cholecystectomy) and 84 patients were lately diagnosed (more than one month after the cholecystectomy). Patients presented with generalized peritonitis, localized peritonitis with fistulae or with progressive jaundice.
229 patients were managed surgically where 217 patients underwent bilio-enteric reconstruction while 122 were managed by endoscopic dilatation and stent out of which 21 patients needed surgical reconstruction after failed repeated dilatations. 87.3% of patients who were managed surgically showed excellent outcomes according to Johns Hopkins criteria compared to 78.6 % for endoscopic management.
Conclusion: As a conclusion, early diagnosis of iatrogenic bile duct injuries together with management by experienced hepatobiliary surgeon greatly improves the patient outcomes.

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Disclosure of Interest: None declared

P0873 APPLICATION OF HEPATOBILIARY SCINTIGRAPHY FOR THE IDENTIFICATION OF HIGH-RISK PATIENTS REQUIRING PREOPERATIVE PORTAL VEIN EMBOLIZATION

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Introduction: Patients with insufficient future remnant liver (FRL) are at risk of developing postoperative liver failure (LF) and are candidates for preoperative portal vein embolization (PVE). ^{99m}Tc-mebrofenin-hepatobiliary-scintigraphy (HBS) is a quantitative method enabling functional assessment of the FRL with a validated cut-off value for safe resection (2.7%/min/m^2). Other, mathematical methods of preoperative FRL-assessment, like FRL/body-weight ratio (FRL-BWR) and standardized (estimated) volumetry, claim to accurately assess the FRL.
Aims & Methods: The aim of this study was to evaluate the above mentioned methods in the identification of patients requiring preoperative PVE. From November 2006 to June 2014, preoperative HBS and CT-volumetry followed

by major liver resection (≥3 segments) were performed in 169 patients. Patients with FRL volume <25% and/or FRL function <2.7%/min/m2 were considered for preoperative PVE. We compared CT-volumetry in combination with HBS with FRL-BWR (cut-off value 0.5% patient's weight) and estimated volumetry (cut-off value 25% of estimated total liver volume). The endpoints were the differences in FRL-evaluation between the methods.
Results: 29/169 (17.2%) patients underwent preoperative PVE. The median FRL percentage of the total liver volume before PVE was 23.7% (IQR 18.7-27.8). The median FRL-function was 1.9%/min/m2 (IQR 1.50-2.36). In 8/29 (27.6%) of these patients, PVE was performed because FRL-function was below the cut-off value in spite of FRL-volume ≥25%. Median FRL-BWR was 0.52% (IQR 0.40-0.70) and median estimated FRL was 24.5% (IQR 18.34-29.43). According to BWR-FRL and estimated volumetry, 16/29 (55.2%) and 14/29 (48.3%) patients, respectively, had sufficient FRL and would not have undergone PVE if the decision was based on these methods. 1/29 (3.4%) patient developed LF resulting in death. This patient had insufficient FRL according to all the above mentioned methods.
Conclusion: Non-functional FRL-assessment may lead to overestimation of the FRL. HBS provides useful information for the identification of patients requiring preoperative portal vein embolization.
Disclosure of Interest: None declared

P0874 ASSESSMENT OF LIVER FUNCTION IN PATIENTS UNDERGOING MAJOR LIVER RESECTION USING HEPATOBILIARY SCINTIGRAPHY

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Introduction: ^{99m}Tc-mebrofenin-hepatobiliary-scintigraphy (HBS) is a quantitative method enabling functional assessment of the future remnant liver (FRL-function). In a previous validation study, we determined a single cut-off value of 2.7%/min/m^2 in patients with non-compromised and compromised liver parenchyma, for the prediction of postoperative liver failure (LF).
Aims & Methods: The aim of this study was to evaluate the value of HBS in the preoperative assessment of patients eligible for major liver resection. From November 2006 to June 2014, 169 patients, of which 71/169 (42.0%) with (peri)hilar cholangiocarcinoma, underwent major liver resection (≥3 segments) after preoperative HBS and CT-volumetry. Patients with FRL-volume <25% and/or FRL-function <2.69%/min/m^2 were considered for preoperative portal vein embolization (PVE). The study endpoints were postoperative LF and LF related mortality.
Results: 29/169 (17.2%) patients underwent preoperative PVE. Median FRL-volume prior to PVE was 23.7% (IQR 18.7-27.8) of total liver volume. Median FRL-function was 1.9%/min/m^2 (IQR 1.50-2.36). In 8/29 (27.6%) of these patients, PVE was performed because FRL-function was below the cut-off value in spite of FRL-volume ≥25%. Major hepatectomies comprised 72 (42.6%) right and 56 (33.1%) left hemihepatectomies, 30 (17.8%) extended right and 6 (3.6%) extended left hemihepatectomies, 2 (1.2%) central resections and 3 (1.8%) segmentectomies of ≥3 liver segments. Overall, clinically relevant complications (≥ Clavien-Dindo grade 3a) were seen in 66/169 (39.1%) patients. LF (overall 2.4%) was seen in 3/140 (2.1%) of the non-PVE patients and in 1/29 (3.4%) of the PVE patients while LF related mortality (overall 1.8%) occurred in 2/140 (1.4%) of non-PVE vs. 1/29 (3.4%) of the PVE patients. There were no significant differences in postoperative outcomes between PVE and non-PVE patients.
Conclusion: Preoperative HBS provides useful functional information on the FRL in patients requiring major liver surgery. Patients with sufficient FRL-volume but decreased FRL-function may benefit from preoperative portal vein embolization.
Disclosure of Interest: None declared

P0875 ARE "TAKE HOME" BOX TRAINERS AS GOOD AS HIGH FIDELITY, VIRTUAL REALITY (HFVR) SIMULATORS IN ACQUIRING LAPAROSCOPIC SURGICAL SKILLS?

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Introduction: High Fidelity Virtual Reality (HFVR) simulators have been proposed as providing optimum training for laparoscopic procedures such as cholecystectomy. However, purchase and maintenance costs have compromised widespread use of this type of equipment. Further, recent short-term studies have demonstrated equal or greater efficacy of supervised training programmes using simple box trainers (BT) compared to HFVR simulators.
Aims & Methods
Aim: This study explores the value of independent learning using a BT over a longer period of training, compared to the same duration of "free access" to HFVR simulators.
Methods: 16 surgical trainees who had performed fewer than 15 laparoscopic cholecystectomies were recruited to this study and randomised into two groups: the BT Group were to be provided their own BT whilst the HFVR Group were subsequently offered free access to a HFVR. Prior to commencing their allocated training programme all trainees performed laparoscopic cholecystectomy on a HFVR simulator from which the simulator-derived matrix scores were collected. Subsequently both groups were asked to practice 3 simple tasks (peg transfer, clip applying and precision cutting) for 6 weeks (20 repetitions of each) using their allotted training tool. Finally trainees performed a second laparoscopic cholecystectomy on the HFVR simulator from which the same matrix scores were determined. Change in performance from baseline to the second assessment was compared between the groups.
Results: The BT group improved significantly in respect of the number of movements (before median, (25th -75th percentile) 1419 (893.5-1689), after 466 (324-888.5), p = 0.021) performed and total path length (PL before mean 2951.58 (2037.6-4258.5) after 1610.57 (906.05-2211.85), p = 0.024). The time to perform cholecystectomy was not statistically reduced (before mean, 1373.22 sec (1057-1880) after 749.22 (294.5-1071.5), p = 0.051). In contrast, there was no statistically significant improvement in any of the matrices in the VR group (time before mean 923.71 sec (317-1238) after 820.29 (430-1264), p = 0.920; NOM before median 760 (430-1264) after 964 (608-1442), p = 0.446; PL after mean 1856.3 (981-2739.4) after 2393.9 (939.9-3056.3), p = 0.425). Inter-group comparison of these parameters showed no difference in the reduction in time to perform cholecystectomy (Time BT mean 624sec (-2-1422) HFVR: -33.24 (-968-639) sec p = 0.137). However the BT group performed significantly better in terms of NOM (BT median 447 (112-1416) HFVR -182 (-811-337), p = 0.031) and PL (BT mean 1341.01 (172.6-2800.7) HFVR -537.6 (-2210-1011.2), p = 0.03). These differences could be explained by the number of repetitions performed by each group (BT: median 20 (20-25) v HFVR: 10 (2-10), p = 0.008).
Conclusion: There are strong indications that longer-term practice on a "take-home" BT may be more effective for the acquisition of laparoscopic skills, compared to VR simulators. This may be explained by the greater opportunity for practice with the BT.
Disclosure of Interest: None declared

P0876 CLINICOPATHLOGICSTUDY OF MINIMUM INVASIVE SURGERY AND ENDOSCOPIC PAPILLECTOMY FOR TUMOR OF THE AMPULLA OF VATER

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Introduction: Ablative therapy is required for patients with pathological abnormalities at The Tumor of the Ampulla of Vater: in particular, carcinomas, adenomas and carcinoids. Adenomas are benign lesions, but because suspicions are raised about adenoma-carcinoma sequence during the process of developing adenoma, a treatment for premalignant lesions also needs to be considered. Local excision of the Ampulla of Vater and partial duodenectomy as Minimum Invasive Surgery for adenomas and early carcinomas have been performed at our hospital since 1989. For the case of adenomas, endoscopic Papillectomy has also been carried out. A decision regarding the adequacy of borderline lesions has been made by a discussion with gastroenterologists in our hospital. In the present study, the adequacy of borderline lesions and results of it were examined by attempting to compare between endoscopic Papillectomy and Local excision of Tumor of the Ampulla of Vater.
Aims & Methods: From 1989 ~ 2014, 18 patients underwent Local excision of the Ampulla of Vater, 2005 ~ 2013, 12 patients underwent endoscopic Papillectomyrespectively. We examined in terms of clinicopathlogical findings, complications?background, curability and the postoperative hospitalization days.
Results: 18 patients underwent Local excision of the Ampulla of Vater, and another 12 patients were given endoscopic Papillectomy. The patients who underwent Local excision were histopathologically diagnosed as follows: 9 patients with papilla cancer, 8 patients with adenoma, and 1 patient with carcinoid; meanwhile, the patients who underwent endoscopic Papillectomy were as follows: 2 patients with papilla cancer, 8 patients with adenoma, 1 patient with carcinoid, and 1 patient with polyp. The number of patients who received a diagnosis of adenoma before surgery but who were recognized as malignancy after surgery was 4 in Local excision of the Ampulla of Vater and 2 in endoscopic Papillectomy. Resection stumps in 3 patients who were given endoscopic Papillectomy were partially unclear, but there was 1 patient with positive surgical margins. The number of patients who suffered complications before surgery was 3 in Local excision, but none were in endoscopic Papillectomy. The average of a hospital stay after surgery was 18.5 days in Local excision of the Ampulla of Vater and 11.6 days in endoscopic Papillectomy. The number of patients who suffered complications after surgery in Local excision of the Ampulla of Vater was 1 patient with pancreatitis, and that in endoscopic Papillectomy was 5 patients with bleeding, 3 patients with inflammation of the gall bladder and the bile duct, and 2 patients with pancreatitis. 1 patient had a prognosis of stump recurrence (adenoma) in endoscopic Papillectomy, but others were alive without evidence of any cancer.
Conclusion: Patients had neither severe complication nor cancer recurrence in both Local excision of the Ampulla of Vater and Endoscopic papillectomy;

therefore, a decision regarding the adequacy of borderline lesions in our hospital was thought to be responsible.
Because patients had a good prognosis in both therapeutic procedures, each benefit was thought to be utilized by greatly considering the adequacy of borderline lesions and choosing surgical procedures, and appropriate medical care for patients was also thought to be provided by means of the lowest operative stress on borderline lesions.
Disclosure of Interest: None declared

P0877 IN SITU HYPOTHERMIC PERFUSION WITH RETROGRADE OUTFLOW DURING RIGHT HEMIHEPATECTOMY: FIRST CLINICAL EXPERIENCES

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Introduction: A new technique of selective in situ hypothermic perfusion with retrograde outflow (IHP-R) was developed. The outcomes of IHP-R were assessed during right hemihepatectomy in a randomized controlled clinical trail.
Aims & Methods: After right liver mobilization, the right branch of the portal vein (RPV) and the right hepatic artery (RHA) were clamped and cut. Following RHA cannulation, the portal triad was clamped, the right hepatic vein was closed and cut, and the middle/left hepatic veins were clamped to exclude the liver from the circulation. The left hemiliver was perfused through the RHA using cold Ringer's lactate solution (target liver temperature of 28°C), allowing retrograde outflow via the cut end of the RPV until parenchymal transection was completed. Fourteen patients were randomized between IHP-R and the standard procedure. Outcomes included laboratory parameters (AST, ALT, total bilirubin), transfusion requirements, complications, ICU stay, functional liver regeneration (assessed preoperatively and at postoperative day (POD) 3 by hepatobiliary scintigraphy with SPECT), and hospital stay.
Results: There were no statistical differences regarding baseline demographic and clinical characteristics. The median/range IHP-R times were 45/43–55 min while the target temperature of 28°C was reached in 6 of 7 IHP-R patients. Ischemia time, resection type, transfusion requirements, ICU stay, complications, and hospital stay were not different between groups. Procedure duration was longer in the IHP-R group (454/371-494 versus 330/256-351 min, p = 0.007). Postoperative AST and bilirubin were not different between groups, however peak ALT levels were higher in the IHP-R group (512/399-667 versus 397/214-415 U/L, p = 0.038). There was significant functional liver regeneration within the IHP-R but not in the control group on POD-3 compared to preoperatively calculated values (p = 0.018), suggesting early and possibly improved functional liver regeneration following IHP-R.
Conclusion: IHP-R allows easy and safe cold liver perfusion. The higher peak in ALT levels following IHP-R might be due to the prolonged procedure duration. Nevertheless, IHP-R induces early, and possibly improved liver regeneration following major liver resection.
Disclosure of Interest: None declared

P0878 PERCUTANEOUS PREOPERATIVE BILIARY DRAINAGE FOR RESECTABLE PERIHILAR CHOLANGIOCARCINOMA: NO ASSOCIATION WITH SURVIVAL AND NO INCREASE IN SEEDING METASTASES

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Introduction: Endoscopic biliary drainage (EBD) and percutaneous transhepatic biliary drainage (PTBD) are both used to resolve jaundice prior to surgery for perihilar cholangiocarcinoma (PHC). PTBD has been associated with seeding metastases.
Aims & Methods: The aim of this study was to compare overall survival (OS), and the incidence of initial seeding metastases that potentially influence survival, in patients with preoperative PTBD versus EBD. Between 1991 and 2012, 278 patients underwent preoperative biliary drainage and resection of PHC at two institutions (Netherlands and USA). Of these, 33 patients were excluded for postoperative mortality. Among the 245 included patients, 88 patients who underwent preoperative PTBD (with or without previous EBD) were compared with 157 patients who underwent EBD-only. Survival analysis was done with Kaplan-Meier and Cox regression with propensity score adjustment.
Results: Unadjusted median OS was comparable between the PTBD group (35 months) and EBD-only group (41 months; $P = 0.26$). After adjustment for propensity score, OS between the PTBD group and EBD-only group was similar (Hazard ratio, 1.05; 95% CI, 0.74-1.49; $P = 0.80$). Seeding metastases in the laparotomy scar occurred as initial recurrence in 7 patients, including 3 patients (3.4%) in the PTBD group and 4 patients (2.7%) in the EBD-only group ($P = 0.71$). No patient had an initial recurrence in percutaneous catheter tracts.
Conclusion: The present study found no effect of PTBD on survival when compared to patients with EBD, and no increase in seeding metastases that develop as initial recurrence. These data suggest that PTBD can safely be used in preoperative management of PHC.
Disclosure of Interest: None declared

P0879 EVALUATION OF THE PREDICTORS OF SURGICAL SITE INFECTION AFTER HEPATECTOMY: A SINGLE-CENTER EXPERIENCE

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Introduction: Surgical site infection (SSI) is the most common infectious complication after hepatectomy for hepato-biliary malignancies or hepatic benign lesions, with leading to longer hospital stays and higher medical costs. To clarify the predictors associated with SSI after hepatectomy, we conducted a retrospective cohort study of the patients who underwent hepatectomy at a single institution.
Aims & Methods: Recent 4 years, from June 2010 to June 2014, 430 patients underwent hepatic resection at our institution. Patient demographics, laboratory parameters, surgical records, and postoperative morbidity were evaluated and the predictors were identified using multivariate analysis between SSI group and non-SSI group.
Results: Of these 430 patients, 66 (15.3%) had SSIs after hepatectomy. 38 were men and 28 were women whose mean age was 66.6 years (range, 27 to 82). The most commonly disease and surgical procedure were hilar cholangiocarcinoma (n = 25, 37.9%) and hemihepatectomy (n = 32, 48.5%), respectively. The following pathogens were isolated by bacterial culture of purulent fluid from the patients of SSI; Enterococcus sp. (n = 31), Staphylococcus sp. (n = 17), Enterobacter sp. (n = 3), and Klebsiella sp. (n = 2), with high concordance of the bacterial culture from bile juice (70%). Postoperative hospital stays of SSI group (n = 66) were significantly longer than that of non-SSI group (n = 364). In a multivariate analysis, biliary reconstruction (odds ratio 6.24, 95% confidence interval 3.10-12.91, $P < 0.001$) and duration of operation (odds ratio 1.01, 95% confidence interval 1.00-1.01, P = 0.01) were identified as independent predictors for SSI after hepatectomy.
Conclusion: Biliary reconstruction and duration of operation were independent predictors of SSI after hepatectomy. Bacterial infections of bile juice was one of the major source of SSI after hepatectomy.
Disclosure of Interest: None declared

P0880 LAPAROSCOPIC VERSUS OPEN REPAIR OF PERFORATED PEPTIC ULCER (PPU)

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Introduction: While open surgery for PPU has long been golden standard, laparoscopic repair is steadily increasing at Danderyd general hospital. Our hypothesis is, in this retrospective descriptive single-center study, that laparoscopic is superior to open repair.
Aims & Methods: All patients who underwent a primary surgical procedure for PPU from January 2011 to December 2014 were included. Our aim is to describe and compare the outcome of different surgical approaches regarding age, ASA, boey score, clavian-dindo and mortality.
Results: 67 patients were treated for PPU, 9 were excluded due to non-operative or endoscopic treatment. Repair was performed laparoscopically in 32 cases, open surgery in 26 among which 8 had been converted from initial laparoscopy. In 2 cases only a peritoneal lavage was performed and in another 2 cases lavage was performed and a duodenal stent was placed. Conversion from laparoscopy was due to adhesions, the size of the perforation or inability to locate it. No significant preoperative differences were found between the groups of patients who underwent open or laparoscopic repair concerning characteristics of patients or ulcer.
The mortality rate was highest among elderly and those with high ASA-scores. In the open repair group the Clavian-Dindo score, mortality and length of hospital stay were significantly higher.
Reoperation had to be performed in 6 cases, 4 for continued leakage, 1 for deep abscess and 1 for suture dehiscence.

	Laparoscopic N = 32	Open approach N = 26	p
Male (n)	16	14	n.s
Age, yrs	63.0 (±19.3)	69.9 (±18.2)	n.s
ASA ≥3 (n)	15	16	n.s
General peritonitis (n)	22	16	0.59
Duodenal ulcer (n)	22	15	0.42

(continued)

Continued

	Laparoscopic N = 32	Open approach N = 26	p
ICU-care (days, median)	2	8	0.016
In hospital (days)	5.5 ± 2.3	9.8 ± 8.0	0.04
Clavian-Dindo≥ 3a (n)	6	10	0.14
Abscess (n)	1	2	0.59
Reoperation (n)	4	2	0.40
Mortality (n)	2	7	0.05

Conclusion: The size and design of this study do not allow too strong conclusions despite the fact that significant differences were found for morbidity, mortality and length of hospital stay. Albeit not having found significant differences for preoperative status (ASA, boey score) several patients in the open repair group underwent open surgery because they were deemed unfit for laparoscopy. Either based on pulmonary disease or multi organ failure, it will bias the outcome between the groups to the advantage of the laparoscopic group. In conclusion, when feasable, laparoscopic repair for PPU seem to be beneficial for the postoperative care.
Disclosure of Interest: None declared

P0881 ENDOSCOPIC RETROGRADE CHOLANGIO-PANCREATICOGRAPHY IN THE HANDS OF HEPATOBILIARY SURGEON FOR MANAGMENT OF CHOLECYSTOCHOLEDOCHOLITHIASIS

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Introduction: This study aims at assessment of the outcome of laparoscopic cholecystectomy (LC) with intraoperative endoscopic sphincterotomy (IOES) as a single session management option for patients with cholecysto-choledocholithiasis (CCL).
Aims & Methods: This is a retrospective analysis of the records and collected data for patients with CCL who were submitted for LC with IOES. Patients were preoperatively diagnosed by clinical presentation, laboratory findings, abdominal ultrasound examination, and magnetic resonance cholangiopancreatography (MRCP). IOES was performed after completion of LC and closure of ports in most cases. ERCP procedure was done by the surgeon with the patient is in the left lateral position.
Results: In the period between June 2009 to June 2013, 140 patients having combined (LC) and (IOES) for CCL were analyzed. One hundred and fourteen patients were females (82%). The mean age was 35.1 years. Mean serum bilirubin level was 7.5 mg/dl. Mean CBD diameter at MRCP was 9.1 mm and the mean CBDS size was 5.1 mm. Mean operation time was 87 minutes. Complete CBD clearance was possible in 134 patients (95.7%). The mean hospital stay was 3.1 days. There was no procedure related mortality. Complications were reported in 15 patients and included bleeding sphincterotomy (n = 6; 4.3%), pancreatitis (n = 7; 5%), and minor bile leak (n = 2; %). All complications were treated by conservative means.
Conclusion: Combining IO-ERCP and sphinctrotomy with LC is a safe and effective single-session minimally invasive treatment strategy for patients with CCL that should be available in the hands of the experienced hepatobiliary surgeon.
Disclosure of Interest: None declared

P0882 SHORT-TERM OUTCOMES OF TOTALLY ROBOTIC ABDOMINOPERINEAL RESECTION FOR LOW RECTAL CANCER: A RETROSPECTIVE COMPARISON WITH LAPAROSCOPIC AND OPEN SURGERY

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Introduction: Currently, robotic surgery for rectal cancer using da Vinci System was common. However, few studies reported robotic approaches in abdominoperineal resections (APRs).
Aims & Methods: This study compared short-term outcomes of totally robotic, laparoscopic and open APRs for low rectal cancer. Between September 2013 and March 2015, a total of 231 consecutive patients received APRs were retrospectively engaged: 66 received totally robotic surgery as TRAP group, 89 received conventional laparoscopic surgery as LAP group, and 76 received open surgery as OS group. Short-term outcomes were analyzed, including length of recovery, quality of total mesorectal excision (TME), morbidity and mortality.
Results: The operating time of TRAP group (209.8 min) and LAP group (205.4 min) were almost the same (P = 0.864), both longer than OS group (166.6 min, P < 0.001). TRAP group had less intraoperative hemorrhage, compared to LAP group (99.2 vs. 129.1 ml, P < 0.001) and OS group (99.2 vs. 141.6 ml, P < 0.001). TRAP resulted in shorter days to first flatus than LAP (1.6 vs. 2.3 days, P < 0.001) and OS (1.6 vs. 2.5 days, P < 0.001). Also, TRAP showed advantage in reducing days of retention catheterization after operation (TRAP vs. LAP, 2.3 vs. 3.3 days, P < 0.001; TRAP vs. OS, 2.3 vs. 3.1 days, P < 0.001). There was no difference among the three groups in open conversion rate, length of hospital stay after surgery, lymph node harvested, positive rate of circumferential resection margin or postoperative mortality. The morbidity rates were 16.7%, 28.1%, and 27.6% in the TRAP, LAP and OS groups respectively, with no significant difference. However, TRAP resulted in potentially less urinary retention than LAP (3.0% vs. 11.2%, P = 0.059), and potentially less wound infection than OS (3.0% vs. 10.5%, P = 0.082).
Conclusion: Totally robotic APRs were safe, and reproduce the equivalent TME quality of conventional laparoscopic and open surgery. Also, it provided less injury and faster functional recovery.
Disclosure of Interest: None declared

P0883 ROBOT-ASSISTED SIMULTANEOUS RESECTION OF COLORECTAL CANCER WITH LIVER METASTASES: A FEASIBLE AND INNOVATIVE TECHNIQUE

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Introduction: The Da Vinci Surgical System may help to overcome some of the difficulties of laparoscopy for complicated abdominal surgery. The aim of this study was to present an innovative technique that is robot-assisted, simultaneous radical resection of both colorectal cancer and liver metastasis (RSRCLM).
Aims & Methods: Between May 2013 and November 2014, we attempted to perform robot-assisted simultaneous resection of liver metastases in 24 patients with sigmoid colon cancer or rectal cancer. Procedure of this technique was described and clinic data of patients were collected and analyzed.
Results: We successfully completed the technique of RSRCLM in 24 patients with no conversions to an open procedure. The mean age was 55.1 ± 11.9 years and BMI (body mass index) was 22.9 ± 1.9 kg/m^2. The mean operation time was 293.3 ± 96.6 minutes and blood loss was 133.7 ± 105.4 ml. An R0 resection was achieved in all patientswith the minimal margin from 2mm to 35 mm. The aver age tumor size of colorectal cancer was4.7 ± 1.3 cm and that of metastatic liver tumor was 3.3 ± 1.9 cm. The aver age number of harvested lymph node was 20.7 ± 7.6. Patients were able to walk in first 2 days of surgery. The mean time get pass gas was 2.2 ± 0.5 days and flow eating start at 3.4 ± 0.9 days. The median duration for indwelling urine Foley catheter was 3.1 ± 1.2 days. The voiding function after removal of the urine Foley catheter was good (International Prostate Score Symptom (IPSS, 0–7) in 20 (83.3%) patients, fair (IPSS, 8–14) in three (12.5%), and poor (IPSS, 15–35) in one (4.2%).The mean postoperative hospital stay was 7.2 ± 2 days and hospital cost was 11325.5 ± 1337.6 US dollars. Overall morbidity and mortality was 8.3% and 0% respectively, within one month after surgery. At a median follow-up of 10 (range, 2-21) months, 23 (95.9%) patients remain disease-free.
Conclusion: This study shows that robot-assisted simultaneous resection is safe and technically feasible in selected patients with sigmoid colon cancer or rectal cancer liver metastases.
Disclosure of Interest: None declared

P0884 TRANSLATIONAL 3D-PRINTED ORGAN MANUFACTURING OF BIO-ELASTIC PATIENT-SPECIFIC ORGAN REPLICA FOR LAPAROSCOPIC SURGERY SIMULATION

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Introduction: Professional 3D printers now incorporate photo-curable resins of various textures, transparency and flexibility. Before procedures, surgeons can now plan complex surgeries with MDCT scan data of a patient's bones, blood vessels or other organs, converted to a 3D-printable digital file (STL) that can be manipulated and studied. But these applications in the operating room are generally limited to a relatively small number of procedure types, though physicians can easily apply the lessons from one surgery to many others.
Aims & Methods: To overcome the limitation, we developed an anatomically accurate translational 3D-printed organ manufacturing system for surgical simulation. Our hybrid 3D imaging and 3D-printed injection molding technology allowed to manufacturing bio-elastic organ and abdominal wall replica.
Based on patient-specific DICOM data from MDCT, after generating its surface polygons using OsiriX application, the multi-material inkjet 3D printer created life-size copies of the 3D organs, blood vessels, and abdominal cavity. The replicas were manufactured bio-elastic by simultaneous jetting of different types of materials and injection molding the polyvinyl alcohol (PVA), which is a water-soluble synthetic resin. Each organ's mold model was given an injection of a synthetic resin that helps make it feel wetter and more lifelike for the surgeon. We evaluated the feasibility of this system in 20 liver, pancreas, and kidney surgery simulations. We programed a printer to create clear models made from acrylic resins that allowed us to visualize and understand the hepatobiliary pancreatic complex internal structures and blood vessels or the exact tumor locations. We printed liver, pancreas, and kidney models compounding the polyvinyl alcohol (PVA) for tensile strength and elongation to break. It allowed these models realistic stand-in for ultrasonic diagnosis, hepatic intervention and surgical procedure such as cutting, suturing and ligation.
Results: The personalized bio-elastic wet organ replicas were useful for visible and tangible surgical simulation and navigation to plan and guide the successful liver, pancreas, and kidney surgeries. Such organ models can be soaked in water to look and feel closer to real organs. With the wet model, surgeons can

experience the softness of organs and see them bleed, to help us in practice on lifelike models before stepping into real surgery. Using abdominal cavity replica, there was a place for using synthetic models in realistic surgical situation including laparoscopic surgery. The use of these replicas reduced the length of the operation and provided better anatomical reference tools for tailor-made navigation surgery, consequently helping to improve training for the operating room staff, students, and trainees.
Conclusion: The translation from 3D imaging to 3D manufacturing provided realistic surgical simulation of specific values of bio-texture in liver, pancreas, and kidney. The PVA was compatible for wet tissue simulation in ultrasonography and intervention in liver, pancreas, and kidney surgeries. These could overcome the limitations of the conventional image-guided navigation. Its combines the advantages of conventional 3D modeling and precise virtual 3D planning in personalized surgical simulation and navigation.
Disclosure of Interest: None declared

P0885 A PROSPECTIVE, RANDOMISED MULTICENTER STUDY COMPARING MINILAPAROTOMY CHOLECYSTECTOMY VERSUS LAPAROSCOPIC CHOLECYSTECTOMY WITH ULTRASONIC DISSECTION IN BOTH GROUPS – POSTOPERATIVE RECOVERY AT 4 WEEKS AFTER SURGERY

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Introduction: Cholecystectomy by minilaparotomy (MC) or by laparoscopy (LC) have been shown to have quite similar early recovery after surgery (Harju et al. 2013, 1). Monopolar electrosurgical energy is the most frequently used form of energy to achieve adequate dissection and haemostasis in the MC and in the LC. We assessed the MC with the ultrasonic dissection (UsD) versus the LC with the monopolar electrosurgical energy and our results suggested a shorter early recovery after surgery (Harju et al. 2013, 2). The outcome after the LC versus the MC with the UsD technique in both groups has not been compared in randomised trials. We therefore investigated the four weeks recovery after the LC and the MC with the UsD in 100 patients (ClinicalTrials.gov Identifier: NCT0172340).
Aims & Methods: Initially 100 patients with non-complicated symptomatic gallstone disease were randomized into the MC with the UsD (n = 50) or the LC with the UsD (n = 50) over a period of 2-years (2013-2015) and 95 of them (95%) were reached for a follow-up interview at four weeks after the surgery. Postoperative recovery at 4 weeks after surgery in the two study groups was assessed with a follow-up questionnaire to be filled and returned in a prepaid envelope, the non-responders were contacted by a phone. Analgesic efficacy was assessed with an 11-point numeric rating scale (NRS, 0 = no pain relief, 10 = total pain relief).
Results: Both groups were similar in terms of the demographic variables and surgical data. Postoperative data for the first four weeks after surgery were available for 95% of patients from both groups. The duration of postoperative pain (in days) was slightly shorter in the LC group, 8.5 (SD, 8.2) days, than in the MC group, 11.1 (SD, 10.8) days, ($p = 0.24$). The mean length of sick leave was five days shorter in the LC group, 14.4 (SD, 10.3) days, than in the MC group, 19.9 (SD, 12.4) days, ($p = 0.05$). The pain at normal activities after four weeks assessed with the NRS showed slightly lower scale values in the MC group, 0.3 (SD, 0.9) versus in the LC group, 0.6 (SD, 1.2), ($p = 0.23$). Total use of analgesics after discharge (in days) was slightly shorter in the LC group, 6.6 (SD, 8.0) versus in the MC group, 7.7 (SD, 10.8), ($p = 0.59$). The satisfaction with surgery was quite similar in the both study groups.
Conclusion: In conclusion, the cholecystectomy by minilaparotomy versus the cholecystectomy by laparoscopy with ultrasonic dissection in both study groups seems to have quite similar four weeks recovery after surgery. A new finding with the clinical relevance in the present work is the applicability of the UsD technique in the MC and the LC procedures.

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Disclosure of Interest: None declared

P0886 MENTAL REHEARSAL WITH PATIENT SPECIFIC IMAGERY ENHANCES LAPAROSCOPIC SURGERY PERFORMANCE: A PILOT STUDY

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Introduction: Mental rehearsal of a task is known to improve performance in sports and music. Recent studies have shown some indications that it can do the same in surgery, with or without visual aids. Our study aims to assess the impact of mental rehearsal with interactive patient specific 3D imagery, on laparoscopic surgery performance.
Aims & Methods: 15 laparoscopic cholecystectomy novices were matched into two groups on 2:1 ratio. Group 1 (n = 10) performed a simulated laparoscopic cholecystectomy on a virtual reality (VR) simulator after watching a didactic video of a real procedure. Group 2 (n = 5) performed the same procedure after structured mental rehearsal with an interactive 3D visual aid. The optic tool was a 3D reconstruction of the relevant surgical anatomy (gallbladder, liver, cystic duct, cystic artery and peritoneal gathering), from an anonymised Computer Tomography. The anatomical features were modified to resemble the anatomy of the simulated model. Performance and safety variables were obtained from the VR simulator database after each procedure and compared between the two groups.
Results: Trainees who performed structured mental rehearsal using a 3D model prior to the operation had significantly less total number of movements (Group 2 median 553, Group 1 1391.5, $p = 0.005$) and total path length of instrument tip (Group 2 mean 1540.24, Group 1 mean 2837 $p = 0.007$). Furthermore, trainees in group 2 performed the procedure significantly faster than the trainees in Group 1 (Group 2 median 667s, Group 1 mean 1283, $p = 0.003$). There was no statistical difference in the safety metrics (number of perforations $p = 0.07$, non-cauterised bleeding $p = 0.114$, damage to vital structures $p = 0.529$).
Conclusion: From this pilot data there are strong indications that viewing a patient-specific 3D model of the relevant anatomy can enhance surgical performance.
Disclosure of Interest: None declared

P0887 LAPAROSCOPIC BASIC SKILLS TRAINING - BLACK BOX OR HIGH FIDELITY SIMULATORS ?

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Introduction: Training in laparoscopic high-fidelity simulators to proficiency levels has been shown to improve laparoscopic cholecystectomy skills (1-3). However, since high-fidelity laparoscopic simulators are expensive the availability is limited which could have a negative impact on the opportunity of laparoscopic training for residents. In countries with a strained economy other priorities within the health sector than buying expensive simulators are made. In countries with a somewhat better economy but with large distances to travel, residents working in or near large academic centers often have a much better access to simulator training. Whether laparoscopic basic skills training in black boxes can be an adequate alternative to corresponding basic skills training in high fidelity simulators for students and residents in this high-tech era is not known.
Aims & Methods
Aim: To analyze how basic skills training in a black box or a high fidelity simulator (LapMentor, Simbionix, USA) motivated medical students and if differences in surgical skills performance were noted when tested in a validated surgical simulator (MIST, Mentice, Sweden).
Methods: Medical students (n = 57) during their surgical semester volunteered to participate in the study. After signing informed consent the students completed a questionnaire regarding their expectations of the simulation training. Their visuospatial ability was also tested. They were then randomized into either basic skills training in a black box (n = 31) or in the LapMentor (n = 26). Following their skills training all the students did three tests in the validated MIST simulator (1) and then finally they completed a questionnaire of how they had experienced the simulator practice sessions regarding how they liked it, if it facilitated their MIST performance and if it had been difficult.
Results: Students training in both the BlackBox and the LapMentor found that the training exceeded their expectations regarding how well they thought that they would like it.
BlackBox estimations increased from an expectation level of 73.1% pre-training on the VAS scale to 80.0% post-training ($P = 0.0365$) and LapMentor from 75.8% pre-training to 82.2% post-training ($P = 0.0225$). There was a significant correlation in the BlackBox group between how difficult they experienced the simulation training was and their MIST-performance ($RSquare = 0.25$; $P = 0.0064$). There was also a positive trend towards how well they thought that the BlackBox training facilitated their MIST-performance ($RSquare = 0.10$; $P = 0.0953$). In the LapMentor group no such correlations existed ($RSquare = 0.02$; $P = 0.61$ "Was difficult" and $RSquare = 0.00$; $P = 0.92$ "Facilitated"). More students in the BlackBox group also completed the MIST excercises (28 vs. 19).
Conclusion: The perhaps more straightforward approach to basic skills training procedures in the low-tech BlackBoxes seems to correlate better with MIST performance. The results indicate a still important role for low-tech and low-cost BlackBoxes in laparoscopic basic skills training of students in an otherwise high-tech surrounding.

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Disclosure of Interest: None declared

P0888 T4 COLON CANCER: AN ABSOLUTE CONTRAINDICATION TO LAPAROSCOPIC RESECTION?

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Introduction: Some retrospective comparative studies have shown that laparoscopic resection (LR) of T4 colon cancer is feasible and oncologically adequate, but it is burdened by high conversion rates to open resection (OR). The selection criteria for the laparoscopic approach to T4 colon cancers are unclear.

Aims & Methods: The aim of this study was to identify possible tumor-related factors that should be considered as contraindication to LR in T4 colon cancer patients. The short-term and the long-term oncologic outcomes of LR or OR were also evaluated.

It is a retrospective analysis of a prospectively collected database. All patients undergoing elective LR or OR for non-metastatic T4 colon cancer were included. Statistical analyses were performed on an ''intention-to-treat'' basis and by actual treatment. Kaplan-Meier curves were compared to analyse overall survival (OS) and disease-free survival (DFS).

Results: OR and LR were performed for T4 colon cancer in 50 and 48 patients, respectively. A complete R0 resection was obtained in 49 (98%) OR and in 48 (100%) LR patients (P = 0.962). Conversion to open surgery occurred in 12 LR patients (25%), due to a tumor larger than 6 cm (75%) or the need for a multivisceral resection (25%). There was a trend towards a higher rate of 30-day morbidity after OR than LR (34% vs. 16.7%; P = 0.083). Thirty-day mortality rate was similar after OR and LR: 4% vs. 0% (P = 0.495). Median postoperative length of stay was longer after OR, than converted resection or LR: 12 (range, 7-60) vs. 9 (range, 6-14) vs. 7 (range, 5-51) days (P = 0.005). No significant differences were observed in the median number of lymph node harvested after OR or LR: 16 (range, 6-29) vs. 14 (range, 7-36), P = 0.455. Median follow-up was 46.5 (range, 3-140) months for OR patients and 37 (range, 6-139) months for LR patients (P = 0.274). Five-year OS and DFS did not differ significantly between OR and LR patients: 66.7% vs. 65.8% (P = 0.828), and 59.7% vs. 58.6% (P = 0.634). Conversion to OR did not affect OS and DFS.

Conclusion: LR is associated with a high conversion rate to OR. Patients with a tumor larger 6 cm and/or infiltrating adjacent organs should be treated by OR. In selected cased, LR for T4 colon cancer has better short-term outcomes and similar oncologic outcomes compared to OR.

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Disclosure of Interest: None declared

P0889 PAN-EUROPEAN SURVEY ON LAPAROSCOPIC PANCREATIC SURGERY

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Introduction: Benefits of minimally invasive pancreatic surgery, especially for cancer, are under debate since no randomized studies have been performed. It is unclear which proportion of pancreatic resections (pancreatoduodenectomy, distal pancreatectomy) is currently performed via a minimally invasive approach and whether these procedures are performed for cancer.

Aims & Methods: An online survey, consisting of 30 questions, was sent to the members of the European Pancreatic Club, the European-African Hepato-Pancreato-Biliary Association and to 5 national pancreatic societies in Europe between June and December 2014. Non-responders received two reminders. Fully completed responses were included. Because of overlapping, confidential membership lists, the number of invitees was unknown.

Results: In total, 237 pancreatic surgeons responded. After excluding 34 for incomplete responses, 203 responses from 27 European countries were analysed. 164 (81%) surgeons were employed at a university hospital, 184 (91%) performed advanced minimally invasive surgery, 148 (73%) performed minimally invasive distal pancreatectomy. Minimally invasive pancreatoduodenectomy was performed by 42 (21%) surgeons whereas only 9 surgeons had performed more than 10 of these procedures. Robot-assisted pancreatic surgery was performed by 28 (14%) surgeons. 63 (31%) surgeons expected minimally invasive distal pancreatectomy for cancer to be inferior to open distal pancreatectomy concerning oncological outcomes. 151 (74%) surgeons expected to benefit from training in laparoscopic distal pancreatectomy and 149 (73%) were willing to participate in a randomized trial on this topic.

Conclusion: Minimally invasive distal pancreatectomy has become a common surgical procedure, although its benefits for cancer are under debate. Minimally invasive pancreatoduodenectomy has not yet been implemented. Specific training in laparoscopic distal pancreatectomy is welcomed and a pan-European randomized controlled trial for pancreatic cancer (DIPLOMA) seems indicated.

Disclosure of Interest: None declared

P0890 CLINICAL OUTCOMES AFTER ENDOSCOPY-ASSISTED LAPAROSCOPIC FULL-THICKNESS RESECTION FOR SUPERFICIAL DUODENAL NEOPLASMS

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Introduction: Superficial duodenal neoplasms (SDNs) are rare, but clinically important disease, whereas whose therapeutic strategies have not been established. Endoscopic resection is technically difficult, due to thin intestinal walls which can be easy to perforated and difficulty of maneuvering endoscope. On the other hand, surgical resection seemed considerably invasive. In addition, it is often difficult to recognize the extent of the lesion precisely during surgical approach. To overcome these problems, we developed a noble approach to treat SDNs which involves a combination of endoscopic and laparoscopic techniques; endoscopy-assisted laparoscopic full-thickness resection (EALFTR).

Aims & Methods: The aim of this study was to assess the clinical outcomes after EALFTR for SDN. Between January 2011 and March 2015, a total of 85 patients with 90 non-amupllary SDNs were enrolled in this study. Patients with familial polyposis syndrome were excluded. Clinocopathological characteristics (e.g. age, sex, tumor location and size) were collected at initial endoscopic examination. The primary outcome was en-bloc R0 resection rate. Secondary outcomes were procedure time, complications and length of hospital stay after EALFTR. Moreover, long-term outcomes of SDNs after EALFTR were also evaluated. EALFTR procedure was previously described in our report. In summary, subsequent to the laparoscopic duodenal mobilization, peripheral margin was marked around the tumor endoscopically and each marking was perforated intentionally using a needle knife in the coagulation mode.After laparoscopic full-thickness incision, closure of the defect in the duodenal wall was performed by a laparoscopic hand-suturing technique.

Results: Lesions were predominately located at the second portion (50/90, 56%), whereas others located at bulb (32/90, 35.6%) and third portion (8/90, 8.9%), respectively. The tumor size was 13.2 ±11.6 mm, and the resected specimen size was 26.0 ±10.5 mm. The mean procedure time was 146 ±43.2 minutes. The mean length of hospital stay after EALFTR was 11.6 ±6.7 days. Although two of 90 cases were converted to open surgery, en-bloc R0 resection was achieved in most of remaining cases (86/88, 98%). Regarding to complications, postoperative anastomotic leakage and stenosis occurred in three (3.5%) and five patients (5.9%), respectively, however all patients recovered conservatively. Histopathological examination confirmed 42 adenomas, 22 adenocarcinomas, 17 neuroendocrine tumors, and 9 others. Of 71 patients whose follow-up period longer than 1 year, no metastasis and/or local recurrence was detected during the median follow-up period of 27 months (range, 12 – 44).

Conclusion: We confirmed favorable clinical outcomes of EALFTR for SDNs. EALFTR enables successful en-bloc R0 resection, with minimally invasive manner. Our results indicated that EALFTR hardly concerns with tumor dissemination. We believe EALFTR can be a effective treatment option for SDNs, although great caution against complications is mandatory.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00–17:00
IBD II – HALL 7

P0891 NATURAL PEPTIDE INHIBITOR OF NEUTRAL ENDOPEPTIDASE (NEP) ALLEVIATES EXPERIMENTAL COLITIS IN MICE AFTER SYSTEMIC ADMINISTRATION

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Introduction: The role of endogenous opioid peptides in the pathophysiology of inflammatory gastrointestinal (GI) disorders is widely recognized, but poorly understood. This is, among others, because of the short half-life of these peptides, which are quickly inactivated by endopeptidases, e.g., neutral endopeptidase (NEP, EC 3.4.24.11). NEP inactivates endogenous Met- and Leu-enkephalins, which are potent regulators of GI motility, secretion and pain

sensation, acting through μ, κ and δ opioid receptors (MOR, KOR and DOR, respectively).
Aims & Methods: The aim of this study was to investigate the effect of the natural peptide inhibitor of NEP, sialorphin and Met- and Leu-enkephalins in mouse models of experimental colitis.
Methods: To assess the anti-inflammatory activity of tested compounds, we used acute and semi-chronic models of inflammation induced by intracolonic administration of TNBS as well as acute model of DSS-induced colitis. Body weight, macroscopic score, ulcer score, colon length, weight and thickness were recorded. Moreover, in all experiments the level of myeloperoxidase (MPO) activity was determined as an indicator of neutrophil infiltration in colonic tissue. In order to determine the mechanism of action of sialorphin, we used selective MOR, KOR and DOR antagonists; β-funaltrexamine (β-FNA), nor-binaltorphimine (norBNI) and naltrindole (NLTR), respectively.
Results: Met- and Leu-enkephalin and sialorphin administered intraperitoneally (i.p.) at the dose of 1 mg/kg twice daily significantly ameliorated colitis in the acute model, as indicated by reduced macroscopic and ulcer scores, as well as bowel length and thickness and MPO activity. In addition, the anti-inflammatory activity of sialorphin was dose-dependent at the dose range from 0.3 to 3 mg/kg (i.p., twice daily). The therapeutic effect of sialorphin (1 mg/kg, i.p. twice daily) in the acute model was blocked by selective MOR and KOR, but not DOR antagonists (all at a dose of 1 mg/kg i.p.). In the semi-chronic model of TNBS-induced colitis sialorphin (1 mg/kg, i.p.) partially improved macroscopic parameters of the disease but this effect was not statistically significant. Interestingly, treatment with sialorphin had no effect in the model of DSS-induced colitis.
Conclusion: We propose a novel anti-IBD therapeutic strategy, based on the treatment with inhibitors of enkephalin-degrading enzymes and the elevation of endogenous enkephalin levels.
Disclosure of Interest: None declared

P0892 IS INTESTINAL DYSBIOSIS A FACTOR LEADING TO COLONIC INFLAMMATION?

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Introduction: Dysbiotic states have been associated to intestinal inflammation. However, a causal relationship has not been established and it is not clear if dysbiosis should be regarded as a cause or a consequence of intestinal inflammation. To further understand the relationship disbiosis-inflammation we assessed immune activation and the appearance of colitis in mice subjected to antibiotics-induced dysbiosis.
Aims & Methods: A dysbiotic state was induced with a 1-wk or 2-wk duration oral treatment with non-absorbable, broad spectrum antibiotics (bacitracin and neomycin) in mice. At the end of the treatment, colonic luminal and wall adhered microbiota (fluorescent in situ hybridization and qPCR), inflammatory markers (RT-qPCR) and macroscopical and microscopinal signs of colonic inflammation were assessed.
Results: 1-wk or 2-wk antibiotic treatment resulted in a similar dysbiotic state; with an increase in the proportion of *Lactobacillus* spp, *Bifidobacterium* spp and coccoid forms of *Clostridium* cluster XIVa. However, total bacterial counts were reduced during a 1-wk treatment (by 50% vs. control conditions, $P < 0.05$), while there was a 2-fold increase during the 2-wk treatment ($P < 0.05$ vs. control). During a 1-wk treatment, bacterial adherence to the colonic epithelium was favored, while no changes were observed during the 2-wk treatment. A local immune activation, as seen by an increase in the luminal levels of secretory IgA (Table) and the up-regulation in the expression of antimicrobial peptides was observed. Although these changes, no macroscopical (except for an enlargement of the cecum) or microscopical signs of colonic inflammation were observed (see Table).**Table: Immune activation and macro and microscopic changes in the colon during antibiotic treatment (Data are mean ± sem, 6-16 animals per group; *: P < 0.05 vs. respective vehicle control.)**

	Secretory IgA (mg/ml)	Weight cecum (mg)	Colon relative weight (mg/cm)	Histopathological score (0-12)
Vehicle 1-wk	7.2 ± 1.4	318.4 ± 16.5	12.6 ± 0.7	1.6 ± 0.4
Antibiotics 1-wk	261.7 ± 6.5 *	661.9 ± 16.5 *	14.8 ± 0.9	1.8 ± 0.6
Vehicle 2-wk	36.7 ± 11.5	409.0 ± 20.2	23.3 ± 1.8	0.7 ± 0.2
Antibiotics 2-wk	362.5 ± 11.5 *	507.7 ± 18.4 *	23.9 ± 1.9	1.3 ± 0.2

Conclusion: Colonic dysbiosis might result in a state of ''low grade inflammation", characterized by a local immune activation in the absence of structural changes. Similar states (disbiosis and low-grade inflammation) are described in patients with functional gastrointestinal disorders, mainly irritable bowel syndrome. Dysbiosis seems to represent a contributing factor to immune colonic responses but, per se, does not result in an overt inflammatory reaction.
Disclosure of Interest: None declared

P0893 EXOSOME: A NEW MEDIATOR OF HOST RESPONSE TO CROHN'S DISEASE-ASSOCIATED ADHERENT-INVASIVE *ESCHERICHIA COLI*

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Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disease of which the etiology involves environmental, genetic and microbial factors. A high prevalence of invasive *Escherichia coli* strains, named AIEC (adherent-invasive *E. coli*), has been reported in the intestinal mucosa of CD patients. Exosomes are small endosomal-derived vesicles involved in cell to cell communication and have been implicated in various diseases including cancer and infectious disorders.
Aims & Methods: Here, we investigated the potential involvement of exosomes in host response to AIEC infection. Exosomes were extracted from human intestinal epithelial T84 cells and human monocyte-derived THP-1 macrophages uninfected or infected with the AIEC reference strain LF82 or the non-pathogenic K-12 C600 strain by using the ExoQuick exosome precipitation kit (System Biosciences). Epithelial permeability was assessed by measuring the TER and the translocation of FITC 4kDa. Intracellular number of AIEC was determined by using the gentamicine protection assay.
Results: Electron microscopy showed that infection with AIEC LF82 increased the release of exosome-like microvesicles of 30-100nm from T84 and THP-1 cells. Immunogold labelling and Western blot analyses confirm the presence of the well-known exosomal marker CD63 in these microvesicles. Characterization of exosomes released from LF82-infected cells showed that they did not affect either intestinal epithelial permeability, or adhesion and invasion capacity of AIEC LF82 in T84 cells, or expression of carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6)-host epithelial receptor for AIEC. However, compared to exosomes released from non-pathogenic K12-infected host cells, those from LF82-infected cells induced in naïve recipient cells increased activation of NF-kappaB and MAPK pro-inflammatory signaling pathways and enhanced production of pro-inflammatory chemokines and cytokines IL-8, TNF-α and IL-6. In contrast, exosomes released from uninfected cells did not exhibit these pro-inflammatory activities. Mass spectrometry analysis revealed that exosomes released from LF82-infected T84 cells carried microbial antigens including the outer membrane protein C (OmpC), a known virulence factor of AIEC bacteria.
Conclusion: In conclusion, our study shows that in response to CD-associated AIEC infection, intestinal epithelial cells and macrophages release exosomes that can trigger pro-inflammatory responses in naïve macrophagic recipient cells.
Disclosure of Interest: None declared

P0894 ACTIVATION OF WNT SIGNALLING BY M2A MACROPHAGES PROMOTES MUCOSAL REPAIR IN MURINE IBD

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Introduction: Mucosal repair is a key goal in Inflammatory Bowel Disease (IBD) treatment and the Wnt signalling pathway plays a crucial role in this process. Macrophages coordinate tissue repair and expression of canonical Wnt ligands has been associated with the M2 phenotype. Recent studies reported an impaired M2 polarization and delayed wound healing in STAT6-/- mice.
Aims & Methods: We aim to evaluate the role of STAT6 in Wnt ligands expression associated with M2 polarization *in vivo* and the relevance of these cells in wound healing in a murine model of colitis. Peritoneal macrophages were isolated from WT and STAT6-/- and polarized towards M1 and M2 phenotype. mRNA expression of canonical Wnt ligands was analyzed by qPCR (fold induction). Colitis was induced in STAT6-/- by an intrarectal injection of TNBS (3.5mg/20g mice) and 2 days later received an i.p. injection of macrophages ($2{\cdot}10^6$ million) obtained from WT and STAT6-/- treated with Il-4 (WT-M2a and STAT6-M2a, respectively). Mice were weighed daily (percentage of body weight at day 4 vs day 0). 4 days after TNBS were sacrificed, colon length was measured and mucosal histology was evaluated according to Wallace Score. Mucosal expression of iNOS, TNFα, IL-1β, c-myc and Lgr5 was analyzed by qPCR and protein levels of nuclear β-catenin by western blot. Data are expressed as Mean ± SEM ($n \geq 5$).
Results: In peritoneal macrophages from WT mice we detected the expression of Wnt2b, Wnt7b, Wnt10a and Wnt10b, while Wnt1, Wnt3a and Wnt6 were not detected. In macrophages obtained from WT mice, polarization towards the M2a phenotype induced a significant increase in the expression of Wnt2b (4.0 ± 1.1) and Wnt7b (2.8 ± 0.3) compared with that detected in non-polarized (1.1 ± 0.2 and 1.1 ± 0.2) and M1 macrophages (1.1 ± 0.4 and 0.8 ± 0.2). However, in macrophages obtained from STAT6-/- mice and polarized towards M2a phenotype the expression of Wnt2b (0.9 ± 0.2) and Wnt7b (0.9 ± 0.3) was not significantly different to that detected neither non-polarized (1.3 ± 0.2 and 0.9 ± 0.2, respectively) nor M1-macrophages (0.9 ± 0.4 and 1.1 ± 0.1, respectively). In STAT6-/- mice treated with TNBS, administration of WT-M2a macrophages accelerated the regain of body weight (98.1 ± 0.6%) compared with the administration of STAT6-M2a macrophages (92.9 ± 1.1%). These cells also enhanced the functional recovery of mice since colons from mice treated with WT-M2a macrophages were significantly longer and exhibited less histological damage score than those colons from mice with STAT6-M2a macrophages. The mRNA expression of pro-inflammatory markers such as iNOS, TNFa and IL-1b was significantly lower in the mucosa of mice treated with WT-M2a macrophages (0.7 ± 0.1, 0.5 ± 0.1 and 0.6 ± 0.2, respectively) than in that of mice treated with STAT6-M2a macrophages (1.0 ± 0.1, 1.1 ± 0.1 and 1.0 ± 0.1, respectively). A significant increase in nuclear b-catenin (1.6 ± 0.1) and mRNA expression of two Wnt target genes, c-myc (1.6 ± 0.2) and Lgr5 (2.1 ± 0.4) was detected in the mucosa of mice treated with WT-M2a macrophages compared whith that of mice with STAT6-M2a macrophages (1.0 ± 0.1, 1.1 ± 0.1 and 1.1 ± 0.1, respectively).
Conclusion: STAT6 mediates the expression of canonical Wnt ligands associated with the M2a macrophage phenotype. Activation of Wnt signalling by a STAT6-dependent macrophage phenotype promotes mucosal repair in murine IBD.
Disclosure of Interest: None declared

P0895 ACTIVATION OF COLONIC AUTOPHAGY WITH TREHALOSE IMPROVES WOUND HEALING IN MURINE COLITIS

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Introduction: Autophagy plays a homeostatic role in intestinal epithelial cells by engulfing intracellular organelles and endogenous pathogens leading to the degradation of their contents. Several polymorphisms in gene loci containing autophagy-related proteins such as ATG16L1, IRGM, and NOD2 have been associated with an increased risk of Crohn's disease and it has been suggested that a defective autophagy may have a role in its pathogenesis.

Aims & Methods: We aim to analyze the expression of autophagic protein markers in a murine model of colitis induced by TNBS and the resultant effects of activating mucosal autophagy on the course of the disease. Mice received an intrarectal injection of TNBS (3.5mg/20g) in order to induce colitis and control animals received an intrarectal injection of TNBS-vehicle (EtOH 40%) (day 0). Some mice received trehalose in the drinking water (3%) during three weeks before TNBS administration. After colitis induction, changes in body weight were determined daily (results are expressed as percentage vs the weigth at day 0) and mice were sacrificed 2 and 4 days after TNBS administration. Mucosal histology was evaluated after an hematoxylin staining according to Wallace Score (1-10). Colons were frozen for protein extraction and Western blot experiments of p62, LC3 and b-actin were performed. Data are expressed as Mean ± SEM ($n \geq 5$).

Results: Treatment of mice with TNBS induced a loss of body weight that peaked 2 days after treatment. Subsequently, mice began to recover and, four days after treatment, body weight reached similar values to those of control animals. The expression of autophagic protein markers reveal a slight accumulation of both p62 and LC3II protein levels in the mucosa of TNBS-treated mice compared with the control mucosa, suggesting a reduction in the autophagic flux in the inflamed mucosa, which was observed 2 and 4 days after TNBS. Chronic treatment with trehalose induced a significant increase in LC3II protein levels and a significant decrease in p62 protein levels in the colonic mucosa of both control and TNBS-treated mice showing that trehalose was increasing the autophagic flux in both conditions. In trehalose-treated mice, the loss of body weight was significantly lower at day 1 and 2 (92.85 ± 1.28 and 96.48 ± 1.42, respectively) compared with that observed in vehicle-treated mice (90.24 ± 0.76 and 91.33 ± 1.72, respectively). The analysis of histological damage score revealed significant differences between trehalose (4.3 ± 0.4) and vehicle-treated mice (5.5 ± 0.6), four days after TNBS administration.

Conclusion: Chronic treatment with trehalose during three weeks activates autophagy in murine colonic mucosa and improves wound healing and functional recovery of TNBS-treated mice.

Disclosure of Interest: None declared

P0896 RESPONSE TO CORTICOSTEROIDS IN ULCERATIVE COLITIS MAY BE RELATED TO MODULATION OF MTOR SIGNALING PATHWAY GENES BY MICRORNAS

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Introduction: Mechanisms of resistance to corticosteroids (CS) in ulcerative colitis (UC) are not well understood. Little is known about the influence of microRNAs (miR) in the response to CS in UC.

Aims & Methods

Aims: To compare the transcriptomic profile in rectal mucosa of patients with active UC responding and non-responding to CS.

Methods: Rectal biopsies were obtained from UC patients before and after three days of CS treatment. Patients were grouped in responders and non-responders according to Montreal's classification. miR were identified by means of a sequencing method *(Illumina)* and RNAm were study by microarrays method (*Illumina*) on those rectal biopsies with high integrity. Those miR and RNAm with a fold change ≥ 1.5 and adjusted p-value ≤ 0.05 were further studied.

Results: 32 out of 48 tissue samples reached an integrity that allowed miR sequencing or microarrays study. Comparison between groups showed a differential miR expression of miR-1246, miR-1291, miR-5701 and miR-625-3p, miR-183-5p, miR-3607-3p, miR-4770, miR-449, miR-145-3p. The only gene with differential expression after microarrays study was DDIT4. *In silico* study reveals that DDIT4 is a potential target of three of the differential expressed miR (miR-183-5p, miR-625-3p, miR-3607-3p) and also that this gene is linked to the mTOR pathway (and indirectly with autophagy).

Conclusion: There is a different profile of rectal microRNAs between responders and non-responders to CS. Our findings suggest that regulation of mTOR and autophagy pathways by miR might be involved in the response to CS in active UC.

Disclosure of Interest: None declared

P0897 ULCERATIVE COLITIS PATIENTS AND THE FAMILY'S ENTEROBACTERIA BUSH COMPARATIVE INVESTIGATION

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Introduction: The role of intestinal microflora in the aetiology of inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease is broadly assumed. The Terminal Restriction Fragment Length Polymorphism (T-RFLP) is a molecular biology technique for profiling microbial communities in faecal samples. We have recently reported the application of T-RFLP to validate the discriminant score of intestinal microbiota as a biomarker of disease activity in patients with UC. However, because T-RFLP cannot distinguish specific bacterial strains, it is not the best technique when one wishes to trace IBD among family members.

Aims & Methods: In the present study, instead of T-RFLP, we were interested to apply the Amplicon Sequence analysis to the intestinal flora in faecal samples from UC patients and patients' relatives as a molecular biology probe. The subjects were 90 patients with UC together with 78 relatives of the same UC patients as a control group. Twenty-seven patients had active UC (group I) and 63 had quiescent UC (group II). The later included 31 with mild inflammation in the large intestine (group IIa), and 32 without inflammation (group IIb). The patients' relatives were consanguineous (group III, n = 45), and non-consanguineous (group IV, n = 33). With the Amplicon Sequence analysis, intestinal microflora in faecal samples from 78 relatives and from the 90 patients with UC were analysed for comparative interpretations. The software we used was an SPSS (IBM Statistics 20.0).

Results: With the technology we applied, it was possible to identify over 600 different bacterial species and analyse quantitatively. Among all groups, Bifidobacterium did not show significant difference. Bacteroides, especially Fragilis and Enterobacteriaceae were markedly increased in patients with active UC. In contrast, Verrucomicrobiales species were markedly decreased in patients with active UC.

Conclusion: The most significant findings of this study include a marked increase in the Bacteroides, Fragilis and Enterobacteriaceae during active UC, while the Verrucomicrobiales species were markedly decreased in active UC patients. Further, in several previously studies, Bifidobacterium has been reported to be decreased in patients with active UC, but we did not find any clinically relevant change in Bifidobacterium in this study. The present method could reveal presence of pathologic as well as beneficial bacterial strains in IBD patients. We believe that further studies including more factors for analyses are warranted to better understand the significance of intestinal microflora in the immunopathogenesis of IBD.

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P0898 DUAL OXIDASE 2, A NOVEL PLAYER IN INFLAMMATORY BOWEL DISEASE: EXPRESSION AND FUNCTIONAL IMPLICATIONS

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Introduction: Inflammatory bowel diseases (IBD) are comprised of Crohn's disease (CD) and ulcerative colitis (UC). Unlike the inflammation in CD that can affect any part of the bowel, inflammation in UC is limited to the large bowel mucosa, thus complete large bowel resection was expected to be curative. Nonetheless, about 60% of patients who undergo total proctocolectomy with an ileal pouch reservoir develop pouchitis. Recently we performed mRNA profiling and detected an increase in Dual Oxidase 2 (DUOX2) expression in inflamed pouch biopsies as well as in CD patients. Duox2 mediates anti pathogen responses in intestinal epithelial cells by secreting reactive oxygen species (ROS) to the lumen, and its expression may be induced by microbiota.

Aims & Methods: We aimed to decipher the mechanism responsible for DUOX2 effects in the intestinal inflammation. Intestinal biopsies from normal controls, inflamed and non-inflamed UC, CD and pouch patients were collected. Disease activity was defined using clinical disease scores, as well as endoscopic and histologic assessment. DUOX2 mRNA and protein levels were assessed by RT-PCR and immunohistochemistry. DUOX2 intracellular localization as well as activity (extracellular ROS production) were assessed by flow cytometry and amplex red assay, respectively, in human intestinal epithelial cell lines (Caco2 and HT-29) in response to inflammatory cytokines (IL1b, TNFa, IFNg, IFNb) and fecal extracts obtained from IBD patients. Microbiota composition in patients with IBD as well as controls was assessed by 16S rRNA gene amplicon pyrosequencing.

Results: DUOX2 expression in the non inflamed colonic mucosa of IBD patients was increased (30 fold, $p < 0.05$). This was further augmented in the inflamed colon (≥ 150 fold, $p < 0.001$), both compared to normal controls. Similar results were obtained in biopsies generated from the ileum. Decrease in key microbial taxa was observed in fecal samples from patients with a normal pouch compared to normal controls ($p < 0.004$). Further decrease was noticed in fecal extracts from patients with pouchitis ($p < 0.0001$). DUOX2 expression

significantly increased in response to inflammatory cytokines (≥300 fold increase, $p < 0.001$) and fecal extracts derived from patients with active IBD (≥10 fold increase, $p < 0.001$). ROS production reflecting Duox2 activity, increased in response to fecal extracts derived from patients with active IBD (3 fold, $p < 0.001$).
Conclusion: Mucosal DUOX2 expression is increased in IBD, and correlates with inflammation. DUOX2 expression in epithelial cells is increased in response to inflammatory stimuli and fecal extracts, specifically from patients with active IBD. ROS production is increased in response to fecal extracts but not to inflammatory cytokines alone. Thus DUOX2 increased expression and aberrant function may have a role in augmenting intestinal inflammation in IBD.
Disclosure of Interest: None declared

P0899 MAPPING BIOPSY OF ENTIRE SMALL INTESTINE REVEALED SPECIFIC GENE EXPRESSION IN CROHN'S DISEASE

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Introduction: The discovery of genetic variants in Crohn's disease (CD) has helped us to understand the pathogenesis of CD. Notably, genetic variants of nucleotide-binding oligomerization domain containing 2(NOD2) and autophagy related 16-like 1 (ATG16L1) have indicated that mucosal barrier dysfunction is one of the most crucial pathogenesis in CD. However, the patients with CD in Asia including Japan and China did not have significant variants of these genes, suggesting that the other molecular mechanism of the pathogenesis might be involved in Asian patients differently from Caucasian patients.
Aims & Methods: In this study, we therefore aimed to elucidate the molecular mechanism of the pathogenesis in Japanese patients with CD, using mapping biopsy of entire small intestine collected by balloon-assisted enteroscopy.
We performed balloon-assisted enteroscopy to the patients with CD and healthy controls. Then we collected five biopsy specimens in equal interval positions through entire small intestine assisted by X-ray. Gene expression pattern in each region of entire small intestine was analyzed by using Self-Organizing Maps (SOM). Specific gene expression in CD was detected by the microarray analysis of 16 biopsy specimens of jejunum in 4 CD patients compared to 4 healthy controls.
Results: RNA was successfully generated from mapping biopsy specimens. SOM analysis compared CD with healthy control revealed that any inflammatory genes were not increased in jejunum of CD patients, suggesting that the pathogenesis at the pre-onset stage of CD might remain in jejunum. Microarray analysis in 16 jejunum biopsy specimens compared between 4 CD patients and 4 healthy controls showed statistically significant gene expression including 11 up regulated genes and 14 down regulated genes in CD patients.
Conclusion: The analysis of comprehensive gene expression using mapping biopsy is useful for understanding the condition in human entire small intestine. Moreover, it might be useful to elucidate the pathogenesis of CD.
Disclosure of Interest: None declared

P0900 CORRELATION OF HISTOLOGICAL ACTIVITY AND BASAL PLASMACYTOSIS WITH MUCOSAL HEALING IN ULCERATIVE COLITIS PATIENTS

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Introduction: Microscopic activity in ulcerative colitis (UC) patients with endoscopic remission is becoming more and more important in the prediction of relapse. The presence of basal plasmacytosis and the increased number of eosinophils and neutrophils in the lamina propria have been supposed to predict clinical relapse in UC patients with complete mucosal healing.
Aims & Methods: The aim of this study was to examine the correlation between the microscopic activity and the disease outcome in patients with endoscopically inactive UC. Sixty-nine UC patients (mean age at diagnosis was 31.4 years, male/female ratio: 27/42) with endoscopic remission (eMayo 0 and 1) and at least 12-month follow-up between 2008 and 2013 were enrolled in this prospective observational study. An expert pathologist evaluated all colonic biopsies for histologic activity (Geboes score) and the presence of basal plasmacytosis. C-reactive protein (CRP), partial Mayo scores and the used medications were documented at the time of the endoscopy, and the follow-up appointments: at months 6, 12 and 24 and at the last visit. Disease relapse was defined as a partial Mayo score ≥3.
Results: Histology revealed focal or diffuse basal plasmacytosis and microscopic inflammatory activity with a Geboes score ≥3.1 in 81.2% and 37.7% of patients with mucosal healing. At 6, 12 and 24 months and at the follow up visit, clinical relapsed occurred in 19%, in 14.5%, in 13%, and in 16% of the patients. The mean time of follow-up was 3 years. Neither of the presence of basal plasmacytosis, nor Geboes score ≥3.1 was predictive of disease relapse at 6, 12, 24 months and at follow-up. No difference was observed if the data were analyzed separately in subgroups of eMayo score of 0 or 1.
Conclusion: Our results did not confirm the previous hypothesis that the presence of basal plasmacytosis and microscopic inflammation predicts UC clinical relapse in patients with mucosal healing.
Disclosure of Interest: None declared

P0901 CRITICAL ROLE OF THE IL-33/ST2 AXIS IN COLITIS-ASSOCIATED COLORECTAL CANCER

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Introduction: It is now well-established that IL-33 and its receptor, ST2, are important factors in the pathogenesis of IBD. Emerging evidence also suggests its critical role in epithelial proliferation and potential contribution to inflammation-driven tumorigenesis that can lead to colorectal cancer (CRC). The aim of our study was to characterize the precise contribution of IL-33/ST2 axis in the azoxymethane (AOM)/dextran sodium sulfate (DSS) model of colitis-associated CRC.
Aims & Methods: C57/BL6 wild-type (WT), IL-33 KO and ST2 KO mice were given a single dose of AOM (7.4 mg/kg) followed by two cycles of 3% DSS for 7d in drinking water. Body weight, occult blood test, and stool consistency were measured daily to calculate the Disease Activity Index (DAI), and endoscopic and histological evaluation of colons were performed using established scoring systems. Aged-matched WT mice, injected with vehicle and given regular drinking water were used as controls (CT). At 8 wks post AOM injection mice were sacrificed. IHC, immunofluorescence (IF) and qPCR were done on full-thickness colons for IL-33 and ST2 localization and identification, and mRNA expression, respectively. FACS analysis was performed on resected, isolated polyps in order to functionally characterize ST2+ cells.
Results: IL-33, ST2L, and sST2 mRNA transcripts were dramatically elevated in WT vs. CT mice. IHC of treated WT mice revealed localization of IL-33 to the colonic epithelium and to cells within the LP morphologically consistent with tissue macrophages. ST2 staining was localized to the intestinal epithelium in tissues immediately adjacent to tumors, while within the tumors themselves, ST2+ cells displayed a spindle/fibroblast-like morphology with a unique distribution throughout the polyps. Little to no staining for both IL-33 and ST2 was present in CT. Using IF, ST2 co-localized with αSMA in polyps; however, ST2 staining was not exclusive for αSMA+ cells. FACS analysis showed a distinct population of CD45+ hematopoietic cells consisting of CD3/CD8+ cytotoxic T cells (CTLs), CD19+ B-lymphocytes, and CD11b+CD11c- and CD11b+CD11c+ myeloid cells. ST2 was mainly expressed by CTLs, CD11b+CD11c- and CD11b+CD11c+ myeloid cells. Non-hematopoietic cells (CD45-) also expressed ST2. DSS challenge in WT mice resulted in increased body weight loss and DAI vs. IL-33 KO and ST2 KO mice. At 5 weeks post AOM injection, experimental mice underwent survival colonoscopy. WT had already developed protruding lesions with abnormal vascular patterns, suggesting pre-tumorous lesions, while IL-33 KO and ST2 KO mice showed the absence of pre-tumorous lesions with a more impressive mucosal inflammation, likely due to reduced epithelial proliferation and repair caused by the absence of IL-33 signaling. At sacrifice, increased number and size of polyps were observed in WT vs. IL-33KO and ST2KO mice.
Conclusion: Our results suggest that activation of the IL-33/ST2 axis sustains tumorigenesis in the murine model of colitis-associated CRC. Further studies are underway to determine mechanisms of action that support these findings.
Disclosure of Interest: None declared

P0902 PSC - IBD IS ASSOCIATED WITH DIFFERENT MICROBIOTA COMPOSITION AS COMPARED TO UC

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Introduction: Primary sclerosing cholangitis (PSC) is a progressive disease of the biliary tree characterised by inflammation, fibrosis and stenoses. Inflammatory bowel disease (IBD) in patients with primary sclerosing cholangitis (PSC – IBD) is considered to be a distinct phenotype of IBD with a multi – factorial origin where microbiota most likely have a substantial role. In our pilot study, our aim was to compare the microbiota composition in PSC and/or IBD groups with ulcerative colitis (UC) and healthy controls.
Aims & Methods: Total number of 15 individuals was used in presented study: 4 control healthy samples, 4 UC patients, 4 PSC-IBD patients and 3 PSC (without IBD). Fecal microbiota composition was assesed by sequencing of variable V4 and V5 region of 16S rRNA gene on Personal Genome Machine platform (Fisher Scientific). Library preparation, template preparation and template sequencing was performed according to manufacturer's protocols. Obtained data were filtered by quality and length and processed for alpha and beta diversity analyses using QIIME software package.
Results: Following significant changes in bacterial numbers were observed among tested groups: PSC versus PSC-IBD: Higher Bifidobacterium sp. (18 vs 2.71 %), Lachnospira (4.58 vs 0.68 %) and Dorea sp (5.7 vs 1.55 %) and lower Enterococcus sp. (0 vs 9.14 %), Faecallibacterium sp. (1.31 vs 4.12 %) and Prevotella/Paraprevotella sp. (0 vs 9.71 %) numbers. PSC-IBD versus UC: Higher Bacteroides sp. (17.13 vs. 4.86 %), Enterococcus sp. (9.14 vs 0 %) and Prevotella/Paraprevotella sp. (9.71 vs 2.13 %) and lower Bifidobacterium sp (2.71 vs 12.95 %) and Faecallibacterium sp. (4.12 vs 16.4 %) numbers. The clustering of samples according to the type is stronger with the unweighted UniFrac metric than with the weighted metric, suggesting that differences in community membership (rather than community structure) discriminate better among groups.

Conclusion: Members of genus Faecallibacterium and Prevotella showed highest variations with regards to PSC /PSC-IBD/UC groups comparison. Control samples showed higher species richness than patients' samples. Our data suggest that microbiota composition differs among patients with PSC (without IBD), PSC – IBD and UC. Presented data should be considered as preliminary, as more samples are needed for statistical analyses to support detected observations.
Disclosure of Interest: None declared

P0903 EVP-6124, A SELECTIVE A7 NICOTINIC ACETYLCHOLINE RECEPTOR PARTIAL AGONIST, IMPROVES EXPERIMENTAL COLITIS IN MICE AND REDUCES IMMUNE CELL INFILTRATION IN THE COLON

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Introduction: The parasympathetic nervous system and vagal nerve in particular are responsible for anti-inflammatory signaling from the central nervous system (CNS) to the periphery. α7 homopentamer nicotinic acetylocholine receptors (nAChRs) have been implicated in the transduction of these signals to the gastrointestinal (GI) tract, but the underlying mechanisms are still unclear.
Aims & Methods: The aim of this study was to investigate the anti-inflammatory effect of the novel, selective α7 nAChR partial agonist, EVP 6124 in mouse models of experimental colitis, and to determine the mechanism underlying its activity. To assess the anti-inflammatory activity of EVP 6124, we used trinitrobenezenesulfonic acid (TNBS)- and dextran sulfate sodium (DSS)-induced models of colitis. Macroscopic score, ulcer score, colon length and thickness, as well as myeloperoxidase (MPO) activity were recorded. To confirm the selectivity of the test compound, we used α7 nAChRs antagonist methyllycaconitine (MLA). Moreover, we used hexamethonium (HEX) to investigate whether centrally- or peripherally-located nAChRs are involved in the effects of EVP6124. Quantitative immunohistochemistry (IHC) was used to measure the infiltration of macrophages, neutrophils, T cells and B cells in the colon. Furthermore, we employed flow cytometry to determine the effect of EVP6124 on frequencies of $FoxP3^+$and $IL\text{-}17A^+$ T cells in the mouse colon. Additionally, we assessed the effect of EVP6124 on the viability of mouse spleen-derived monocytes. Changes in α7 nAChR mRNA expression in the colonic tissue during colitis and after treatment with EVP 6124 were quantified by real time RT PCR.
Results: The intraperitoneal (i.p.) administration of EVP6124 (3 mg/kg, twice daily) attenuated TNBS- and DSS-induced colitis in mice, as indicated by significantly reduced macroscopic parameters and MPO activity; this effect was blocked by the i.p. administration of MLA (3 mg/kg, twice daily). Treatment with EVP6124 significantly reduced the infiltration of macrophages, neutrophils and B cells in the colon of TNBS-treated animals, as indicated by the quantitative IHC. In the TNBS model the frequency of pro-inflammatory $FoxP3^+IL\text{-}17A^+T$ cells was significantly reduced in the colon of EVP6124-treated animals. In the DSS model treatment with EVP6124 increased the frequency of immunosuppressive $FoxP3^+T$ cells and reduced pro-inflammatory $IL\text{-}17A^+T$ cells. Moreover, EVP6124 reduced the viability of mouse spleen-derived monocytes in a dose-dependent manner. α7 nAChR mRNA was significantly increased in the colitic animals vs. healthy controls.
Conclusion: We show that stimulation of α7 nAChR with a partial agonist EVP6124 alleviates colitis via alteration of the number and/or activation status of the immune cells in the gut. Therefore, we highlight the potential of EVP6124 to become an anti-IBD drug, especially given that initial studies with EVP6124 in healthy volunteers showed that this compound is safe and well-tolerable.
Disclosure of Interest: None declared

P0904 CHARACTERIZATION OF BACTEROIDETES ASSOCIATED WITH INTESTINAL MICROBIOTA IN PATIENTS WITH CROHN'S DISEASE AND ANALYSIS OF ITS EFFECT IN THE INDUCTION OF INTESTINAL INFLAMMATION IN MICE

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Introduction: The pathogenesis of inflammatory bowel disease (IBD) involves an imbalance of the gut microbiota generating an inappropriate activation of the mucosal immune system in genetically predisposed individuals. The human commensal microbiota contains a large number of Bacteroidetes species that may cause inflammation in animal models.
Aims & Methods: The aim of this study was to detect and evaluate the influence of a major type of intestinal commensal bacteria belonging specifically to the order Bacteroidales on the activity of Crohn disease (CD). In addition, the effect of these bacteria isolated from CD patients on gut inflammation was evaluated in mice after transplantation.
Methods: We performed a case control study on the intestinal bacteria of the phylum Bacteroidetes from faeces of CD and healthy controls (HC) using a polymerase chain reaction (PCR) designed to detect human-specific genetic markers targeting Bacteroidetes-like 16S rRNA genes in fecal DNA samples. The PCR products from the 16S rRNA genes were digested with *Hinf*I, *Pci*I, *Dpn*II and *Aci*I enzymes and restriction fragment length polymorphism (RFLP) were determined. RFLP and sequencing analysis indicated that a total of 6 bacterial genotypes do exist: N1, C1, C2, C3, C4 and C5 (of which N1 genotype is probably a strain of *Bacteroides dorei* and C1, and maybe C2, strains of *B. vulgatus*). The relationship between CD activity (CDAI > 150) and microbiota was also evaluated. Microbiota from CD patients was transplanted into mice gut to evaluate their ability to induce inflammation. Results are shown in percentages.
Results: 11 CD patients (8 with active CD -aCD- (CDAI > 150), and 3 with inactive CD –iCD-), and 11 HC were included. The predominant Bacteroidetes genotype in feces from HC and iCD was N1 (in 100% of samples), whereas this genotype was found in only 28% of patients with aCD. 18% aCD patients showed the C1 genotype, 9% the C1 and C3 genotypes together, 18% the C4 genotype, and 27% the C1 and C4 genotypes together. The transplant of bacteria from CD patients to mice led to large bowel inflammation, and the stool of the transplanted mice consisted in 30% C4 genotype and had a high level of Bacteroidetes cluster in comparison with the mice transplanted with bacteria from HC.
Conclusion: The fecal microbiota of CD patients is different from those of HC in that they present a wide variety of Bacteroidetes cluster genotypes. The C4 genotype by itself, or together with the C1 genotype, seems to be intimately related to the activity of the disease. These results were also confirmed in transplanted mice.
Disclosure of Interest: None declared

P0905 INTESTINAL ORGANOIDS DERIVED FROM INFLAMMATORY BOWEL DISEASE PATIENTS SHOW UNALTERED TRANSCRIPTIONAL PROFILES WHEN COMPARED TO HEALTHY CONTROL ORGANOIDS

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Introduction: Various mechanisms contribute to the pathogenesis of inflammatory bowel diseases (IBD), including defects in epithelial barrier function, Paneth cell or goblet cell dysfunction, and a microbial dysbiosis. The epithelium is constantly renewed by intestinal stem cells (ISCs) located at the bottom of the crypts. The *ex vivo* ISC-containing organoids, have demonstrated to be a suitable model to investigate cancer and cystic fibrosis.
Aims & Methods: Given the reported defects in epithelial barrier and Paneth cell function, we evaluated if the organoid forming capacity of colonic crypts, as well as organoid transcriptional profiles, from IBD patients differ from that of healthy controls (HC).
Colonic mucosal biopsies from 9 HC, 14 ulcerative colitis (UC) patients, and 12 Crohn's disease (CD) patients were used to culture organoids as previously described.[1, 2] After the second passage, organoids were differentiated for 4 days by withdrawal of Wnt3a, nicotinamide and p38-inhibitor from the medium. RNA and histology samples were then processed and analysed using qPCR (SYBR Green qPCR SuperMix-UDG, Invitrogen) and immunohistochemistry for ISCs and differentiated cell types (goblet cells, entero-endocrine cells, Paneth cells, enterocytes), as well as proliferation and apoptosis (Ki-67 and cleaved caspase 3 staining).
Results: There was no difference in initial organoid forming capacity between controls and IBD patients (HC 85.9%; UC 78.6%; CD 83.1%, HC vs. UC $P = 0.2794$, HC vs. CD $P = 0.2204$, and UC vs. CD 0.8370). Additionally, no intrinsic differences in expression of the ISC-marker Lgr5 or differentiated cell types were detected. However, in the undifferentiated organoids there was a significant increase in chromogranin A (CHGA) expression in CD patient-derived organoids ($P = 0.0384$, table 1). In differentiated organoids there was a significantly decreased expression of proliferating cell nuclear agent (PCNA) in organoids from CD patients when compared to HC organoids ($P = 0.0099$). The biological implications of these findings are currently being evaluated by immune-stainings of organoid sections.

Table 1: Comparison of deltaCt values per group. UC = ulcerative colitis (n = 7), CD = Crohn's disease (n = 8), HC = healthy control (n = 9).

Comparison colonic organoids	Gene	P-value
UC vs HC undifferentiated	Chromogranin A	0.8125
CD vs HC undifferentiated	Chromogranin A	**0.0384**
UC vs CD undifferentiated	Chromogranin A	0.1137
UC vs HC differentiated	PCNA	0.0541
CD vs HC differentiated	PCNA	**0.0099**
UC vs CD differentiated	PCNA	0.4179
UC vs HC undifferentiated	Mucin2	0.0939

Conclusion: Our data shows that intestinal crypts isolated from IBD patients form organoids as efficient as crypts from healthy controls. Gene expression of markers of stemness and differentiation showed only subtle differences, and the biological implications remain to be clarified via immunohistochemistry.

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Abstract number: P0906 Table: Correlations between CD99 and CyPA in non-inflamed and inflamed colon areas in UC and CD patients.

	UC r^2		CD r^2	
mRNA level	Protein level	mRNA level	Protein level	
CyPA [ng/ml] in plasma vs. CD99 in non-inflamed colon areas	***+0.770***	+0.530	-0.651	-0.274
CyPA [ng/ml] in plasma vs. CD99 in inflamed colon areas	-0.535	+0.090	-0.344	-0.478
CyPA [ng/ml] in non-inflamed vs. CD99 in non-inflamed colon areas	-0.580	-0.086	-0.357	***-0.756***
CyPA [ng/ml] in inflamed vs. CD99 in inflamed colon areas	***+0.796***	+0.488	+0.436	-0.333

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P0906 DIFFRENT CORRELATION OF CD99 AND CYCLOPHILIN A IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Inflammatory bowel diseases (IBD) are characterized by crypt infiltration with neutrophils, which can be stimulated by externalization of an adhesion molecule CD99. Neutrophil infiltration is associated with upregulation of cyclophilin A (CyPA). However, studies on CD99 and CyPA in IBD patients have not been performed yet.
Aims & Methods: The aim of the study was to determine the CD99 gene and protein expression and extra- and intracellular concentration of CyPA in ulcerative colitis (UC) and Crohn's disease (CD) patients in comparison to healthy subjects. Patients with Crohn's disease (CD) and ulcerative colitis (UC) as well as healthy controls were enrolled in our study. All participating subjects were matched by age and gender. The samples comprised serum and colonoscopy biopsies from non-inflamed and inflamed (in UC or CD) colon areas. The CD99 mRNA was analyzed by RT-PCR, and CD99 and CyPA protein levels by immunoenzymatic methods (ELISA and Western blot).
Results: In UC patients, a tendency towards lower CD99 protein ($p = 0.084$), but not mRNA was observed compared with control. There was no relationship between CD and control in CD99 mRNA and protein level ($p = 0.735$ and $p = 0.446$, respectively). The UC patients had significantly lower CD99 mRNA in non-inflamed tissue and higher in inflamed colon areas compared with CD ($p = 0.035$ and $p = 0.021$, respectively). The extracellular CyPA level was 4.6- and 2.8-times higher in UC and CD than in control ($p = 0.017$ and $p = 0.137$, respectively). Reversed correlations were found between CyPA and CD99 in inflamed tissues of UC and CD patients.
Conclusion: Our study indicated that patients with UC had increased CD99 and CyPA both in plasma and tissue. Moreover, CD99 gene expression correlated inversely with intracellular CyPA level in inflamed and non-inflamed colon tissue in UC, but not CD. We suggest that there may be a link between CD99 and CyPA in IBD etiology. It is likely that CD99-CyPA interaction influences the inflammatory process in colitis, as in our study both CD99 and CyPA were increased in inflamed colon areas from UC patients. However, further studies are necessary to confirm those observations and to describe how, if at all, CyPA releasing influences CD99 signaling in IBD.
Disclosure of Interest: None declared

P0907 IMMUNE-SURVEILLANCE FAILURE PREDICTS DYSPLASIA PERSISTENCE IN ULCERATIVE COLITIS

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Introduction: In patients with ulcerative colitis (UC) chronic inflammation leads to dysplasia development in 10-20% of cases. Our previous studies demostrated that immunesurveillance mechanisms mediated by CD80-CD28 signalling may lead to dysplasia regression [1]. The persistence of low-grade dysplasia (LGD) in UC in two consecutive observations may be an indication for restorative proctocolectomy.
Aims & Methods: Our hypothesis is that a failure of immune surveillance mechanism may play a role in dysplasia persistence and we aimed to identify possible immunological markers of LGD persistence in colonic mucosa not affected by dysplasia.
We prospectively enrolled 95 UC patients who underwent screening colonoscopy who had biopsies taken from their sigmoid colon. Forty of them had at least a second colonoscopy and 6 patients had dysplasia in both exams suggesting a persistence of LGD in their colon. Real-time RT-PCR for TLR4, CD4, CD38, CD69, CD80 and CD8beta mRNA expression was performed. Flow cytofluorimetry for CD8+ lymphocytes expressing CD28 or CD38 and for epithelial cells expressing CD80 or HLA ABC were performed. Non parametric statistics, ROC curves analysis and logistic multiple regression analysis were used.
Results: We observed a lower CD38 and CD8beta mRNA expression in the healthy colonic mucosa of patients with LGD persistence ($p = 0.027$ and $p = 0.005$, respectively) as well as a lower level of activated cytotoxic T-cells (CD8 + CD38+) ($p = 0.042$). ROC curve analysis showed that lower level of activated cytotoxic T-cells (CD8 + CD38+) as well as low CD4, CD38, and CD8beta mRNA expression predicted with adequate accuracy the LGD persistence at a second colonoscopy. In particular, CD8beta mRNA levels showed the best accuracy (AUC = 0.87 [95%CI = 0.70-0.96], $p < 0.001$). At multivariate survival analysis in a model including CD8beta mRNA levels, disease duration and inflammatory grade showed that only CD8beta mRNA levels were independent predictor of dysplasia at follow up (OR = 0.033 [95%CI = 0.002-0.433], $p = 0.01$).
Conclusion: These data suggest a failure in immunesurveillance mechanisms in the colonic mucosa of UC patients who do not manage to clear dysplasia. Thus, low level of CD8beta mRNA expression in not dysplastic colonic mucosa might be used in the decision making of UC management as a predictor of persistence of dysplasia.

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Disclosure of Interest: None declared

P0908 COMPARATIVE GENOMICS BETWEEN AIEC/NON-AIEC STRAIN PAIRS FOR THE DETECTION OF GENETIC ELEMENTS IMPLICATED IN THE ADHERENT-INVASIVE E. COLI PHENOTYPE

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Introduction: Adherent-invasive *Escherichia coli* (AIEC) have been implicated in the aetiology of Crohn's disease (CD) but the molecular basis of its pathogenicity is still not well resolved. Obtaining molecular tools specific for AIEC is of great relevance as the current available techniques to identify the pathotype are based exclusively in phenotypic screening of cultured bacteria, which is highly time-consuming.
Aims & Methods: Our aim was to identify genetic elements that could be involved in the AIEC phenotype in order to gain insight into the mechanisms of pathogenicity of the pathotype and to find out molecular targets for its identification. The genome of three pairs of *E. coli* strains with identical pulsed field gel electrophoresis fingerprints and virulence gene profiles but differing in the AIEC phenotype (AIEC and Non-AIEC respectively) was sequenced *de novo* combining HiSeq and PacBio using paired-end libraries. The three pairs covered different phylogenetic groups and, with the exception of one strain, each pair shared the same serogroup. Genome assembly, functional annotation and comparative genomics between pairs was performed to obtain genetic differences between AIEC and non-AIEC strains. Additionally, single nucleotide polymorphisms (SNPs) were searched by comparing the Non-AIEC strains with both their AIEC pair and a reference AIEC of the same phylogroup. We used the genome of AIEC LF82 for the O6:H1-B2 pair, the AIEC 576-1 for the ONT:HNT/O46:H32-D pair, and the AIEC 541-1for the O22:H7-B1 pair.
Results: Quality analysis indicated the reads achieved quality scores above Q30, thus the inferred base call accuracy was above 99.9%. Genome length of AIEC strains O6:H1-B2, ONT:HNT-D and O22:H7-B1 was 5.16, 4.86 and 4.79 MB respectively. Their non-AIEC counterpart presented +30,515bp, +12,270bp and –54,427bp respectively. After a selection of confirmed differences *in silico* we have identified 11, 15 and 28 genetic differences respectively, including SNPs, insertions and deletions. Of them, 29 were found in genes that were in commonly shared in all the strains but the mutations were not AIEC-specific. New SNPs calling comparing the three pairs with reference AIEC strains of the same phylogroup allowed the identification of 185, 182 and 354 SNPs commonly shared by AIEC strains and not found in the Non-AIEC pair respectively, which lead to missense variants. To the moment, no AIEC-specific sequence widely distributed in all AIEC was found among the selected genes. Selected genes included

adhesins, transporters, enzymes, toxins and transcriptional regulators that could be involved in the pathogenicity of the strains.
Conclusion: New genes that could be involved in the pathogenicity of AIEC have been identified. *In vitro* studies are needed to demonstrate their role. Additional coding and non-coding sequences must be analyzed to find out putative genetic markers for AIEC. Identifying the genetic elements associated with the AIEC phenotype may help to better understand the mechanisms of pathogenicity of the pathotype and also could imply a significant advance in the detection of new therapeutic targets for CD.
Disclosure of Interest: None declared

P0909 EVALUATION OF MALE SEXUAL FUNCTION IN MEN WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The inflammatory bowel disease (IBD) per se and the therapies used for the treatment of this disease could have effect on the sex and sexuality of male patients. Also, as medical therapy in IBD has advanced, more patients are healthy enough to consider conception. The aim of the present study was to evaluate the impact of IBD on the male sexual function and satisfaction.
Aims & Methods: A multicentre, transversal study was performed in male subjects with IBD and controls (CTR) between April 2010 and March 2014. All the participants had between 18 and 45 years old and were assessed by a medical history and physical examination before inclusion. The presence of varicocele, altered FSH, LH, prolactine or testosterone levels or having any pathology related to subfertility was considered as exclusion criteria. To evaluate the male sexual function *The International Index Erectile Function questionnaire* (IIEF-15) validated in Spanish language were used. The global score and the five items about sexual function (erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall sastisfaction) were calculated from each patient. To investigate if anti-TNF therapy affected male sexual function, the IIEF-15 scores were calculated in CD patients with biological therapy and compared with patients without this therapy.
Results: Fifty-two patients with IBD (30 CD, 22 ulcerative colitis (UC)) and 22 CTR were included. When the 3 groups (CD, UC and CTRL) were compared, no significant statistical differences were found respect to global score (IEEF15 CD 66.1 ± 7.7; UC 62.5 ± 12.9; CTRL 68.3 ± 8.7; $p > 0.05$), erectile function (CD 26.1 ± 7.5; UC 25.2 ± 7.6, CTRL 28.6 ± 3.6, $p > 0.05$), sexual satisfaction (CD 11.3 ± 4.6, UC 10.6 ± 4.4, CTRL 13.1 ± 3.5; $p = > 0.05$), orgasmic function (CD 9.2 ± 2.1; UC 9.6 ± 0.6; CTRL 10 ± 0. $p > 0.05$) or sexual desire (CD 7.1 ± 2.0, UC 7.2 ± 2.2, CTRL 7.5 ± 1.8, $p > 0.05$). However, patients with UC had worse global satisfaction in IEF15 than CD patients (CD 8.5 ± 1.2; UC 7.2 ± 2.4; CTRL 9.1 ± 1.1 $p = 0.03$). The IIEF-15 score was no difference in patients with CD with ($n = 10$) and without anti-TNF ($n = 20$) therapy ($p < 0.05$).
Conclusion: The male sexual function based on IIEF-15 questionnaire is not affected by IBD or anti-TNF drugs. Nevertheless, patients with UC have lower sexual satisfaction than patients with CD or controls.
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P0910 AN IBD-ASSOCIATED VARIANT IN PTPN22 PROTECTS FROM DISEASE ONSET IN MOUSE MODELS OF COLITIS

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Introduction: Single nucleotide polymorphisms (SNP) in the gene locus encoding protein tyrosine phosphatase non-receptor type 22 (PTPN22) have been associated with inflammatory disorders, including IBD. Presence of the SNP rs2476601 results in a gain-of-function PTPN22 protein product and is associated with increased risk to develop autoimmune disorders, such as type 1 diabetes, rheumatoid arthritis, and systemic lupus erythematosus, but reduces the risk for Crohn's disease (CD) onset. We have previously shown that protein and mRNA levels of PTPN22 are reduced in intestinal biopsies from CD patients, and that loss of PTPN22 results in enhanced inflammatory cytokine secretion from mononuclear cells treated with interferon-gamma or the bacterial product muramyl dipeptide. In this study, we now addressed how presence of the gain-of-function variant in PTPN22 influences the susceptibility to intestinal inflammation in mouse models of colitis.
Aims & Methods: Colitis was induced in 10-12 week old female mice by administration of 2% DSS for 7 days (acute DSS colitis), administration of four cycles of DSS (1.5% DSS for 7 days, followed by 10 days normal drinking water each; chronic DSS colitis), or by transferring naïve T cells into RAG2-/- recipients. Wild-type (WT), PTPN22 deficient (PTPN22-/-), or mice expressing the IBD associated gain-of-function variant in PTPN22 (PTPN22-619W mice) were used for the study.
Results: While PTPN22-/- mice suffered from aggravated acute DSS colitis as determined by pronounced weight loss, increased endoscopic and histologic colitis scores ($p < 0.05$ each), PTPN22-619W mice reacted only weak to the DSS treatment when compared to WT littermates ($p < 0.05$ for weigh development, $p < 0.01$ for other parameters). In chronic DSS colitis however, PTPN22-/- mice suffered from a milder disease course (characterized by reduced weight loss [$p < 0.05$], decreased histological severity [$p < 0.05$]) from the third cycle on, while PTPN22-619W mice tended to show a more pronounced disease course from the third DSS cycle on. In the T cell transfer model, PTPN22-/- T cells induced a more severe colitis as observed by an enhanced histological pathology ($p < 0.05$), while weight loss was not affected when compared to mice receiving WT T cells. In contrast, mice transfected with PTPN22-619W T cells were protected from disease development in the first four weeks, and later on developed a mild disease course (moderate weight loss [$p < 0.01$], reduced shortening of the colon [$p < 0.05$], mild histological disease scores [$p < 0.05$]) when compared to mice receiving WT T cells.
Conclusion: During acute inflammation, loss of PTPN22 results in enhanced colitis severity, while presence of the gain-of-function PTPN22 variant protects from colitis development. In chronic disease, compensatory mechanisms are able to reverse the increased disease susceptibility in PTPN22-/- mice, finally resulting in reduced disease severity, while presence of the gain-of-function variant is no longer able to protect from colitis. We here describe for the first time how the IBD-associated variant in PTPN22 affects colitis development what helps to explain why this variant is associated with a reduced risk for CD onset.
Disclosure of Interest: None declared

P0911 ENTERIC GLIAL ALTERATIONS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Enteric glial cells are the most abundant cells of the enteric nervous system. In inflamatory bowel disease (IBD) patients, enteric glial cells (EGC) present some differences in the expression level of glial markers. Whether these changes are determined by the pathological environment or represent a constitutive feature of pathological EGC is unknown. The purpose of our study is (i) to determine *ex vivo*, the expression of glial markers in colonic biopsies from patients who have a Crohn's disease (CD), an ulcerative colitis (UC) and from control patients (CONT); (ii) to determine if the stimulation of EGC from rats in a primary culture by an inflamed environment could reproduce glial changes observed on human biopsies; (iii) try to reproduce glial changes observed in biopsies by the treatment of EGC from control patient in a primary culture, with supernatant from biopsies previously analyzed.
Aims & Methods: Biopsies of IBD patients (18 CD, 9 UC and 15 CONT) were performed by endoscopic procedures in inflamed area (I) and in non inflamed area (NI) for each patient. Culture of rat EGC were subjected to chronic inflammatory stress represented by TNFα and interleukin-1β (TI; 1ng/ml) or lipopolysacharide (LPS; 0.1µg/ml) for 4 days. Culture of human EGC from control patients (CONT) were obtained from surgical specimens. They were treated with supernatant from colonic biopsies at the concentration of 5% in a serum free medium. Supernantants were obtained after incubation of each colonic biopsie from IBD patient (I area and NI areas biopsies). Expression of the glial markers Sox10, S100β and glial fibrillary acid protein (GFAP) were assessed by quantitative real time PCR and Western blot analysis.
Results: Concerning the biopsies, the mRNA expression levels of Sox 10 and S100β were significantly elevated in I and NI areas of CD patients compared to UC patients ($p < 0.001$) and to CONT patients ($p < 0.001$). Intermediate isoform of GFAP was increased in inflamed area of CD patients compared to controls ($p < 0.05$). TI treatment of EGC from rats induced a significant overexpression of the three glial markers. LPS stimulation of EGC from rats also induced an over-expression of Sox10 and S100β but did not affect GFAP expression. We have not reproduced the increased expression of Sox 10 and S100β mRNA expression by human EGC treatment with supernantant from colonic biopsies of CD patient.
Conclusion: Our work shows that GFAP expression was differentially regulated by inflammatory cytokines and endotoxins. *Ex vivo*, LPS treatment reproduces the over-expression of Sox 10 and S100β in EGC cultures from rats, as observed *in vivo* in colonic biopsies of CD patients. However, treatment of human EGC in a primary culture with supernatant obtained from these biopsies, did not change the glial marker expression in human EGC .
Disclosure of Interest: None declared

P0912 INTRALUMINAL INFUSION OF MESENCHYMAL STROMAL CELLS IN SPHEROIDS ATTENUATES EXPERIMENTAL COLITIS

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Introduction: Mesenchymal stromal cells (MSCs) have emerged as a promising therapeutic option for various diseases due to their immunomodulatory properties and ability to actively participate in tissue repair processes. However, these

abilities are not intrinsic and therefore different strategies to induce and enhance their beneficial effects are currently under investigation. Recently, we observed that intraperitoneally injected MSCs settled as spherical shaped clusters, i.e. spheroids, onto the serosal fat surrounding the colon in experimental colitis.
Aims & Methods: In the present study we assessed whether luminal administration of MSCs in spheroids has a therapeutic effect. We infused 200 or 800 *in vitro* generated MSC spheroids, each consisting of 2,500 MSCs, intraluminally in C57BL/6 mice with established dextran sulphate sodium (DSS)-induced colitis. Body weight was measured daily and disease score consisting of the presence of loose stool, visible faecal blood and macroscopic inflammation was determined at sacrifice. Endoscopy was performed to evaluate mucosal damage and subsequent healing. Mucosal cytokine levels were measured in the homogenates of distal colon. In addition, myeloperoxidase activity in the homogenates of distal colon was measured as an index for neutrophil infiltration. Furthermore, we counted the number of macrophages in the lamina propria of the distal colon.
Results: MSC spheroids alleviated DSS-induced colitis when infused intraluminally resulting in less body weight reduction (9.2% after treatment with 800 MSC spheroids versus 16.4% and 15.9% after treatment with 200 MSC spheroids and PBS-treated mice, respectively; both $p = 0.02$), a lower endoscopic activity score and lower disease activity scores at sacrifice, related to the dose of MSC spheroids infused. Mucosal cytokine levels of interleukin-6 and interferon-gamma as well as numbers of macrophages and neutrophils in the distal colons were decreased particularly after intraluminal infusion of the high dose MSC spheroids.
Conclusion: Intraluminally infused MSC spheroids promote mucosal wound healing and attenuate experimental colitis, accompanied by less phagocytes and proinflammmatory cytokines in the mucosa.
Disclosure of Interest: None declared

P0913 ALTERED TISSUE GLUCOCRTICOID METABOLISM IS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Glucocorticoids (GCS) are known to modulate a number of immunological responses. Within tissues expressing glucocorticoid and mineralocorticoid receptors including the colon, GCS metabolism is regulated by the isozymes of 11 beta hydroxysteroid dehydrogenase (11βHSD). 11βHSD 1 acts as an oxoreductase, converting inactive cortisone into active cortisol while 11βHSD 2 acts as a dehydrogenase producing cortisone. Variations in expression may have a role in Inflammatory Bowel Disease (IBD).
Aims & Methods: To examine the expression of 11βHSD 1 & 2 in IBD.
Following informed consent, patients with known IBD aged 18-80yrs were recruited; exclusion criteria (1) Steroid ≤6 weeks, (2) Coagulopathy, (3) Pregnancy, (4) Cushing/Conns Syndrome (5) Quiescent disease. Disease activity was assessed using biochemical (C Reactive Protein (CRP)), clinical (Harvey-Bradshaw Index/Mayo Score) & histological parameters. Controls with a normal colonoscopy without a history of IBD were also recruited. Two additional biopsies were obtained including inflamed & non-inflamed samples from IBD patients where possible, whereas a single additional colonic biopsy was obtained from controls. Biopsies were stored in RNA later & analyzed in batch, using Quantitative real time RT-PCR (TaqMan) & commercially available Probes & Primers (Invitrogen). Relative transcript levels were determined using 18S as a reference gene. Relative expression of 11βHSD 1 & 2 were expressed as a mean and compared between groups using a student t test and 11βHSD 1:2 ratios were calculated and compared between groups using a Mann-Whitney U test with a p value of <0.05 considered significant.
Results: To date 28 IBD (16 Crohn's Colitis and 12 Ulcerative Colitis) and 15 control patients have been recruited. IBD and control cohorts were demographically similar with 55% (n = 15) vs. 67% (n = 10) being female, with a mean age of 45 years (17-76 years) and 55 years (19-70 years) respectively. Overall based on histology 46% (n = 13) had mild disease, 43% (n = 12) had moderate disease and 11% (n = 3) had severe disease. In all 68% (n = 19) and 57% (n = 16) had elevations in their HBI/Mayo scores (HBI range 0-21, Mayo 0-12) and CRP (range 1-192.5mg/l) respectively. Overall mean levels of 11βHSD1 in IBD patients and controls were 197 au and 261 au respectively and were not significantly different while mean 11βHSD2 expression levels were significantly lower in IBD patients vs. controls (35 au vs. 176 au, p = 0.001, 95% CI -226- -57.8). Of interest 11βHSD1:2 ratios were much higher in patients with IBD compared with controls (52:1 vs. 1.6: 1, p = 0.001). Overall within the IBD cohort disease activity did not affect 11βHSD1 or 2 levels, however among IBD subjects with matched histological inflamed and non inflamed tissue samples (n = 15) there was a trend towards lower 11βHSD2 levels (51au vs. 10 au, p = 0.051).
Conclusion: Patients with IBD have altered glucocorticoid metabolism with increase 11βHSD1: 11βHSD2 ratios mainly due to a reduction in 11βHSD2 expression. Further work on 11βHSD2 regulation is warranted and may represent a novel therapeutic pathway in IBD patients.
Disclosure of Interest: None declared

P0914 LOW-DOSE LINDANE INGESTION AGGRAVATES SUSCEPTIBILITY TO COLONIC AND INTESTINAL INFLAMMATION IN MICE MODELS OF CROHN'S DISEASE

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Introduction: Lindane (LIN) is an organochlorine pesticide. Although LIN has not been used as insecticide in Europe and USA since the 1970s, it is still currently included in the constitution of more than 500 commercial products. In addition, LIN is still used in developing countries. Because of its bioaccumulation potential, LIN is found in high concentrations in environment and food chain. The main contamination way in humans is consumption of lipid-rich diet such as fish and dairy products.
Aims & Methods: Our aim was to assess the effects of oral intoxication with low doses of LIN on gut inflammation in 3 different murine models.
C57Bl6 males were exposed during 1 month to oral intoxication with LIN (0, 5 and 50 µg/kg bw/day). Then 2 types of colitis were induced, either by single intrarectal injection of Trinitro benzene sulfonic acid (TNBS, 100 mg/kg bw), or by oral administration of dextran sodium sulfate (DSS, 2.5%) during 9 days. Besides, enteritis was induced by single gavage of indomethacin (10 mg/kg bw). Then mice were euthanized and gut inflammation intensity was assessed by macroscopic, histological and molecular parameters.
Results: In TNBS-induced colitis, mice intoxicated with LIN showed colitis macroscopic scores significantly higher (+228 % at 5 µg/kg/j, p = 0.001, and +145 % at 50 µg/kg/j, p = 0.03) compared to untreated mice with colitis only. Myeloperoxidase activity in colon of intoxicated mice was significantly enhanced in the 2 groups treated with LIN compared to untreated mice (+588 %, p = 0.002 at 5 µg, and + 153 %, p = 0.003 at 50 µg). Colitis histological score and *IL-1 b* mRNA levels were also higher in colons of mice intoxicated with LIN, with a significant 160 % (p = 0.03) and 762% (p = 0.003) increase respectively at the dosage of 5 µg compared to untreated mice with colitis only. Similar results were obtained in DSS-induced colitis, as mice having received the 2 dosages of LIN showed an increase of their colon weight/size ratio of 121 and 128% for the dosages 5 et 50 µg (p = 0.005 and p = 0.001 respectively), and an increase of colon myeloperoxidase activity (+301 and 287 %, p = 0.0007 and p = 0.009 respectively). Mice intoxicated with 5 µg showed also a significant increase of colitis histological score and colon *IL1-b* mRNA levels (+177%, p = 0.01, and +762%, p = 0.01, respectively). Following indomethacin-induced enteritis, jejunum of mice exposed to 5 and 50 µg LIN showed a significant increase of lesions areas (+171% p = 0.03 and +253% p = 0.003), lesions numbers (+146%, p = 0.008 and +180%, p = 0.0002) and *Il1-b* mRNA levels (+192%, p = 0.02, and +350%, p = 0.04).
Conclusion: Oral intoxication with low doses of lindane induces an aggravation of gut inflammation in 2 murine models of colitis and in 1 model of enteritis. The role of this persistent organic pollutant in inflammatory bowel diseases deserves further investigations.
Disclosure of Interest: None declared

P0915 ALTERED MUCOSAL 5-HT SIGNALING IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The gastrointestinal (GI) tract is the largest producer of serotonin (5-hydroxytrptamine; 5-HT) in the human body. Enterochromaffin (EC) cells are the best characterized subset of enteric endocrine cells and are the main source of 5-HT in the gut; tryptophan hydroxylase (*Tph*)1 is the rate-limiting enzyme involved in the bio-synthesis of 5-HT by EC cells. The diverse effects of 5-HT on various GI functions is mediated by multiple 5-HT receptor subtypes present on a variety of cells in the gut. Previously, we have shown that mice which have significantly reduced gut 5-HT levels exhibit reduced severity of experimental colitis, while replenishing gut 5-HT increased the severity of colitis. These seminal findings identified 5-HT as a key molecule in the pathogenesis of experimental colitis, but further research is needed to translate these observations for clinical utilization. While there are segregated reports on the changes of different components of 5-HT signaling in inflammatory bowel disease (IBD), there is a lack of studies with thorough examination on the changes of 5-HT content and 5-HT receptors in IBD.
Aims & Methods: A comprehensive assessment of key elements of gut 5-HT signalling in patients with Crohn's disease (CD) with a view to validate 5-HT as a new target for improved therapeutic strategy in CD. This study was approved by the local ethics committee. Mucosal biopsies were collected from the colon of consenting patients with CD and from healthy controls (HC), undergoing routine colonoscopy for colorectal cancer. Inactive specimens were collected from CD patients in remission, or from non-inflamed regions of patient with active disease. Non-inflamed regions were designated as those without any endoscopic features of inflammation and at least 10 cm from any area of active inflammation. A pathologist unaware of the diagnosis performed histological evaluation of the biopsies collected (n = 10, 11 and 8 from HC, inactive and active CD segments, respectively). Additionally, relative gene expression of *Tph1*, serotonin reuptake transporter (SERT) and 5-HT receptors (5-HTR_1, 5-HTR_3, 5-HTR_4; 5-HTR_7) were determined by quantitative polymerase chain reaction (qPCR).
Results: Histological evaluation of biopsies confirmed the macroscopic assessments of the endoscopist during sample collection. There was significant upregulation of *Tph1* and downregulation of SERT expression in active CD samples compared to both inactive and control samples. Investigations into 5-HT receptor expression by qPCR revealed significant increases in 5-HTR_{3A} and 5-HTR_7 expression in active CD samples compared to inactive and control samples. 5-

HTR_4 expression was significantly elevated in both active and inactive CD samples compared to control, irrespective of disease activity and 5-HTR_{1A} expression was minimal in all groups compared.
Conclusion: Our findings establish that increased inflammation in patients with CD is associated with alterations in various aspects of 5-HT signalling (5-HTR_{3A}, 5-HTR_7, 5-HTR_4, *Tph1*, and SERT). Given the emerging role of 5-HT as a powerful modulator of inflammation and immune response, a better understanding of 5-HT signaling in intestinal inflammation in CD may ultimately lead to effective strategies targeting this pathway in CD.
Disclosure of Interest: None declared

P0916 LINKING TLRS ACTIVATION BY THE MICROBIOTA WITH CHANGES IN SENSORY-RELATED MARKERS IN IBS PATIENTS AND RATS

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Introduction: Visceral pain is a hallmark of Irritable Bowel Syndrome (IBS). Dysbiotic states of the gut microbiota and alterations in host-bacterial interaction systems appear to contribute to the pathology of IBS. However, the exact mechanisms underlying these pathways are unknown.[1,2,3]
Aims & Methods: The aim of this study was to investigate the relationship between the intestinal nociceptive system and Toll-like receptors (TLRs) in colonic tissue of IBS patients and to assess if this relationship is also altered when simulating a dysbiosis due to TLR-hyper-stimulation in rats. The expression of sensory-related [cannabinoid receptor 1 (CB1) and 2 (CB2) and vanilloid receptor type 1 (TRPV1)] and host-bacterial interaction markers (TLR2, TLR4, TLR5, TLR7) and antimicrobial peptides (AMPs, defensins) in sigmoidal colonic biopsies of IBS patients (n = 12) and healthy controls (n = 11) was assessed (qRTPCR). Additionally, Sprague Dawley male rats were treated intracolonically with a TLR4 agonist (LPS, Escherichia coli O5:B55, 0.2 mg/rat) or a TLR7 agonist [Imiquimod (IMQ), 0.1 mg/rat], (n = 6 each group) for 5 days. Colons were collected for analysis of sensory markers, TLRs, AMPs and cytokines (qRT-PCR), quantification of secretory-IgA levels (s-IgA; ELISA) and histopathological analysis.
Results: Colonic biopsies of IBS patients showed a significant up-regulation of CB1 and CB2 (both $P < 0.001$), TRPV1 ($P < 0.05$) and TLR2 and TLR7 (both $P < 0.001$) expression when compared to healthy individuals. CB1, CB2 and TRPV1expression positively correlated with TLR2 and 7 expression in IBS patients ($P < 0.001$ in all cases). Minor changes were seen in the expression of TLR4, TLR5 and defensin 5.
Using TLR4 and 7 agonists to mimic a dysbiotic state in rats and the TLR-induced responses associated to IBS samples, we found that selective repetitive TLR stimulation induced a mild colonic immune activation characterized by an increase of pro- and anti-inflammatory cytokines expression and changes in levels of s-IgA without overt histological changes, compatible with features associated to IBS. Both TLR agonists also up-regulated the colonic expression of host TLRs (TLR2 > TLR7 > TLR5 > TLR4). Moreover, intracolonic instillation of LPS induced a significant increment in the colonic expression of CB1, CB2 and TRPV1, while IMQ down-regulated the expression of TRPV1. In general, higher changes were seen when stimulating with LPS when compared to IMQ. Similar to IBS biopsies, TLRs stimulation lead to minor changes in the expression of AMPs (defensins).
Conclusion: Altogether, our findings point towards an active communication between the microbiota and intestinal neuro-immune pathways, mainly by connecting the immune TLR-dependent signalling to the intestinal nociceptive system (endocannabinoid and vanilloid systems). Additionally, stimulation of TLRs by luminal factors (simulating dysbiosis) appears to be enough to induce intestinal immune and nociceptive signalling pathways which may be part of the underlying pathophysiological mechanisms of IBS, thereby linking the microbiota to intestinal neuro-immune pathways and visceral pain.

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P0917 20 YEAR FOLLOW UP OF BRITISH TWIN PAIRS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: IBD twin studies have shown similar disease phenotype within concordant pairs. Longitudinal follow up suggests pairs with CD remain concordant for location whereas twins with UC diverge (1). This study is a retrospective longitudinal analysis of UK twin pairs with IBD.
Aims & Methods: The UK IBD Twin and Multiplex Registry was searched for twin pairs who took part in a previous twin study. Data from 1994 and 2014 was reviewed. The following were analysed: zygosity, concordance, Montreal classification, admissions, surgical history.
Results: The UK IBD Twin and Multiplex Registry was searched for twin pairs who took part in a previous twin study. Data from 1994 and 2014 was reviewed. The following were analysed: zygosity, concordance, Montreal classification, admissions, surgical history.
Results
Demographics: N = 94 twin pairs. UC:CD 48:46. Mean age 59.
Pair Concordance:

	CD 1994	CD 2014	UC 1994	UC 2014
MZ	33.3% (4:12)	41.7% (5:12)	21.4% (3:14)	21.4% (3:14)
DZ	9.1% (3:33)	9.1% (3:33)	11.4% (4:35)	17.1% (6:35)

3 previously discordant pairs became concordant. The mean time between diagnosis was 9.1 years.

Montreal Classification
Concordant Pairs: There were no mixed CD:UC pairs. Of the 17 concordant pairs, 10 had complete information from both twins in both datasets.
IBD: A was identical in 6/12 (50%) concordant pairs.
CD: L was identical in 3/6 (50%) pairs in both 1994 and 2014. B was only available from 2014, and was identical in 3/6 (50%) pairs. P was identical in 2/5 (40%) twins in 1994 and 3/7 (43%) twins in 2014.
UC: A was identical in 3/4 pairs (74%). L was identical in 4/4 (100%) pairs in 1994 and 2014.
All IBD sufferers
UC: Disease classified as proctitis decreased from 1994 to 2014 (30.4% vs 17.9%), with a corresponding increase in pancolitis (41.1% vs 50%)
CD: Cases classified as L3 increased from 6/52 (11.5%) to 22/53 (41.5%). Presence of perianal disease also increased (9.6% vs 23.1%).
Extraluminal manifestations increased from 4/109 (3.7%) to 13/112 (11.6%).
Surgery
Concordant pairs: Concordant twin pairs were concordant for history of previous surgery in 9/12 (75%) pairs in 1994 and 7/14 (50%) pairs in 2014.
All IBD: In 1994 32/109 (29.4%) IBD sufferers had undergone surgery, increasing to 52/112 (49.1%) in 2014.
Admission
Concordant pairs: Concordant twins were concordant for history of admission in 10/14 (71.4%) pairs in 1994 and 10/15 (66.7%) pairs in 2014.
All IBD: 46/109 (42.2%) IBD sufferers had at least one admission in 1994; this increased to 76/112 (67.9%) in 2014.
Conclusion: Pair concordance of this cohort supports that heritability of CD is greater than UC. Within concordant pairs with CD, disease location is less correlated than in other cohorts. Conversely, concordant pairs within UC were more similar and converged over time. Sample size limited analysis. Disease progressed over time.

Reference

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Disclosure of Interest: None declared

P0918 RISING INCIDENCE OF INFLAMMATORY BOWEL DISEASE IN CANTERBURY, NEW ZEALAND

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Introduction: A population-based study of inflammatory bowel disease (IBD) in the Canterbury province of New Zealand demonstrated an incidence of Crohn's disease (CD) in this region of 16.5 per 100,000 population in 2004, along with a high rate of IBD overall. At the time, this was one of the highest rates of CD in the world.
Aims & Methods: The current study aimed to ascertain the incidence of IBD in the same geographical area of New Zealand ten years later (during the 2014 calendar year). Patients diagnosed with IBD between January 1st 2014 and December 31st 2014 within the Canterbury region in the private and public sectors were identified and characterised. Diagnosis and disease classification was ascertained using standard accepted criteria. Projected population data for age and gender for the region were utilised to calculate incidence rates for IBD overall and for CD, ulcerative colitis (UC) and inflammatory bowel disease-unclassified (IBDU). Incidence rates were also age-standardized using the World Health Organization Standard Population. Furthermore, all patients were phenotyped according to the Montreal Classification.
Results: During the 2014 year, 205 patients were diagnosed with IBD in Canterbury. This group comprised 134 patients with CD, 69 with UC and 2 with IBDU. Patients were aged between 5 and 88 years, with most patients with CD and UC diagnosed between 20 and 54 years of age. The crude incidence rate

for IBD for 2014 was 39.8 per 100,000 (95% CI, 34.4 – 45.3). In addition, the incidence rates for CD was 26.0 (95% CI, 21.6 – 30.4), for UC 13.4 (95% CI, 10.2 – 16.6), and for IBDU 0.39 (95% CI, -0.15 – 0.93) per 100,000 population. For patients with CD, disease location was evenly distributed (ileal 30%, colonic 36% and ileocolonic 34%) and 94% had inflammatory disease, with only 6% having stricturing or penetrating disease at diagnosis. Twenty-two percent of patients with CD had upper gut involvement, whilst 13% had perianal disease at diagnosis. Similarly, patients with UC had even distribution of pancolonic, left-sided and proctitis.
Conclusion: This population-based study demonstrates further substantial increases in the incidence of IBD in this well-delineated area of New Zealand. Overall, incidence rates were 1.5 fold greater than when assessed ten years earlier, with an even greater increase in the incidence of UC. The reasons contributing to these continued increases remain unclear. However, further increases in rates of IBD indicate growing health system demands in the coming years.
Disclosure of Interest: None declared

P0919 NEOPLASIA RISK AFTER COLECTOMY IN INFLAMMATORY BOWEL DISEASE PATIENTS – A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Although colectomy substantially reduces the risk to develop colorectal cancer (CRC) in inflammatory bowel disease (IBD) patients, neoplasia may still develop following colectomy in the residual rectum or ileal pouch. Conclusive data regarding this risk are scarce, which has resulted in the absence of evidence-based postoperative endoscopic surveillance recommendations. We therefore conducted a systematic review and meta-analysis in order to determine prevalence, incidence, and risk factors for neoplasia development in the different post-surgical scenarios after colectomy, including: 1. patients with a permanent end ileostomy and rectal stump, 2. patients with an ileorectal anastomosis (IRA) 3. patients with an ileal pouch-anal anastomosis (IPAA).
Aims & Methods: PubMed, Embase, Web of Science and Cochrane Library were searched to identify studies which reported prevalences or incidences of colorectal neoplasia following colectomy or specifically assessed risk factors for neoplasia development. Two researchers independently performed study selection, quality assessment and data extraction. Prevalence's were pooled and compared across subgroups with a logistic regression model. Risk factors were analyzed in a pooled random effect model, if possible, or otherwise critically appraised.
Results: Thirteen, 35 and 33 articles, including 1011, 2762 and 8403 patients, for respectively the rectal stump, IRA and IPAA group, were included for prevalence and incidence calculations. CRC prevalence following colectomy was significantly higher in the rectal stump group (2.1%, 95% CI 1.3-3.0) and IRA group (2.4%, 95% CI 1.7-3) compared to the IPAA group (0.46%, 95% confidence interval (CI) 0.32-0.61), with an odds ratio (OR) of 6.4 (95% CI 4.33-9.50). In the IPAA group, the pooled cumulative incidence of pouch/cuff carcinoma 25 years after IPAA construction was 3.4%. A history of CRC was the most important risk factor (IRA: OR 12.8, 95% CI 3.3-49.2; IPAA: OR 15.0, 95% CI 6.6-34.4). Furthermore, IBD duration and ulcerative colitis rather than a diagnosis of Crohn's disease (OR 10.2) emerged as risk factors for rectum or pouch neoplasia.
Conclusion: The calculated prevalence and incidence for colorectal neoplasia following colectomy appeared relatively low, especially in the IPAA group. Major determinants for cancer development following colectomy were the presence of a residual rectum with a 6.4-fold increased risk, and a CRC-history with a 15.0- (IPAA) or 12.8-fold (IRA) increased risk. These findings may aid in developing individualized post surgical endoscopic surveillance strategies in order to optimize prevention of CRC in this patient population.
Disclosure of Interest: None declared

P0920 THE IMPACT OF GENDER ON WORK ACTIVITY IMPAIRMENT AND QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE (IBD) IN SOUTHERN ITALY

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Introduction: IBD impact on patients' major life activities, such as school, work, self-care, and quality of life. Published literature has reported higher rate of unemployment, sickleave and working disability. Data on gender influence are scanty, especially in Mediterranean countries.
Aims & Methods: Aim of our study was to compare work activity impairment and quality of life between female and male patients with IBD followed-up in a referral center from southern Italy. 102 patients with IBD (53 females, 49 males) consecutively observed in the IBD clinic were recruited. Data on clinical and demographic characteristics (age, type of IBD, disease behavior (Montreal) and activity (HBI, Mayo score), smoking habits, familial predisposition, current treatment, educational and marital status, current employment) were registered on a dedicated database. All patients agreed to fill in the WPAI (Work Productivity and Activity Impairment) questionnaire and the EQol-5D (European Quality of Life – 5Dimension) VAS scale.Data of the National Institute of Statistics (ISTAT) on employmentrates in Italy were used for comparison.
Results: There were no significant differences between males and females regarding age, educational and marital status and disease characteristics except disease activity rate, which was higher in males. There was a significant difference in the employment status since 58.5% of women were unemployed versus 34.7% of men ($p = 0.02$). Overall, there were no differences in WPAI scores (absenteeism, presenteism, overall work and regular activities impairment) and EQoL between males and females. In male patients with active disease absenteeism ($p = 0.04$), presenteism ($p = 0.02$) and work productivity impairment ($p = 0.04$) rates were significantly higher as compared to patients in remission, quality of life was not affected, in females with active disease we observed a higher rate of absenteeism ($p = 0.04$) and impaired daily regular activities ($p = 0.04$) as well as quality of life ($p = 0.015$).
Conclusion: Gender significantly influences occupational status in IBD, since women are more often unemployed. Work productivity is impaired in both men and women with active disease, but in women daily regular activities and quality of life are more significantly affected than in men. These data, if confirmed in other geographical areas, should be kept in mind in clinical management of IBD female patients.
Disclosure of Interest: None declared

P0921 COLONIC METAPLASIA OF THE ILEUM AS A PREDICTIVE MARKER OF CLINICAL RELAPSE AFTER ILEO-COLONIC RESECTION FOR CROHN'S DISEASE: A PROSPECTIVE STUDY AT 4 YEARS

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Introduction: Colonic metaplasia of ileum has been reported in Crohn's Disease (IBD), particularly in severe/established ileal lesions. Differently, CD ileum with no lesions or with early post-operative recurrence showed to express the small intestine type mucin phenotype (1).
Aims & Methods: In a prospective study at 4 years, we aimed to address whether colonic metaplasia of the ileum may represent a marker of clinical relapse after ileo-colonic resection for CD. At this purpose, a cohort of CD patients (pts.) already followed up for 1 year (1), was clinically followed up for additional 3 years after surgery. Clinical recurrence at 4 years was assessed in the same cohort of 19 CD pts. with recurrence and colonic metaplasia assessed at 6 (T1) and 12 months (mos) (T2)(1). In the same pts. colonic metaplasia of the ileum was already evaluated at surgery (T0), at T1 and T2 (1). The expression of sulfomucins (colon phenotype) and sialomucins (small intestine mucin and phenotype) in the ileum was evaluated by immunohistochemistry (1). In the present study, compliant CD pts. were followed up for 4 years after surgery, with clinical recurrence (CDAI > 150) assessed yearly. The correlation between the percentage of expression of sulphomucin and clinical recurrence at4 years was assessed. Statistic: Results were expressed as median (range). Coefficient of correlation, the unpaired T test used as appropriate.
Results: Clinical follow up at 4 yrs was completed by 17 CD pts. (12 males, age 41 yrs, range 17-57). Endoscopic recurrence occurred in 13/17 pts. at T1 and in 14/17 pts. at T2. (median: T1: 2., range 0-4; at T2: 0, range 0-4). Clinical recurrence was assessed at 6 mos, 1.2.3 and 4years (pts. $n = 1, 3, 3, 2, 1$, respectively). A significant correlation was observed between the percentage of expression of sulphomucin in the ileal surgical samples and the CDAI at 4 yrs ($r = 0.62$ $p = 0.007$), but not at 6 mos, 1, 2 or 3 yrs. A significant correlation was also observed between the percentage of expression of sulphomucin in the ileal biopsies at 6 mos and the CDAI at 6 mos ($r = 0.68$; $p = 0.003$), but not at 1, 2, 3 and, 4 yrs. The percentage of expression of sulphomucin in the ileal biopsies at 12 mos was significantly correlated with the CDAI at 2 yrs ($r = 0.53$; $p = 0.02$). The median expression of sulphomucins in the ileal surgical samples was significantly higher in the subgroup of pts. developing clinical recurrence at 2 yrs. (40, 10-99 vs 5, 0-50; $p = 0.04$), but not at the other observations. The median expression of sulphomucins in the ileal samples at 12 mos was higher in the subgroup of pts. developing clinical recurrence at 1 and 2 yrs (median, range: 30, 1-40 *vs* 0, 0-35; $p = 0.025$ and 30, 0-40 vs 0, 0-35; $p = 0.029$, respectively), but not at 3 yrs (15, 0-30 *vs* 0, 0-40; $p =$ n.s.).
Conclusion: In CD ileum, the development of a "metaplastic" colonic-mucosa phenotype, as observed in the surgical specimens and in severe early post-operative recurrence, may represent a predictive marker of clinical relapse in pts under regular follow up after ileo-colonic resection.

Reference

1. *Inflamm Bowel Dis*. 2014; 20(9): 1555-61.

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P0922 SMALL BOWEL CANCER ASSOCIATED WITH CROHN'S DISEASE

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Introduction: Population-based studies revealed that patients with Crohn's disease (CD) have increased risk of developing small bowel cancer in comparison with the background population. However, little is known concerning to the cancer in detail, because the number of the patients are relatively small.
Aims & Methods: This study aimed to clarify the clinicopathological characteristics between small bowel cancer and colorectal cancer in CD.
We performed a literature search in Ichushi (Japanese medical literature database) between 1983 and March, 2015 for small bowel cancer and colorectal cancer associated with CD. Two hundred and seventy-one cases were picked up, and we excluded six cases, because the location of the cancer was not specified clearly. Thus, 265 cases were included in this study. The cases were classified to two groups: patients who had small bowel cancer(s) (S group: n = 55) and those with only colorectal cancer(s) (C group: n = 210), which included perianal fistula cancer.
Results: The age at cancer diagnosis was higher in S group (53.5 (29-81); median (range)) than in C group (43 (25-89); $p < 0.0001$). The duration of CD was similar between S group (16 (0-40) years) and C group (15 (0-52) years; $p = 0.41$). The age at CD diagnosis was also higher in S group (39(12-69)) compared with C group (25 (9-84)). S group had more proportion of ileitis than C group (58% vs. 10%), whereas 81% of the patients in C group had ileocolitis, and the difference was statistically significant ($p < 0.0001$). In S group, the cancer diagnosis was made before treatment only in 16%, and 70% of these patients had not been diagnosed before pathological examination of the resected specimen. Well differentiated and moderately differentiated adenocarcinoma occupied three quarters of the tumor in S group whereas only 44% in C group ($p < 0.0001$). On the other hand, the proportion of mucinous carcinoma was only 4% in S group, and that was 40% in C group ($p < 0.0001$). The clinical stage according to the Union for International Cancer Control classification was 4%/8%/39%/12%/39% (stage 0/1/2/3/4) in S group, and that was 3%/14%/35%/29%/19% in C group, and the proportion of stage 4 was significantly higher in S group. Although the resection rate was higher in S group than in C group (98% vs. 87%; $p = 0.0055$), the prognosis was equivalent (41% were alive in S group and 44% in C group).
Conclusion: We found some differences between the two groups with regard to the age at cancer detection, the age at CD onset, the timing of cancer diagnosis, the histology of the cancer, and clinical stage of the cancer. We should always give attention not to miss small bowel cancer at CD operation.
Disclosure of Interest: None declared

P0923 NATURAL HISTORY OF CROHN'S DISEASE IN ELDERLY PATIENTS DIAGNOSED OVER THE AGE OF 70 YEARS: A POPULATION-BASED STUDY

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Introduction: Elderly-onset (>60 years at diagnosis) Crohn's disease (CD) seems to be associated with a better outcome than CD diagnosed earlier in life.
Aims & Methods: Our aim was to compare the natural history of CD in elderly patients older than 70 years (y) at diagnosis with that of elderly patients diagnosed between the age of 60 and 70 y in the EPIMAD population-based registry. Three-hundred and seventy patients with elderly-onset CD diagnosed between January 1988 and December 2006 were identified. Among them, 188 (63%) were older than 70 y at diagnosis. Characteristics at diagnosis as well as natural history, surgery needs and drug exposure were recorded with a median follow up of respectively 4.5 y [1.1;8.3] in CD diagnosed after 70 y and 7.8 years [3.3;12.1] in CD diagnosed between 60 and 70 y.
Results: CD incidence in patients older than 70 y was 2.3/100 000 inhabitants. The proportion of males was lower in patients diagnosed after 70 y than in those diagnosed between 60 and 70 y (31% vs 45%, $p = 0.006$). Clinical presentation at diagnosis was similar in both groups with respect to symptoms as bloody stools, perianal location and extra-intestinal manifestations. Pure colonic location (L2) was more frequent among patients > 70 y both at diagnosis (73% vs 57%, $p = 0.004$) and maximal follow-up (70% vs 47%, $p < 0.0001$). Disease extension (from L1 or L2, to L3) was less frequent in patients > 70 y (7% to 15%, $p = 0.03$). The most frequent behavior in the two groups was inflammatory both at diagnosis (75% vs 80%, $p = 0.43$) and maximal follow up (69 vs 70%, $p = 0.55$). There was no significant difference in patients > 70 y compared to those between 60 and 70 y regarding treatment with 5ASA (71% vs 76%, $p = 0.27$), oral corticosteroids (39% vs 45%, $p = 0.86$), and anti-TNF (4% vs 7%, $p = 0.63$). However, the use of immunosuppressants was significantly less frequent in patients > 70 y (12% vs 25%, $p < 0.001$). Risk for surgery was similar in both groups (29% vs 28% $p = 0.35$).
Conclusion: Natural history of CD in elderly patients diagnosed over the age of 70 y seems to be milder than that in elderly patients diagnosed between 60 and 70 y. The exposure to immunosuppressants and biologics is low in patients diagnosed over 70 y with no difference in surgery needs. This needs to be taken into account when establishing therapeutic strategies.
Disclosure of Interest: None declared

P0924 DESCRIPTION OVER TIME AND STUDY OF ASSOCIATED FACTORS FOR THE DIAGNOSTIC DELAYIN CROHN'S DISEASE: A 21-YEAR POPULATION BASED STUDY

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Introduction: Delay in diagnosis (DD) of Crohn's disease (CD) may be responsible for complications and for poor response to treatment. The description of DD over time in a population-based CD cohort and its determining factors are unknown and may help implementing corrective measures. The aim of this study was to report in a 21-year population-based cohort the variation over time of DD and to identify associated factors including sociodemographic factors.
Aims & Methods: Sociodemographic and clinical characteristics of all CD patients issued from the EPIMAD registry and diagnosed from 1990 to 2010 were included. DD was defined as the time between onset of symptoms and CD diagnosis (months). DD was considered as long when in the upper quartile of this time period. Sociodemographic data included the living area of each patient at the time of diagnosis (urban, periurban or rural), the distance between the patient's living area and the nearest gastroenterologist, and the deprivation index of the living area (FDep99). Clinical data were classified according to the Montreal classification. Univariate and multivariate analyses were performed using a logistic regression to identify the baseline characteristics of patients associated with a long DD.
Results: 8,704 patients with CD were recorded including 57% of females; 10% of them had < 17 years at CD diagnosis (A1), 67% between 18 and 59 years (A2) and 23% >60 years (A3). The majority (65%) of patients had an ileocolonic CD and 5% had perianal lesions; 17% had a stricturing and 10% a penetrating behaviour. During the whole study period, median DD was 3 months [Q1 = 1; Q3 = 7] with no change over time. A long DD was > 7 months and was associated in univariate analysis with the absence of weight loss ($p = 0.04$), the presence of extra-intestinal manifestations ($p = 0.02$), pure ileal involvement (L1) ($p < 0.0001$) and stricturing behaviour ($p = 0.002$). In multivariate analysis, only the absence of weight loss (OR = 1.16 [1.04-1.28]) and pure ileal location (OR = 1.36 [1.18-1.56]) were associated with a long DD. Socioeconomic characteristics were not associated with a long DD.
Conclusion: In this 21-year population-based study of CD patients, median DD was 3 months with no change over time and no influence of socioeconomic baseline characteristics. Only two clinical features (absence of weight loss and L1 location) were associated with a long DD.
Disclosure of Interest: None declared

P0925 FACTORS THAT ARE ASSOCIATED WITH THE OCCURRENCE OF FISTULAE AND STENOSIS IN CROHN'S DISEASE PATIENTS IN THE SWISS IBD COHORT

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Introduction: Fistulae and stenosis represent a frequent and severe complication in Crohn's disease (CD) patients. For an optimal treatment it is essential to identify factors being associated with the development of CD-associated fistulae and stenosis to guide the clinical management or, ideally, prevent their occurrence. Our study aimed to identify independent predictors of fistulae and stenosis in CD patients from the patient collective of the Swiss inflammatory bowel disease cohort study (SIBDCS).
Aims & Methods: We retrieved data of 1'600 CD patients (47.6% males, median age: 39ys) from the nationwide SIBDCS. The development of fistulae and stenosis in relation to smoking status, disease location, age at diagnosis, medications and history of intestinal resection surgery were analyzed.
Results: In the univariate analysis female gender was associated with a lower risk for perianal fistulae (OR 0.64; CI 0.48-0.86; $p = 0.003$) while younger age at diagnosis of CD was associated with perianal (OR 0.98; CI 0.97-0.99; $p = 0.002$ and OR 0.98; CI 0.97-0.99; $p = 0.002$) and multiple fistulae (OR 0.98; CI 0.96-0.99; $p = 0.027$ and OR 0.98; CI 0.96-0.99; $p = 0.035$). Colonic and ileo-colonic manifestation at the time of initial CD diagnosis was associated with the occurrence of perianal or multiple fistula (OR 2.30; CI 1.41-3.77; $p = 0.001$ and OR 2.18; CI 1.40-3.77; $p = 0.001$). Independent factors that were associated with perianal fistulae by multivariate analysis were smoking at time of CD diagnosis (OR 1.508, CI 1.103-2.061, $p = 0.010$), presence of stenosis (OR 1.422, CI 1.023-1.978, $p = 0.036$), colonic (OR 2.505; CI 1.489-4.215, $p = 0.001$) or ileo-colonic CD at diagnosis (OR 1.797 CI 1.137-2.844, $p = 0.012$) and ever treatment with either antibiotics (OR 2.167, CI 1.594-2.945, $p < 0.001$) or anti-TNF antibodies (OR 2.296, CI 1.678-3.141, $p < 0.001$). The latter four aspects are also associated with the presence of multiple fistulae. Multiple fistulae are further associated with a history of intestinal resection (OR 3.098, CI 1.890-5.079, $p < 0.001$). Female gender protects form perianal fistulae (OR 0.571, CI 0.420-0.775, $p < 0.001$).

Colonic involvement at CD diagnosis (OR 0.531, CI 0.305-0.925, $p < 0.026$) protects from the onset of stenosis. History of intestinal resection (OR 6.476; CI 4.866-8.617, $p < 0.001$), anemia (OR 1.529; CI 1.106-2.115, $p = 0.010$), presence of fistulae (OR 1.424; CI 1.075-1.887, $p = 0.014$), disease duration per year (OR 1.018; CI 1.003-1.032, $p = 0.016$) and treatment with antibiotics (OR 1.524; CI 1.167-1.990, $p = 0.002$) or steroids (OR 1.756; CI 1.242-2.481, $p = 0.001$) were independently associated with the occurrence of stenosis.
Conclusion: In particular markers of a severe disease course, such as younger age at diagnosis, history of intestinal resection, use of steroids or anti-TNF antibodies are associated with the occurrence of CD-associated fistulae and stenosis.
Disclosure of Interest: None declared

P0926 THE ROLE OF SMOKING IN THE NATURAL HISTORY OF CROHN'S DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: There is strong evidence that smoking is a strong risk factor for the development of Crohn's disease. The role of smoking on disease progression is less definitive. Some studies support the notion that it increases the risk of complications, resulting in more flares of disease activity and surgical intervention. However, the results of other studies are conflicting. We therefore conducted a systematic review and meta-analysis of current available data to examine this issue.
Aims & Methods: We carried out a search of MEDLINE, EMBASE and EMBASE. Eligible studies were cross-sectional surveys, cohort studies, or case-control studies examining the impact of smoking on the natural history of Crohn's disease, defined according to clinical, radiological, histological, or endoscopic criteria in a minimum of 50 patients. Outcomes of interest were flares of disease activity, or need for surgery, according to smoking status. There were no language restrictions, and a recursive search of bibliographies of all eligible articles was performed. Two independent investigators judged eligibility and extracted data on each article, with a third investigator resolving any disagreements between the two. Study quality was assessed according to published criteria. Dichotomous data were pooled using a random effects model, and the association between smoking status and flare of disease activity, or need for surgery, was summarized using an odds ratio (OR) with a 95% confidence interval (CI).
Results: The search strategy identified 3374 citations, of which 164 appeared relevant to the study question, and were retrieved for further evaluation. Of these, 40 were eligible for inclusion, including a total of 2769 patients. Overall, 1243 (69.5%) of 1788 smokers had a flare of disease activity, compared with 1431 (64.3%) of 2225 non-smokers (OR = 1.56; 95% CI 1.21-2.01). Following a "curative" resection for Crohn's, 165 (59.6%) of 277 smokers had a subsequent flare, compared with 138 (45.8%) of 301 non-smokers (OR = 1.66; 95% CI 0.99-2.79). There were 882 (33.1%) of 2661 smokers who required any surgery during follow-up, compared with 982 (30.4%) of 3235 non-smokers (OR = 1.19; 95% CI 0.99-1.44). When the association between smoking and need for first surgery was examined, there were 508 (51.4%) of 989 smokers who required a first operation, compared with 575 (30.5%) of 1883 non-smokers (OR = 1.71; 95% CI 1.30-2.41). Finally, in those who had undergone a first operation, 404 (47.5%) of 850 smokers underwent a second operation, compared with 276 (30.2%) of 913 non-smokers (OR = 1.61; 95% CI 1.40-1.85).
Conclusion: As has previously been described, smoking adversely impacts the natural history of Crohn's disease, with a 56% increase in flares of disease activity during follow-up, and a 19% increase in need for surgery. First surgery rates are increased by 71% in smokers, and reoperation rates after first surgery by 61%. Smoking cessation interventions should be implemented in all patients with Crohn's disease who smoke.
Disclosure of Interest: None declared

P0927 MOTIVATIONAL INTERVIEWING IN INFLAMMATORY BOWEL DISEASE PATIENTS COUNSELLING: DATA FROM A LARGE CASE-CONTROL STUDY

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Introduction: Motivational interviewing (MI) is a patient-centered counselling also proven useful in inflammatory bowel disease patients. Some skills are at the base of a successful MI: the ability to ask open ended questions, the ability to provide affirmations, the capacity for reflective listening, and the ability to periodically provide summary statements to the patients.
Aims & Methods: We report data from a case-control study (1:1 ratio) on MI applied to IBD patients. Between June 2014 and March 2015 we collected data from 2 IBD referral centers both with knowledge on MI skills but only one of these (case group) currently applied this technique during the visits. At the end of visit all patients filled out an anonymous questionnaire.
Results: 200 patients (108 males [54%]) with a mean age of 40.3 ± 15.5 years were evaluated. Ninety-two patients were affected by Crohn's disease (46%), 96 by ulcerative colitis (48%), and 12 by indeterminate colitis (6%). Patients' characteristics were quite similar between case and controls: male 51% vs. 57%, mean age $35.5.1 \pm 14.1$ vs. 44 ± 15.1, Crohn's disease 48% vs. 44%, ulcerative colitis 46% vs.50%, indeterminate colitis 6% vs. 6%. At final analysis 162 patients (81%) were previously evaluated by a gastroenterologist with an acceptable satisfaction rate (68%) which significantly decreased in those at the first outpatient visit (54%, $p < 0.001$). Satisfaction rate on general practitioner was low both in all patients and in those at the first visit (48% and 28%). The lowest satisfaction rate was reported in patients at the first visit ($p < 0.001$), in patients affected by indeterminate colitis ($p = 0.003$), in patients with long disease duration ($p = 0.004$); 78% of patients would have liked the use of explanatory pictures during the visits. Patients already followed-up in the referral centers reported a good overall satisfaction rate (87%) which reached 100% in those at the first visit. Nevertheless in the latter group, on a scale from 1 to 5, "5" (100% satisfied) was reported by 97% of patients on MI-group (case group) compared to 54% of controls: $p < 0.001$. No differences in terms "physician's communication skills", "perceived empathy" and duration of visits (41.9 ± 8.6 vs. 40.2 ± 9.4 minutes) were observed.
Conclusion: Our study showed as IBD patients followed-up in referral centers are satisfied of their physician rather than gastroenterologists without experience on IBD. MI is a communication tool very well appreciated by IBD patients and can help "IBD experts" to reach the best communication skills especially in pts at the first visit. Explanatory pictures should be used to help patients to better understand their clinical condition.
Disclosure of Interest: None declared

P0928 CONTRAST-ENHANCED ULTRASONOGRAPHY IN THE EVALUATION OF CROHN'S DISEASE ACTIVITY: CORRELATION WITH ILEOCOLONOSCOPY

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Introduction: The role of contrast-enhanced ultrasonography (CEUS) for assessing CD activity is still evolving.
Aims & Methods: Our aim was to determine the performance of conventional US and CEUS to detect CD activity assessed by ileocolonoscopy taken as the reference.
Thirty-five patients with small bowel CD were prospectively studied. Clinical disease activity was assessed by the Harvey–Bradshaw Index (HBI). All patients underwent ileocolonoscopy and also a conventional US followed by a CEUS using a microbubble contrast agent (SonoVue®). US examinations was performed using a Hitachi HI VISION Avius®, employing a multi frequency convex abdominal transducer. Disease small bowel activity was assessed by ileocolonoscopy (reference) and patients were graded, for the purpose of statistical analysis, as inactive (normal or mild disease) or active (moderate or severe inflammation). Qualitative and quantitative parameters from the sonographic analysis included maximum bowel wall thickness, vascularity pattern by Doppler US and quantitative measurements of contrast bowel wall enhancement using CEUS (peak intensity and time to peak). Statistics were performed with SPSS v.20.0.
Results: Disease severity was as follow: no inflammation in 10 patients (29%), mild in 5 patients (14%), moderate in 4 patients (11%) and severe in 16 patients (46%). Only 6 patients (17%) had significant clinical activity (HBI $\geq$ 5 points). In patients with active endoscopic disease, wall bowel thickness of the terminal ileum was higher than in patients with inactive disease (7mm vs 5mm, $p = 0.029$), the same association was observed for the presence of moderate to severe vascularity by Doppler ($p = 0.006$). For CEUS the peak intensity was related with disease severity (10.5 vs 21.5, $p = 0.001$) with an excellent capability to predict endoscopic activity in ileoscopy (area under the ROC curve 0.896, 95% CI 0.786-1.0). The time to peak could not predict endoscopic activity in ileoscopy (23.2 sec vs 22.7 sec, $p = 0.7$).
Conclusion: Wall bowel thickness, Doppler US and CEUS peak intensity are valuable parameters for an accurate detection of small bowel inflammatory activity in CD. Conventional US and Contrast-enhanced US could in the future have a major role in the assessment of inflammatory activity in CD patients, and probably in the evaluation of therapeutic response.
Disclosure of Interest: None declared

P0929 CHANGE IN CLINICAL PRESENTATION OF IBD PATIENT ADMITTED TO THE HOSPITAL FROM EMERGENCY DEPARTMENT AND/OR OUTPATIENT CLINIC: RESULTS FROM A 1996-2013 RETROSPECTIVE STUDY FROM AN ITALIAN TERTIARY CENTER

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Introduction: Recently a big change in management and organization of IBD patients occurred thought Europe, including Italy, because of introduction of anti-TNF-a, introduction of IBD units, etc. Few studies exist on clinical features of IBD admitted to hospital and its change during the time.
Aims & Methods: Aim of this study was to describe clinical presentation, outcome of hospitalization, need for surgery and complications of IBD patient

admitted to the hospital from emergency or outpatient clinic. 5407 admissions from 1996 to 2013 at Policlinico "A. Gemelli" hospital were analyzed, identified from ICD-9-CM code referring to IBD. All records were classified to define: type of access (if from outpatient clinic or from emergency department); admission code if suspicion of IBD or flare or Complications or Unrelated Reason); diagnosis at the discharge according to ICD-9-CM; clinical outcome of the hospitalization if diagnosis/follow-up, Treatment, outcome not related; surgical outcome if no/ unrelated surgery, Related surgery, complications. Data are stratified for type of IBD, type of access, time (Pre vs. Post-biological, being the cut-off year 2003 for the CD and 2007 for the UC). Statistical analysis was performed by chi2 test for qualitative variables and the Student's t test for quantitative variables. Statistical significance was defined for p values less than 0.05.

Results: IBD represent around 1% of all admission to tertiary center. 557 out of 5407 patients (10.3%) were admitted for abdominal pain and were then diagnosed for IBD. Admission rate from emergency were 19 % ot total for both CD and UC, with a mean admission per patient of 2.5 ± 3.9 (min 1 and max 53 admissions). In CD patients complications were higher if admitted from emergency department while in UC higher if admitted from outpatient clinic; fistulas and obstruction were complication associated primarily to CD while bowel cancer and osteo-articular diseases for UC. Stratifying for admission before and after introduction of anti-TNF we observed an increase of admission for recurrence of the disease; an increase in medical and surgical treatments; an overall increase in complications, with a decrease of some important complications and the rise of extra-intestinal cancer in UC.

Conclusion: Clinical presentation, outcome of hospitalization, need for surgery and complications in IBD patient varied in recent years differently according to type of disease, type of admission at the hospital and also timeframe, being introduction of anti-TMF-a and re-organization of outpatient clinic major determinants of it. This is a starting point for a better cost-effective and integrated management of IBD.

Disclosure of Interest: None declared

P0930 HEALTH-RELATED QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE IN SOUTH-EAST NORWAY 20 YEARS AFTER DIAGNOSIS

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Introduction: Inflammatory bowel disease (IBD) can reduce patient's health-related quality of life (HRQoL). The aim of the present study was to compare HRQoL in ulcerative colitis (UC) and Crohn's disease (CD) 20 years after diagnosis with the background population, and to identify factors associated with reduced HRQoL.

Aims & Methods: IBD patients from a population-based inception cohort (IBSEN) were invited to a follow-up visit 20 years after diagnosis. In addition to a structured interview, clinical examination, blood and stool samples and a colonoscopy, patients answered the Short Form 36 (SF-36), the Norwegian Inflammatory Bowel Disease Questionnaire (N-IBDQ) and the Fatigue Questionnaire.

Results: 72% (438/604) of patients with a confirmed UC or CD diagnosis completed the HRQoL questionnaires. Females scored lower than males in SF-36 dimensions and N-IBDQ total scores, stratified by diagnosis (Table 1). Seven out of eight SF-36 dimensional scores were statistically significantly reduced compared to the Norwegian reference population. However, only the difference in the general health (GH) dimension between CD patients and the reference population (67.3 vs. 77.4) appeared to be of clinical importance with a z-score of 0.65, which is a moderate difference according to Cohen's effect size. C-reactive protein > 5, current symptoms and not working were independent factors associated with reduced scores in SF-36 dimensions in CD patients (CRP > 5: role physical (RP) 72 vs. 42, bodily pain (BP) 72 vs. 60, GH 66 vs. 54; current symptoms: RP 79 vs. 52, BP 80 vs. 61, GH 72 vs. 56, vitality (VT) 60 vs. 44, $p < 0.01$; not working: physical functioning (PF) and BP (91 vs. 76 and 78 vs. 57, $p < 0.001$)). In UC patients a simple clinical colitis activity index (SCCAI) > 2.5 and having chronic fatigue (CF) were associated with reduced SF-36 dimension scores (SCCAI: RP 81 vs. 48, BP 75 vs. 53, GH 72 vs. 53, VT 61 vs. 47; CF: PF 89 vs. 74, RP 80 vs. 45, BP 74 vs. 50, GH 72 vs. 51, VT 62 vs. 38, $p < 0.01$).

Table 1: : SF-36 dimensional scores and N-IBDQ total scores

UC			CD		
	Male	Female		Male	Female
PF* **	91 (88-93)	82 (79-85)	**PF*** **	91 (87-96)	79 (74-83)
RP* **	81 (75-87)	65 (59-71)	**RP***	73 (64-82)	56 (47-65)
BP**	74 (70-78)	65 (61-69)	**BP***	75 (69-80)	65 (59-71)
GH*	70 (67-74)	65 (61-69)	**GH***	68 (63-73)	58 (53-63)
VT* **	62 (59-66)	53 (50-56)	**VT****	57 (52-62)	46 (40-51)
SF*	87 (83-90)	81 (77-84)	**SF**	83 (77-89)	75 (69-81)
RE**	87 (81-92)	74 (69-80)	**RE**	77 (68-86)	67 (58-77)
MH	81 (78-83)	78 (75-80)	**MH***	80 (76-84)	72 (68-76)
N-IBDQ total score**	187 (183-191)	178 (174-182)	**N-IBDQ****	185 (179-196)	172 (166-178)

Estimated marginal mean scores adjusted for age and education. PF physical function, RP role physical, BP body pain, GH general health, VT vitality, SF social function, RE role emotional, MH mental health. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$. (95%CI) 95% confidence intervals.

Conclusion: In this population-based IBD cohort HRQoL measured 20 years after diagnosis was in general comparable to the reference population. However, HRQoL in female IBD patients was lower than in males. Independent factors associated with reduced HRQoL were: CRP > 5, current symptoms and not working in CD, SCCAI > 2.5 and chronic fatigue in UC.

Disclosure of Interest: None declared

P0931 OVERVIEW OF HEPATITIS B IMMUNIZATION PRACTICE AND VACCINATION RESPONSE IN GREEK INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Low vaccination rates against hepatitis B virus (HBV) have been reported in patients with IBD, as well as sub-optimal responses to vaccination. ECCO has currently advised for vaccination of non-immune IBD patients with an aim of achieving levels of anti-HBs > 100 IU/l for adequate seroprotection, in particular when immunosuppressive therapy is planned. The appropriate management in this setting remains to be fully specified.

Aims & Methods: We have initiated a multi-centre study in the metropolitan area of Athens, Greece, to evaluate a) the percentage of Greek IBD patients with protective anti-HBs levels; b) the response to vaccination; and, c) the effect of various patient and disease-related parameters on the efficacy of vaccination. We reviewed the clinical records of all IBD patients with a regular follow-up at 4 tertiary hospitals at the Athens Metropolitan area. All patients were tested for HBsAg, anti-HBs and anti-HBc antibodies. Patients younger than 65-y-old with negative tests for both HBsAg and anti-HBc were managed as follows: a) negative anti-HBs without/unknown history of vaccination: 3-dose vaccination (0, 1, 6 mo) with 20 μg, b) history of vaccination: anti-HBs levels >100iu/l: annual follow-up of anti-HBs levels; anti-HBs 10-100iu/l, 1-3 20 μg doses with anti-HBs measurement after each dose; no anti-HBs, 1-3 40 μg doses with anti-HBs measurement after each dose. Vaccination was considered complete when anti-HBs > 100iu/l were detected. In patients with negative anti-HBs levels after 3x20 μg doses, vaccination was repeated with a double dose (40 μg) with anti-HBs measurement after each dose.

Results: We have included 446 IBD patients so far in our study (CD = 267, UC = 176, IC = 3, male = 226, age: 42.2 ± 15.3, 16-89). Among 328 patients with recent HBV serology, there were 5 with chronic HBV infection (HBsAg+) and 29 patients with previous exposure to HBV (HBsAg-, anti-HBc+). Protective immunity due to previous vaccination (HBsAg-, anti-HBc-, anti-HBs+ > 100iu/L) was detected in 23.8% (n = 78). Sub-optimal anti-HBs levels were seen in 10.1% (n = 33). The majority of tested patients were negative for all three markers (HBsAg, anti-HBc, and anti-HBs), indicating lack of effective vaccination (n = 183, 55.8%). If only patients less than 65-y-old were analyzed (n = 280), effective immunity was still absent in 54.3%. There was significant association ($p < 0.001$) between age and presence of protective immunity that is probably due to the widespread application of HB vaccination at early ages in the last 2 decades in Greece. Vaccination was commenced in 125 patients so far, with 64 having finished their regimen. Response has been assessed in 31 patients with 18 (58.1%) achieving sufficient response and 13 requiring double dose vaccination.

Conclusion: A significant percentage of Greek IBD patients lack protective immunity against HBV. The "classical" vaccination regimen often fails to induce adequate levels of anti-HBs antibodies. Increased awareness, intensified vaccination protocols and frequent testing of response may be required in this population.

Disclosure of Interest: None declared

P0932 EXPRESSION OF INTESTINAL ALKALINE PHOSPHATASE (IAP) IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Intestinal alkaline phosphatase (iAP) functions as a gut mucosal defense factor by detoxifying pro-inflammatory bacterial and endogenous components. The aim of this study was to compare the expression of iAP in inflamed colon mucosa to that in non-inflamed colon mucosa of inflammatory bowel disease (IBD) patients.
Aims & Methods: Colon mucosal specimens were obtained from IBD [18 with ulcerative colitis (UC), 17 with Crohn's disease (CD)] during colonoscopy. iAP from each specimen was quantified using ELISA. The expression levels of profinflammatory cytokins in IBD patients were determined by real-time polymerase chain reaction. The activation of iAP in cells treated with enteropathogenic *Escherichia coli* (EPEC) was determined by Western blo
Results: A total of 35 consecutive patients (18 UC, 17 CD) were included in this study. In IBD patients, the protein level of iAP in inflamed mucosa was significantly (average fold: 2.34; $p < 0.001$) higher than that in non-inflamed mucosa. The mRNA levels of inflammatory genes IL-6, TNF-α and TLR-4 in inflamed mucosa were significantly higher than those in non-inflamed mucosa ($p < 0.05$). There was significant correlation between endogenous iap and CDAI in CD patients ($p = 0.038$, $r = 0.506$). In EPEC-treated epithelial cells, the protein levels of iAP were significantly higher than that in cells not treated by EPEC ($p < 0.05$).
Conclusion: Endogenous iAP was increased in inflammatory mucosa in IBD patients with protective role against gut inflammation at suboptimal levels. Further study is needed to determine the role of iAP in patients with IBD.
Disclosure of Interest: None declared

P0933 PREVALENCE AND DISEASE COURSE OF INFLAMMATORY BOWEL DISEASE DIAGNOSED IN ASYMPTOMATIC PATIENTS DURING SCREENING COLONOSCOPY

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Introduction: There is sparse evidence about the prevalence of Inflammatory Bowel Disease (IBD) in asymptomatic patients. We have data from retrospective studies in different countries ranging from 0.7 to 1.6%. Interestingly most of the patients developed symptoms related to the disease during the next 5 to 10 years of follow up. We have conducted a study to evaluate the prevalence, disease characteristics and treatment requirements in patients diagnosed of IBD during screening colonoscopy in asymptomatic patients in our area.
Aims & Methods: We have retrospectively reviewed the medical chart of all the patients who underwent a colonoscopy under the colon cancer screening programme in the Basque Country (Spain). This study was designed and conducted in two hospitals from the IBD Study Group from the Basque – Navarre Society of Gastrointestinal Diseases. The screening in our area started in 2009 and it covers people between 50 and 69 years from a population of 2.2 million people. All patients were assessed with fecal occult blood test (FOBT) and, if this test was positive, a colonoscopy was performed. The inclusion criteria in the present study included a diagnosis of IBD established by endoscopy and confirmed by histology during the colon cancer screening programme.
Results: A total of 70.299 FOBT were done in our two hospitals. In 4.717 (6.7%) of these cases a colonoscopy was performed. We have found 14 patients (0.3%) diagnosis of IBD: Ten cases of ulcerative colitis (UC), two of Crohn's disease (CD) and two of indeterminate colitis. Nine of them are women, and most of them have never smoked. The median age at diagnosis was 55 years [51.5-60]. UC extension was classified as E1 in 3 patients, in 4 as E2 and in 3 as E3. All four patients with CD and IBD unclassified suffered only colonic involvement. Endoscopic activity was scored as UCEIS 5 [4-5.5]. Only one patient suffered perianal disease and extraintestinal manifestations, both at diagnosis. Median follow-up time since the diagnosis was 12 months [8.5-29.5]. Five patients (35%) developed symptoms during this period (rectal symptoms/ diarrhoea/ rectal bleeding). Treatment was indicated with mesalazine in 11 cases, steroids in 3 and 2 with azathioprine. No patients required methotrexate or biologics. Only one patient required surgery because of a mass in transverse colon at diagnosis to rule out an underlying cancer.
Conclusion: We have found a 0.3% prevalence of IBD during screening colonoscopies in our area. All cases had exclusive colonic involvement. After a medium – term follow – up the disease behaviour is relatively mild. Our preliminary data need to be explored in future studies with a greater number of patients and a longer – follow up.

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P0934 CLINICAL INEFFICACY OF GOLIMUMAB IN ULCERATIVE COLITIS PATIENTS IS INDEPENDENT OF IMMUNOGENICITY

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Introduction: Golimumab (GOM, Simponi®), a therapeutic antibody targeting tumor necrosis factor (TNF) alpha, has recently been approved for treatment of moderate to severe Ulcerative Colitis (UC). The PURSUIT-SC induction study showed that 51.0% of patients responded clinically upon sub-cutaneous administration of GOM 200/100 mg at weeks 0 and 2.
Aims & Methods: (1) To develop monoclonal antibody (MA)-based immunoassays for the determination of GOM and anti-GOM concentrations (2) To evaluate the clinical significance of these assays in a small cohort of 15 UC patients receiving GOM maintenance dosing (50 mg or 100 mg) after induction of therapy. For the quantification of GOM serum concentrations, both a MA-based TNF-coated ELISA and a MA/MA-based sandwich-type ELISA were developed. Assay performance was assessed using 64 patient serum samples. External analytical validation was performed through collaboration with Sanquin. For quantification of the anti-GOM antibody response, a bridging ELISA was developed and samples were analyzed neat and after an acid-treatment step. Clinical response and C-reactive protein (CRP) were determined.
Results: Analyzing 64 serum concentrations of GOM-treated UC patients revealed an excellent correlation between the two immunoassays: Spearman's rho 0.981, $p < 0.0001$; intra-class correlation coefficient (ICC) of 0.972. The sandwich-type ELISA demonstrated higher sensitivity and specificity as compared to the TNF-coated ELISA and is therefore our preferred assay. External validation of the sandwich-type ELISA using 20 patient serum concentrations showed a good Pearson's r (0.969, $p < 0.0001$) and ICC (0.926). Treatment of seven out of 15 UC patients was terminated within 14 weeks due to inefficacy. However, in all serum samples tested, anti-GOM levels were <3.2 ng/mL even when an acid dissociation step was included to dissociate the GOM/anti-GOM complexes. Comparing consecutive GOM levels of a representative responder *versus* a representative non-responder revealed significantly different pharmacokinetics, which were also reflected in the clinical and biochemical response parameters of these patients (Table 1).
Conclusion: In this study, highly sensitive MA-based immunoassays were developed for the specific quantification of serum GOM and anti-GOM concentrations and applied on a cohort of 15 UC patients. Despite major differences in pharmacokinetics between responders and non-responders, no antibodies against GOM were detected. Based on these preliminary results, we hypothesize that efficacy could be improved by higher or more frequent GOM doses for patients with inadequate treatment responses or by increasing GOM absorption.
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Abstract number: P0934 Table 1: Clinical, biological and biochemical characteristics of a typical responder and non-responder

Week	responder Dose (mg)	TC (μg/mL)	ATG (ng/mL)	Partial Mayo	CRP (mg/L)	non-responder Dose (mg)	TC (μg/mL)	ATG (ng/mL)	Partial Mayo	CRP (mg/L)
W0	200	<0.1	<3.2	6	8.7	200	ND	<3.2	8	8.0
W1		9.8	<3.2				9.9	<3.2		
W2	100	10.4	<3.2	ND	4.2	100	4.6	<3.2	8	4.0
W4		14.9	<3.2				3.8	<3.2		
W6	50	8.4	<3.2	2	5.4	50	1.5	<3.2	6	4.6
W14	50	6.2	<3.2	0	4.8	0	1.0	<3.2	ND	16.6

TC, Trough concentration;ATG, antibodies towards GOM;CRP, C-reactive protein;ND, not determined

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P0935 PRESENCE OF LIVER TEST ABNORMALITIES AT DIAGNOSIS IS ASSOCIATED WITH OCCURENCE OF COMPLICATED DISEASE BEHAVIOR IN PATIENTS WITH CROHN'S DISEASE

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Introduction: In patients with Crohn's disease, liver test abnormalities (LTA) are a frequent phenomenon. Although clinical experience may suggest a relationship between disease severity and presence of LTA, this has not been extensively studied. In celiac disease, presence of LTA has been associated with the degree of mucosal damage. In Crohn's disease, the degree of mucosal damage is associated with a poor prognosis. In this study, we aim to investigate whether the presence of LTA is associated with a poor prognosis in newly diagnosed Crohn's disease patients.

Aims & Methods: We performed a retrospective cohort study in all patients diagnosed between 2004 and 2011 in a tertiary IBD centre and 2 large teaching hospitals. All new cases of Crohn's disease were included in the study when liver test results from before the start of treatment were available. Patients with liver disease, manifest at diagnosis or during follow up, were excluded. Patients were scored for patient characteristics, occurence of complications (such as stenosis or perforation), hospitalizations and surgeries. Liver test abnormalities (LTA) were defined as a value of either alkaline phosphatase (AP), Gamma Glutamyl transferase (GGT), Aspartate Aminotransferase (AST) or Alanine Aminotransferas (ALT) above the upper limit of normal. Complicated behavior at diagnosis was defined as having any form of non-B1 behavior at diagnosis.

Follow-up was ended after 60 months or at the occurence of a complication.

Results: In 383 newly-diagnosed patients with Crohn's disease, LTA were found in 135 patients.

No differences in Montreal classification at diagnosis were found between patients with and without LTA. Patients with LTA more often developed complications compared to patients without LTA (either stenosis or perforation; 33% vs 15% resp., $p < 0.001$). Using a multivariate analysis, LTA ($p < 0.001$, Hazard ratio (HR)2.3), complicated behavior at diagnosis ($p = 0.019$, HR 1.7), CRP at diagnosis ($p = 0.032$, HR 1.003) and involvement of the small bowel ($p = 0.05$, HR 1.9) were associated with the occurence of a new stenosis or perforation.

During the 5 year follow-up period, 54% of patients with LTA were hospitalized, compared to 35% of non-LTA patients ($p = 0.001$). Using a multivariate analysis, both presence of LTA at diagnosis ($p = 0.005$, HR 1.56) and complicated behavior at diagnosis ($p = 0.003$, HR 1.5) were associated with an increased risk for hospitalization.

Eighty out of 135 patients with LTA had an increased AP, and 27 of these 80 patients developed complicated disease behavior compared to 54 out of the 303 patients without LTA (33% vs. 15%, $p = 0.003$). Out of the 80 patients with an increased AP, 44 were hospitalized during the 5 years follow up compared to 117 of 303 patients with normal AP (55% vs 38%, $p = 0.011$).

Conclusion: In this study we have demonstrated that presence of LTA at diagnosis is associated with a poor prognosis, as both the risk for developing a new complication or the need for hospitalization were higher in the LTA-group. Presence of an increased AP at diagnosis has the highest predictive value.

Disclosure of Interest: None declared

P0936 NORMALIZED HS-CRP AND EARLY MUCOSAL HEALING AFTER INDUCTION CAN PREDICT SUSTAINED RESPONSE IN PATIENTS WITH CROHN'S DISEASE AFTER ONE YEAR INFLIXIMAB THERAPY

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Introduction: High sensitive C-reactive protein (hs-CRP) and early mucosal healing are thought to be usefulin monitoring disease activity during infliximab therapy, but how to combine these two index to be a more useful tool to predict sustained response remains unclear. We aimed to investigate the predict value of hs-CRP combined with early mucosal healing in patients undergoing infliximab therapy.

Aims & Methods: 76 patients were retrospectively enrolled after initiating infliximab therapy in our center. All patients responded to infliximab after induction had been scheduled for every 8 weeks shooting. Hs-CRP was tested at 14wks after induction. Normalized hs-CRP was defined as hs-CRP = 0-3mg/L. Endoscopic examinations were carried out at 14wks and 52wks. Mucosal healing was defined as no ulcer or only scar.

Results: Hs-CRP was normalized in 57%(44/76) of all patients. Patients with normalized hs-CRP had higher mucosal healing rate and lower loss response rate than the other group at 52wks (53%vs37.50%, $P = 0.04$; 15%vs40%, $P = 0.02$). 55% (42/76) of all patients reached mucosal healing at 14 wks. Patients with early mucosal healing also had higher mucosal healing rates and lower loss of response rate at 52wks (64%vs17%, $P < 0.01$; 17%vs42%, $P = 0.04$). Normalized hs-CRP combined with early mucosal healing had significant value in predicting sustained response and mucosal healing at 52wks. 70% (21/30)patients with normalized hs-CRP and early mucosal healing reached mucosal healing and 93% (28/30) of them maintained a sustained response to infliximab at 52wks.

Conclusion: Normalized hs-CRP and early mucosal healing after induction can effectively predict mucosal healing andsustained response in patients undergoing infliximab therapy.

Disclosure of Interest: None declared

P0937 POST-INDUCTION SERUM INFLIXIMAB TROUGH LEVEL AND ANTIBODYARE ASSOCIATED WITH ONE YEAR OUTCOME AFTER INITIATING THERAPY IN CROHN'S DISEASE

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Introduction: Serum infliximab trough level(S-IFX) and antibody were documented to correlate with sustained infliximab response. Aim of this study was to identify relationship between trough levels, antibodies and clinical outcome in a cohort on maintenance infliximab therapy.

Aims & Methods: 64 patients were retrospectively enrolled. All received a scheduled maintenance therapy after response to infliximab induction. S-IFX and antibodies were tested in at 14 weeks after initiating treatment. Rate of loss response and endoscopic activity were evaluated at 52weeks.

Results: At week14, S-IFX was 5.28 ± 7.24ug/ml and 23%(15/64) of all patients developed antibodies. S-IFX was significantly lower in patients with antibody (2.91 ± 5.40ug/ml vs 6.00 ± 7.61ug/ml, $P = 0.02$). During 52 weeks follow up, 28% (18/64) patients lost of response to infliximab. The patients who lost of response had lower S-IFX than patients had sustained response (2.16 ± 3.05ug/ml vs 6.50 ± 8.02ug/ml, $P = 0.03$) while no significant difference was found on drug antibodies (38% vs 22%, $X = 2.50$, $P = 0.11$). At week 52, 62 patients had undergone ileo-colonoscopy and 30 patients reached mucosal healing. Mucosal healing group had relatively higher S-IFX than who did not reach mucosal healing (8.11 ± 9.33ug/ml vs 2.56 ± 2.90ug/ml, $P < 0.01$) but no statistical difference for antibodies between these two groups (17% vs 28%, $P = 0.28$). S-IFX had a predictive value on sustained response and mucosal healing in 52 weeks follow up. When S-IFX > 2ug/ml, the sensitivity for predicting sustained response and mucosal healing were76% and 83%, the specificity were 72% and 56% (AUC = 0.76, $P < 0.01$;AUC = 0.78, $P < 0.01$). Baseline albumin level and BMI were 41.44 ± 6.95g/l and 21.45 ± 3.56 in sustained remission patients. S-IFX was correlated to albumin level and BMI (r = -0.79, $P < 0.01$;r = -0.46, $P < 0.01$).

Conclusion: Post-induction serum IFX trough level could predict sustained response and mucosal healing in CD patients undergoing IFX treatment. Nutritional status before treatment was correlated to serum IFX trough level.

Disclosure of Interest: None declared

P0939 EARLY POST-OPERATIVE ENDOSCOPIC EVALUATION AFTER ILEOCECAL RESECTION IN CROHN'S DISEASE REDUCES CLINICAL RECURRENCE

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Introduction: In Crohn's disease, the recurrence rate after ileocecal resection is high, around 20-25% per year without therapy[1,2], and is best predicted by endoscopy rather than clinical indeces[1]. Since 2010, the *European Crohn's and Colitis Organization guidelines* recommends performing ileocolonoscopy 6 to 12 months after surgery to predict clinical behavior[3], which has therapeutic implications.

Aims & Methods: The aim of this study is to evaluate the impact of this endoscopic evaluation on early post-operative clinical recurrence.

This is a retrospective analysis of a cohort of Crohn's disease patients submitted to ileocecal resection at our Hospital with updated follow-up until 2014. Patients were distributed into two groups, whether they had or not performed ileocolononoscopy within 12 months after surgery, group P or NP respectively. We evaluated different levels of reccurence: clinical, defined as symptomatic disease needing corticotherapy or an escalating immunossupresive regimen; endoscopic, defined by Rutgeert's endoscopic score; and surgical, defined as necessity of surgical reintervention.

Results: We included 66 patients, of whom 34 (51.5%) women, with an average age at diagnosis of 34.5 ± 13.6 years, average age at surgery of 37.1 ± 13.7 years, median follow-up time after surgery of 152 ± 120 months; 35 (53%) with penetrating disease and 10 (15.2%) with perianal disease. Previous to surgery, 9 (13.6%) patients were on immunosupressive therapy, 4 (6%) of them on combined therapy. All patients have undergone post-operative prophylaxis with messalazine, in 16 (24.2%) of them azathioprine was added and in 4 (6%) biologic therapy was started. There were 27 (41%) patients on group P and 39 (59.1%) on group NP. We have found endoscopic reccurence in 46 (69%), clinical reccurence in 35 (53%) and surgical reccurence in 8(12.1%). Patients on group P had less clinical reccurence than group NP (66.6% vs. 33%; $p = 0.01$).

Conclusion: Early endoscopic evaluation after ileocecal resection in Crohn's disease has a positive impact on clinical evaluation as this group of patients shows less clinical reccurence than patients that are not systematically submitted to this evaluation and this is in accordance to previous published data[4].

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Disclosure of Interest: None declared

P0940 COMPARISON MR ENTEROGRAPHY AND COLONOSCOPY IN DETECTING FINDINGS OF INFLAMMATORY BOWEL DISEASE IN CHILDREN

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Introduction: Diagnostic process for Inflammatory bowel disease (IBD) based on magnetic resonance of small bowel and endoscopy. Magnetic resonance is considered as the first-line imaging modality because of high efficacy for detecting IBD findings and lack of ionizing radiation. Before colonoscopy bowel cleansing is necessary. It is often problematic and bad tolerated by young patients. Specially in children the procedure of general anesthesia is needed.

Aims & Methods: The aim of this study was to compare detecting findings of disease by colonoscopy with MR-enterography proceeded for small bowel assessment. We tried to asses utility of MR-enterography in detecting lesions in the colon.

A retrospective assessment of 59 children with suspected or diagnosed IBD was done. All of the patients underwent colonoscopy and MR-enterography for small bowel disease localization within no longer than 23 weeks (only 1 patient had gap between studies 41 weeks). Localization of disease was described in 7 segments of the end part of small and large bowel: terminal ileum, cecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum. During MR procedure was assessed wall thickening bowel wall enhancement and presence lesions after DWI.

Results: The most common localization of findings of disease viewed by colonoscopy was ileum (88%). In rectum disease was in 56% of patients. The sensitivity and specificity for detecting lesions in the rectum bowel wall enhancement was in 42.3% and 96.7%, DWI 32% and 93.6%, wall thickening 26.9% and 96.7%; sigmoid colon 45.5% and 97.1%, DWI 40.9% and 88.6%, wall thickening 36.4% and 97.1%; descending colon 41.2% and 97.5%, DWI 29.4% and 95%, wall thickening 41.2% and 97.5%; transverse colon 50% and 100%; 43.8% and 100% for DWI and 43.8% and 100% for wall thickening; ascending colon 53.3% and 95.4%; DWI 46.7% and 95.4%, wall thickening 53.3% and 100%; cecum 57.1% and 93.1%, 50% and 93.2% for DWI, 50% and 97.7% for wall thickening; terminal ileum 53.9% and 79.6%, 61.5% and 77.3%, 61.5% and 77.3% respectively.

Conclusion: MRI characterized very high specificity in detecting disease lesion in colon. Unfortunately sensitivity wasn't enough high. Lack of IBD findings in MR does not exclude presence of disease. The sensitivity was better in higher segments of the bowel, what can suggest that additional rectal contrast may be obligatory for better detection of lesions in lower part of the colon.

Disclosure of Interest: None declared

P0941 ROUTINE COLONOSOPIC BIOPSIES – SHOULD PRACTICE CHANGE?

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Introduction: American society for gastrointestinal endoscopy[1] (ASGE) and Joint advisory group on Gastointestinal endoscopy (JAG) suggest routine colonic biopsies as quality indicator and auditing our practice to identify microscopic colitis. UK studies suggest low incidence of microscopic colitis[2] and additional costs making one wonder whether we should be doing this routinely and/or auditing our practice?

Aims & Methods: We perfomed a retrospective database search of colonoscopy requests from July-December 2013 with keywords diarrhoea, loose stools & change in bowel habits to audit our practice as a quality indicator as per ASGE and JAG. Demographics, endoscopic findings & histology were collected from electronic records.

Results: From the 1124 requests, 407 colonoscopies were performed with the indication for diarrhoea, loose stools or change in bowel habit. Colonic biopsies were taken in 325 cases (79.9%) and right sided biopsies were specifically taken in 279 cases (68.6%). 60% of our colonoscopies were reported as macroscopically normal (241/407) and only 5.2% (17/325 colonoscopy biopsies) cases of microscopic colitis were picked up on routine biopsies. Among diagnosed with microscopic colitis, the mean age was 60.1 years (range 38-80, 76% > 50 years) with a female to male ratio of 14:3. Micropsopic colitis was diagnosed at an average biopsy cost of £1545 (total £26,266 spent on biopsies to identify 17 patients, not factoring colonoscopy tariffs or endoscopist/histopathologist time).

Conclusion: Our rate of routine colonoscopic biopsies in patients with diarrhoea[3] and the pickup rate of microscopic colitis[4] is similar to previous reports. We conclude that one case of microscopic colitis (5.2%) is diagnosed for every 20 colonoscopy perfomed for diarrhoea at a biopsy cost of £1545; age/sex may help in increasing pickup rate and to decrease routine biopsy rates.

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Disclosure of Interest: None declared

P0942 COMPARISON OF COMMERCIALLY AVAILABLE ASSAYS FOR INFLIXIMAB CONCENTRATIONS AND ANTIBODIES TO INFLIXIMAB WITH ASSAYS DEVELOPED AT JANSSEN AND USED IN CLINICAL STUDIES OF REMICADE® (INFLIXIMAB) IN IBD PATIENTS

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Introduction: Infliximab(IFX) concentrations and antibodies to IFX(ATI) titers can be informative in assessing IBD response.
Aims & Methods: In collaboration with KU Leuven(Belgium), Sanquin(The Netherlands), Dynacare(Canada) and LabCorp(USA), the accuracy and reliability of commercially available IFX and ATI assays were compared to assays used by Janssen for Remicade®(IFX) IBD studies. Test samples were prepared by Janssen, blinded and frozen at -70°C and shipped to the labs; blinded analysis was also performed at Janssen. IFX concentration (49 samples) and ATI titer (32 samples) were assessed. KU Leuven* and Dynacare utilized enzyme-linked immunosorbent assay (ELISA) to measure IFX and ATI. Sanquin used ELISA to measure IFX and a radioimmunoassay to measure ATI.LabCorp used electrochemiluminescence immunoassay (ECLIA) to measure IFX and ATI. Janssen used ELISA for IFX quantification, and ELISA (''old'') and ECLIA (''new'') for ATI assessments.
Results: IFX Assays: Specificity:All assays were specific as they detected IFX alone, but not 5μg/mL of adalimumab, certolizumab pegol, golimumab or siltuximab. Selectivity: TNFα (0.5 – 50 ng/mL) did not interfere with IFX detection in any assays, whereas the presence of ATI titers > 10 interfered with IFX assessment in all assays. Accuracy: Accuracy was confirmed by 3 independent measurements of IFX (0.125-20μg/mL) spiked sera from untreated IBD patients and with IFX measured in sera from IFX-treated IBD patients. Precision: All IFX assays were precise as determined by inter-occasion reproducibility (2wks between assays of IFX-spiked IBD sera; Dynacare assessed the samples the same day). Pearson R values describing the correlation of Janssen IFX results to IFX results from Sanquin, Dynacare, KU Leuven, and LabCorp were 0.936, 0.945, 0.968 and 0.972, respectively.
ATI assays: Specificity: Assays from all labs and Janssen were specific in detecting anti-IFX antibodies; results were not affected by high titers of antibodies against other human monoclonal antibody drugs (ustekinumab and golimumab). Selectivity: The Sanquin, LabCorp and new Janssen methods were drug tolerant (IFX > 10ug/mL); ATI results from Dynacare and KU Leuven were affected by IFX concentrations at 2ug/mL or higher. Concentrations of free or bound TNFα (< 5ng/mL) did not interfere with ATI detection; but a high (supraphysiologic) TNFα concentration (50ng/mL) resulted in false positive results in all assays except Sanquin's. Precision: All ATI assays were reproducible (2wks between assays of human sera containing ATI; Dynacare assessed samples the same day).
Conclusion: Results from KU Leuven, Sanquin, Dynacare and LabCorp were similar and significantly correlated to the results of Janssen assays. These results may aid in interpretation of data from commercial assays and assays used in IBD clinical studies of Remicade®(IFX).
*assay distributed by apDia and R-biopharm
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P0943 PERFORMANCE OF FECAL LACTOFERRIN, CALPROTECTIN, PMN-ELASTASIS AND CRP AND WBC COMPARED TO HISTOLOGICALLY DEFINED HEALING IN ULCERATIVE COLITIS

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Introduction: Microscopic, histological healing may be a better predictor than the macroscopic appearance or clinical criteria for course of disease in ulcerative colitis (UC). Histological assessment revealed that indicators of acute mucosal inflammation, including crypt abscesses, mucin depletion or an acute inflammatory cell infiltrate were associated with a 2-3fold increase in the risk of UC relapse during 12 months' follow-up. Fecal inflammation biomarkers are increasingly popular because they are noninvasive and individual patients can serve as their own control. However an evaluation of a panel of biomarkers in their performance compared to a histological assessment in UC is lacking.
Aims & Methods: Three sigmoidal and rectal biopsies each were taken randomly or at the site of macroscopic active inflammation for histopathological work-up. Riley score (each category 0-3pts) was performed for signs of acute inflammation including **acute inflammatory cell infiltrate**, **crypt abscesses**, **mucin depletion** and **breaches in the surface epithelium**. The 4 categories were combined as **acute HistoScore** with a score = 0 indicating histologically defined healing and a score > 0 indicating acute inflammation**.** In addition, **chronic inflammatory cell infiltrate** and **architectural irregularities** were added and combined as HistoSumScore. The 3 fecal biomarker Lactoferrin (LF; > 7.25μg/g), Calprotectin (Cal; > 50μg/g), PMN-elastasis (PMN-e; > 0.062μg/g) as well as CRP (≥0.5mg/dl) and WBC (> 8500/μl) were correlated to the HistoSumScore and median (inactive/active), sensitivity, specificity, PPV, NPV and diagnostic accuracy were calculated based on the acute HistoScore.
Results: In 150 UC patients (79 female; age 18-75 years) 238 endoscopic procedures (75 colonoscopies; 163 sigmoidoscopies) were performed. Correlation (Spearman) with the **complete HistoSumScore** was LF cc = .408; p < 0.0001; PMN-e cc = .447; p < 0.0001; CAL cc = .458; p < 0.0001; CRP cc = .307; p < 0.0001; WBC cc = .203; p = 0.002. Comparison to the **acute HistoScore** showed the following results: **LF**: median (inactive/active): 3.9/36.5μg/g; sensitivity 71.2%; specificity 64.7%; PPV 71.2%; NPV 64.7%; diagostic accuracy: 68%; optimized cut-off: 10.2μg/g; **CAL**: median: 10.7/25.7μg/g; sens 27.2%; spec 96.1%; PPV 89.5%; NPV 51.9% diag acc: 58%; opt. cut-off: 16.6μg/g; **PMN-e**: median: 0.02/0.05; sens 38.2%; spec 84.0%; PPV 72.4%; NPV 55.3%; diag acc: 60%; opt. cut-off: 0.033μg/g; **CRP**: median: 0.1/0.4mg/dl; sens 43.3%; spec 85.3%; PPV 78.6%; NPV 54.7%; diag acc: 62%; opt. cut-off: 0.25mg/dl; **WBC**: median: 6500/6750; sens 23.2%; spec 90.3%; ppv 75.0%; npv 48.4%; diag acc: 53%; opt. cut-off: 6620.
Conclusion: The fecal biomarker show sufficient correlation and diagnostic accuracy outperforming CRP and WBC when compared to histology. Only fecal Lactoferrin shows median above the predefined cut-off in histologically active inflammation.
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P0944 ENDOSCOPIC SURVEILLANCE OF COLITIS IN A DISTRICT GENERAL HOSPITAL

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Introduction: The British Society of Gastroenterology (BSG) recommends 2-4 biopsies from every 10cm of the colon in patients undergoing colonoscopy for surveillance in patients with inflammatory bowel disease (IBD) (1). The timing of follow-up surveillance colonoscopies should be based on the risk group determined in part by macroscopic findings.
Aims & Methods: 1. To establish compliance with BSG Guidelines for IBD endoscopic surveillance in a district general hospital. 2. To conduct a questionnaire regarding IBD surveillance to direct an improvement in the service.
All endoscopy reports between 1999 and January 2015 coded as ''IBD surveillance'' were reviewed. The total number of biopsies taken in each procedure and the number of individual sites biopsied throughout the colon was recorded. This was compared to a target of a minimum of 2 biopsies at 6 sites (total of 12 biopsies). The number of colonoscopies which met this target was recorded.
Secondly, the endoscopy report was reviewed. The patients were separated into low, intermediate and high-risk groups according to the macroscopic findings. The time until their next surveillance endoscopy was recorded and compared to the BSG guidelines for each risk group.
Once the results of the above analysis were established, a questionnaire was designed to explore the reasons behind any failings in the service by asking endoscopists a number of questions.
Results: A total of 278 colonoscopies involving 108 patients were reviewed. The mean total number of biopsies taken was 11.05, and the mean number of sites biopsied was 3.28. Out of the colonoscopies reviewed, 46 out of 278 (17%), met the BSG target for biopsies.
Of the 278 colonoscopies, 55 (20%) were higher risk, 92 (33%) intermediate and 130 (47%) were lower risk. One patient had unknown category. For each colonoscopy, the number of years until the next screening colonoscopy was calculated. This was compared to the BSG target for follow up. 79% met the target year according to risk group. Of note, if the intended date for the next surveillance colonoscopy was after January 2015, the target was said to have been met.
A questionnaire was sent to 12 endoscopists and replies were received from 8. All that replied were aware of the guidelines and agreed with their importance. Time pressure was thought to play a role in failure to meet biopsy targets, with an average score of 2, where a score of 5 indicates that time pressure always plays a role.

There was also a unanimous agreement that a centralised computer database to ensure timely follow up would be beneficial. Other suggestions for service improvement included the use of pan-colonic dye spray, designated surveillance endoscopy lists and a printed version of the protocol on request cards.
Conclusion: Currently our hospital is not meeting the BSG target for IBD surveillance colonoscopies, with a failure to take adequate numbers of biopsies. The opinions of the endoscopists suggest that this is in part due to time pressure, and there could be a role for pan-colonic dye spray, which is not routinely used in our hospital presently.
The hospital is more successful in arranging appropriate follow up colonoscopies. However, there is room for improvement in the service. Feedback suggests that this could be carried out using a computerised database.

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Disclosure of Interest: None declared

P0945 QUALITY OF LIFE IN ULCERATIVE COLITIS IS ALREADY IMPAIRED BY MILD DISEASE ACTIVITY

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Introduction: The EuroQol (EQ)-5D-5L is a generic instrument measuring health-related quality of life that correlates with disease activity. We have previously described a high agreement between the simple clinical colitis activity index (SCCAI) self-administered by UC patients from home through an online tool with that administered in-clinic by the physician (1). Our aim was to measure which level of disease activity has an impact on QoL in patients with UC.
Aims & Methods: Patients were followed-up for 6 months. At month 3 and 6, they completed the SCCAI at home through a website(CRONICA tool), and thereafter (<48 hours later) the EQ-5D-5L at a visit in which SCCAI was also completed onsite by gastroenterologist, who was blinded to patient's score. EQ-5D-5L was analyzed as an index value according to the prespecified values for Spanish population with value 1 indicating the best health status and -0.652 the worst. SCCAI scores were analyzed as a continuous variable(from 0 to 19). Spearman's Rho correlation coefficients were used to assess the correlation between EQ5D-5L and SCCAI measured by patients online and by physician in clinic.
Results: 199 patients (mean age: 39 years [SD 11]; min: 18; max: 67, 55.8% women), contributed with 330 pairs of online completed SCCAI - EQ-5D-5L questionnaires and with 337 pairs of physician SCCAI - EQ-5D-5L questionnaires. The correlation between patients online completed self-administered SCCAI with EQ-5D-5L was moderate (Spearman's Rho correlation coefficient: 0.49 [$p < 0.001$]) and similar to that between the SCCAI assessed by the physician in-clinic and the EQ-5D-5L (Spearman's Rho: 0.53 [$p < 0.001$]).The correlations between the EQ-5D-5L scores versus the SCCAI scores were all consistent, with a lower SCCAI score corresponding to a higher EQ 5D-5L index, and approximately linear, both when comparing patient online completed SCCAI and SCCAI assessed by the physician in-clinic. (Table 1) An increase on EQ 5D-5L was already observed with a SCCAI of 2, which commonly is considered as remission.Relationship between the EQ-5D-5L and the SCCAI score measured by patients online or by physicians in the clinic.

EQ 5D-5L total Patient online SCCAI	Mean	SD	Physician in- clinic SCCAI	Mean	SD
0	0.96	0.11	0	0.97	0.05
1	0.95	0.08	1	0.93	0.13
2	0.90	0.09	2	0.88	0.13
3	0.89	0.13	3	0.87	0.14
4	0.87	0.12	4	0.84	0.13
5	0.83	0.15	5	0.83	0.12
6	0.80	0.16	6	0.75	0.17
7	0.85	0.12	7	0.79	0.15
8	0.84	0.23	8	0.56	0.26
9	0.71	0.02	9	0.91	0.01
Total	0.90	0.13	Total	0.90	0.13

Conclusion: In the CRONICA-UC study, QoL measured by the EQ-5D-5L questionnaire is affected proportionally with disease activity. Mild symptoms that are categorized as remission have an impact in QoL. This observation calls for a complete control of all symptoms in patients with UC as a requisite to obtain maximal improvement in QoL.

Reference

1. Marín-Jimenez et al. P261 *ECCO* 2015.

Disclosure of Interest: None declared

P0946 RETROSPECTIVE EVALUATION OF CLINICAL PRESENTATION OF COLLAGENOUS COLITIS IN JAPAN

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Introduction: Collagenous colitis (CC) often results from the use of proton pump inhibitors (PPIs) in Japan. Non-steroid anti-inflammatory drugs (NSAIDs) or selective serotonin reuptake inhibitors (SSRIs) have also been reported as trigger drugs, but less frequently. Recently, sporadic cases of CC without chronic diarrhea, that were only suspected from endoscopic findings and confirmed by histopathological examination, have been reported.
Aims & Methods: We examined the medication history, endoscopic findings, and clinical features of 93 patients who had been diagnosed with CC at our hospital and joint research institutions.
Results: The mean age of patients was 70.2 years, of which 30 were male and 63 female. Seventy-three patients (78.5%) had a history of PPI treatment. For the remaining 20 patients (21.5%) not administered PPIs, trigger drugs were NSAID in 11, SSRI in 2, and ticlopidine in 1, although a relation of CC to drugs was unknown in 6 patients. Longitudinal ulcers that were characteristic of lansoprazole (LPZ)-induced CC were observed in 20 (29.0%) of 69 patients diagnosed with LPZ-induced CC. An NSAID was concomitantly used in 11 out of these 20 patients. Four patients with longitudinal ulcers had no history of LPZ, including 2 and 1 patient with CC triggered by an NSAID and SSRI, respectively (the trigger drug was unknown in 1 patient). Six patients had no diarrheal symptoms, including 2 with severe abdominal pain and 4 with no symptom of CC. All these 6 patients had longitudinal ulcers detected on endoscopy and were diagnosed with CC on histopathological examination of biopsy specimen.
Conclusion: PPIs are recognized as being the most common trigger drugs for development of CC in the vast majority of patients in Japan. However, this study revealed other drugs to be also involved in about 20% cases. Some patients had CC without chronic diarrhea. In these cases, CC was suspected only from longitudinal ulcers found on endoscopy, which were later confirmed by histopathological examination. Our study suggests that CC is liable to be overlooked

Abstract number: P0947
Table 1: Diagnostic accuracy of POCUS compared to Endoscopy, radiologist performed Ultrasound (US), Computed Tomography (CT), and Magnetic Resonance (MR)

	Endoscopy	US	CT	MR
Sensitivity %(CI %)	89.66 (71.50 -97.29)	96.15 (78.42-99.80)	90.91 (57.12-99.52)	88.89 (51.75- 99.72)
Specificity %(CI %)	81.48 (61.25-92.97)	100.00 (59.78-100.00)	100.00 (31.00-100.00)	100.00 (39.76-100.00)
PPV %(CI %)	83.87 (65.53-93.91)	100.00 (83.42-100.00)	100.00 (65.55-100.00)	100.00 (63.06-100.00)
NPV %(CI %)	88.00 (67.66-96.85)	88.89 (50.67-99.42)	75.00 (21.94-98.68)	80.00 (28.36-99.49)

in patients who have only minor endoscopic findings or those not investigated by endoscopic examination.
Our study highlights the need for reviewing the clinical protocols and diagnostic criteria for CC, as asymptomatic CC or cases with only acute abdominal pain and no chronic diarrhea, may be overlooked if the existing diagnostic criteria for CC are followed
Disclosure of Interest: None declared

P0947 USE OF POINT OF CARE TRANSABDOMINAL ULTRASOUND TO MONITOR INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is characterized by periods of disease activity not always reflected by clinical symptoms, interposed with quiescence. Early and appropriate medical intervention aimed to control disease can reduce disease progression and mitigate complications that may result in surgery and hospitalization. Ultrasound (US) is a favorable monitoring strategy, as it is safe, accurate, non-invasive, repeatable and inexpensive. In North America, computed tomography (CT) and magnetic resonance (MR) are preferred imaging modalities to monitor IBD, with limited access to US. Gastroenterologists can accurately perform bedside ultrasound during routine clinic visits for monitoring disease activity and thus facilitate early medical intervention.
Aims & Methods: The aim of this single-centre, prospective study was to evaluate the accuracy of point of care ultrasound (POCUS) performed to detect disease activity in patients with established IBD, relative to gold standard, ileocolonoscopy as well as cross-sectional imaging modalities MR/ MR Enterography, US and CT/CTE. A trained gastroenterologist performed POCUS followed by standard of care monitoring with any of the above modalities, within 3 months. Disease activity was based on presence of increased bowel wall thickness, presence of mesenteric inflammatory fat and lymph nodes, and/or blood flow as seen by color Doppler. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with 95% confidence intervals (CI) were calculated for each comparator modality.
Results: A total of 117 patients were included with 56 (48%) endoscopies, 14 (12%) CT, 34 (29%) US, and 13 (11%) MR completed within 3 months of POCUS examination. The average age was 42.7 years, 72 were female and 45 male. The accuracy of POCUS in detecting disease activity was high, with minimum sensitivity, specificity, PPV and NPV of 88.89%, 81.48%, 83.87%, and 75.0% respectively, found in all comparisons (Table 1).
Conclusion: Gastroenterologists can accurately perform bedside US during clinic to detect inflammatory activity in established IBD patients. POCUS may be an effective tool to guide early, goal directed management for these patients.
Disclosure of Interest: None declared

P0948 EARLY AND LATE-ONSET CROHN'S DISEASE: DIFFERENT PHENOTYPE AND COURSE, AN ITALIAN COHORT STUDY

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Introduction: Disease heterogeneity, according to age of onset, may be observed in Crohn's disease (CD). The prevalence of CD is increasing worldwide. Although the peak incidence is between the second and fourth decade of life, we are observing a significant growth in the number of patients presenting at diagnosis more than 60 or less than 17 years. These ages represent the most critical ones when evaluating the risks and benefits of treatment choices and little is known about their disease history.
Aims & Methods: The aim of the present study was to compare CD phenotype at diagnosis and disease course in diagnosed patients ≤ 17 years (early) and ≥ 60 years (late). Cases included all CD patients diagnosed ≤ 17 years and ≥ 60 years with follow-up > 2 years, recorded in the registry of two IBD referral Centres in Rome. Data reported at diagnosis included gender, smoking habits, IBD family history, IBD location and CD behavior, according to the Montreal classification, extraintestinal manifestations and medical/surgical treatments performed during the follow-up period. Statistical analysis: Chi-squared test, Kaplan-Meier survival method.
Results: Of the entire cohort of 2321 CD, 160 patients met criteria for the inclusion in the study: 92 in the early-onset (EO) and 68 in the late-onset (LO) group. The median follow-up was 10 years (range 2- 34 years). A family history of IBD occurred more frequently in EO compared to LO (26% vs 4%; $p < 0.0007$). Ileocolonic location, upper gastrointestinal involvement and perianal disease occurred more frequently in EO compared to LO (56% vs 21% $p < 0.0001$; 17% vs 3% $p < 0.009$; 38% vs 19% $p < 0.01$ respectively). Disease behavior at diagnosis was inflammatory in approximately 60% in both group, however progression to complicated disease during follow-up occurred more frequently in EO (40% vs 10% $p < 0.002$). Compared to LO, EO had increased need for steroids and anti-tumor necrosis factor (TNF) alpha during the first two years from diagnosis (41% vs 6%, $p < 0.003$ and 15% vs 4%, $p < 0.05$ respectively). The cumulative probability of receiving steroids, immunosuppressant and anti-TNF alpha within 10 years from diagnosis in EO and LO was 81% and 58% ($p = 0.004$), 58% and 35% ($p = 0.04$), 36% and 16% ($p = 0.01$) respectively. There was no significant difference between the two groups regarding the cumulative probability of surgery within 10 years.
Conclusion: At our knowledge, this is the first Italian study on clinical presentation and course of CD according to age of onset. Our data are consistent with the literature being ileocolonic location and greater proportion of complicated behavior more common in EO CD. The course of disease in LO CD is more stable and less aggressive than EO CD and should be taken into account when discussing therapeutic choices.
Disclosure of Interest: None declared

P0949 DIAGNOSTIC DELAY IN IBD: A COMPARISON IN THE LAST THIRTY YEARS, AN ITALIAN MULTICENTRIC STUDY

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Introduction: The diagnosis of inflammatory bowel disease (IBD) continues to present difficulties due to unspecific symptoms and limited test accuracies. Therefore IBD patients are still under-diagnosed or diagnosed with serious delay. Diagnostic delay, particularly in Crohn's disease (CD), seems to have an important clinical impact
Aims & Methods: The aim of our study was to examine whether diagnostic delay in IBD has changed over the last thirty-three years and to investigate its correlation with CD phenotype and Ulcerative Colitis (UC) location at diagnosis. Cases included all IBD patients recorded in the registry of four IBD referral Centres in Italy. Diagnostic delay was calculated from the onset of the symptoms indicative of CD or UC to the definitive diagnosis. Data reported included date of birth, gender, IBD location and CD behavior at diagnosis, according to the Montreal classification.
Results: Of 3393 IBD patients, 2499 (74%) had a diagnostic delay ≥ 1 month, 1046 (31%) ≥ 12 month. Median diagnostic delay was 3 months, interquartile range (IQR) 0 to 13 (7 months in CD, IQR 1 to 25 and 2 months in UC, IQR 0 to 7). Mean diagnostic delay was 19, standard deviation (SD) 45, (significantly higher in CD than UC, 29 vs 11 months, SD 54 vs 34, $p < 0.0005$). In CD, mean diagnostic delay was higher in patients with penetrating/stricturing behavior at diagnosis ($n = 870$) compared to patients with inflammatory behavior at diagnosis ($n = 667$), (32 vs 23 months, SD 49 vs 57, $p < 0.0005$). 242 patients were diagnosed between 1952-1979 (historical cohort), while 3151 were diagnosed between 1980 and 2013 (modern cohort). Mean diagnostic delay was significantly higher in the historical cohort in comparison to the modern cohort (31 vs 18 months, SD 58 vs 44, $p < 0.0005$). IBD patients belonging to the modern cohort were stratified according to the time of diagnosis into three subgroups diagnosis (1980-89, 1990-99, 2000-13). There was no significant difference in the mean diagnostic delay between the three periods (18, 17 and 19 months, SD 41,37 and 50 respectively). Mean diagnostic delay in CD of modern cohort is significantly higher in the subgroup of patients ≥ 40 years at diagnosis(A3) in comparison to patients ≤ 40 years, 39(SD 74) vs 20(SD 33) months, $p < 0.001$. No significant difference was found in the mean diagnostic delay according to gender or disease location at diagnosis. No significant difference was found in the mean diagnostic delay according to gender or disease location at diagnosis.
Conclusion: Diagnostic delay in IBD was significantly decreased in recent years (1980-2013) in comparison to the past (1952-1979), however it did not change over the last thirty-three years, despite increasing the diagnostic tools. Compared with UC, diagnostic delay is higher in CD especially in penetrating/stricturing phenotype at diagnosis or age at diagnosis higher than 40 years.
Disclosure of Interest: None declared

P0950 IN-VIVO AXIAL-STRAIN SONOELASTOGRAPHY HELPS DISTINGUISH ACUTELY-INFLAMED FROM FIBROTIC TERMINAL ILEUM STRICTURES IN PATIENTS WITH CROHN'S DISEASE

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Introduction: A number of radiological examinations are available to evaluate the terminal ileum, all with different accuracy in detecting ileal stenosis. A critical issue, however, is the possibility of differentiating inflammatory from fibrotic strictures in patients affected by terminal ileum Crohn's Disease.
Aims & Methods: To ascertain whether RTS could *in-vivo* differentiate fibrotic from inflammatory terminal ileum strictures in patients with Crohn's disease, using magnetic resonance enterography (MRE) as a reference standard, 13 patients (10m,3f; median[interquartile interval]age = 40[33-48]years; median C-reactive protein (CRP) = 0.9[0-1.8]mg/dl; median disease duration = 46[29-205]months; median Harvey-Bradshaw Index (HSI) = 3[2.75-5.25]) affected by terminal ileum Crohn's disease were prospectively included. Patients underwent MRE, evaluating T2 hyperintensity, perivisceritis, transmural contrast uptake. RTS was performed on terminal ileum. Short-axis scans were performed, each cross-section was ideally subdivided into eight circular sectors. Colour map provided by RTS was translated into a semiquantitative scale (1 = red; 2 = green; 3 = blue).

Results: At MRE, T2 hyperintensity was seen in 7 patients, perivisceritis in 7, contrast uptake in 7. Accordingly, 7 patients were classified as having an inflammatory stricture and 6 a fibrotic one. Total median RTS score was significantly lower in patients with inflammatory stricture (16[14-16]) than that (19[18-20.75]) in patients with fibrosis ($P = 0.002$). The same result was found when the four most superficial quadrants of the loop were considered (7[6-7]vs.10[9.25-10]; $P = 0.003$). No significant correlation was seen between RTS-HSI ($r = -0.153$; $P = 0.635$), RTS-CRP ($r = 0.362$; $P = 0.247$), RTS-disease duration ($r = 0.224$; $P = 0.483$).
Conclusion: RTS is a promising imaging modality to differentiate *in-vivo* inflammatory from fibrotic terminal ileum strictures in patients with Crohn's disease.
Disclosure of Interest: None declared

P0951 COULD HISTOLOGICAL LESIONS PREDICT REACTIVATION IN ULCERATIVE COLITIS PATIENTS WITH MUCOSAL HEALING?

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Introduction: Mucosal healing (MH) is a potential target in the treatment of patients with ulcerative colitis (UC), reducing the need for surgery and the risk of colorectal cancer. MH lowers the risk of disease reactivation, but some patients relapse in spite of the presence of MH. It is reasonable to think that the microscopic disease activity beyond MH could explain these cases.
Aims & Methods: Our aim is to assess how many patients with MH have a microscopic disease activity and what kind of lesions are associated with mid-term n (after 6 and 12 months).
Our aim is to assess how many patients with MH have a microscopic disease activity and what kind of lesions are associated with mid-term reactivation (after 6 and 12 months).
We retrospectively enrolled UC patients showing MH, expressed as Mayo 0 at colonoscopy, and undergone multiple biopsies during the same exam. We reviewed the corresponding histological lesions evaluating the presence of the typical histological lesions associated with UC, such as acute or chronic inflammatory infiltrate, basal plasmacytosis, basal lymphoid aggregates, stromal changes, lamina propria eosinophils, crypt branching, crypt distortion, crypt atrophy/depletion, cryptitis, crypt abscesses, surface irregularity, mucin depletion, erosions and Paneth cell metaplasia. We evaluated the number of clinical reactivation 6 and 12 months after baseline colonoscopy.
Results: Among 63 enrolled patients, only 2 showed no histological lesions. The most common lesion was chronic inflammatory infiltrate (81%) followed by basal lymphoid aggregates (60%), acute inflammatory infiltrate (46%) and crypt distortion (33%). After 6 and 12 months, 14% and 22% of patients relapsed, respectively. The most prevalent lesion in patients relapsing after 6 months was chronic inflammatory infiltrate (100% of relapsers vs 76% of non-relapser), followed by acute inflammatory infiltrate (63% vs 40%), basal lymphoid aggregates (63% vs 62%), basal plasmacytosis (50% vs 12%, $p < 0.05$) and lamina propria eosinophils (50% vs 10%, $p < 0.05$). After 12 months, chronic inflammatory infiltrate was found in 90% of relapsers vs 83% of non-relapsers, basal lymphoid aggregates in 70% vs 53% and acute inflammatory infiltrate in 50% vs 44%, basal plasmacytosis (50% vs 8%, $p < 0.05$) and lamina propria eosinophils (40% vs 11%, $p < 0.05$), respectively.
Conclusion: A microscopic disease activity persists in the major part of patients with MH. Basal plasmacytosis and lamina propria eosinophils are more frequent in patients with disease reactivation after 6 and 12 months.
Disclosure of Interest: None declared

P0952 INFLIXIMAB LEVEL AND ANTI-DRUG ANTIBODY IN INFLAMMATORY BOWEL DISEASE PATIENTS LOSING RESPONSE: ASSAY AFTER OPTIMIZATION AND OUTCOME AT ONE YEAR

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Introduction: Therapeutic drug monitoring is claimed to be an important tool in tailoring infliximab therapy to the clinical status of inflammatory bowel disease (IBD) patients. However, cut-off values for infliximab trough levels (TL) and anti-drug antibodies (ATI) need to be established for each assay method and validated in the clinical setting.
Aims & Methods: Aim of our study was to evaluate infliximab TL and ATI in patients losing response and to identify cut-off values after drug optimization, which could be significantly related to clinical outcomes at one year. We studied 71 IBD patients, 42 affected by Crohn's disease (CD) and 29 by ulcerative colitis (UC). They were on maintenance treatment with infliximab after initial response to the induction course and had experienced a loss of response defined as worsening of clinical symptoms and rise in CRP or evidence of endoscopic disease activity. We collected blood for assay of trough levels and antibodies to infliximab by ELISA method (LisaTracker-Duo Infliximab, Theradiag, Marne-la-Vallée, France). According to manufacturer instructions, levels of detection were 0.1 μg/ml for TL and 10 ng/ml for ATI. We recorded clinical status and CRP levels after drug optimization (dose increase and/or interval shortening), after six months and after one year. All TL and ATI determinations were performed in a single laboratory session and the clinicians were blinded to the results, which did not influence the clinical decisions.
Results: Of the 71 IBD patients, 15 (21%) were on concomitant treatment with azathioprine/6MP and 55 (77%) were studied after infliximab optimization. Clinical follow-up at 12 months was available for 49 of them. ATI were detected in 26/71 patients (36%) while TL were undetectable in 13/71 (17%). ATI and TL were negatively correlated (Spearman's rho -0.53, $p = 0.0001$). By ROC analysis we found that achieving a TL > 4.05 μg/ml after optimization was predictive of clinical response after 12 months (AUC 0.648, sensitivity 60%, specificity 75%, $p = 0.05$). The same cut-off was predictive of normal CRP both after 6 months (AUC 0.652, sensitivity 59%, specificity 77%, $p = 0.05$) and after 12 months (AUC 0.677, sensitivity 59%, specificity 80%, $p = 0.02$). The presence of ATI levels > 11 ng/ml was predictive of high CRP at 6 months (AUC 0.653, sensitivity 48%, specificity 82%, $p = 0.029$).
Conclusion: Monitoring infliximab TL after dose optimization and/or interval shortening for loss of response could help in predicting those patients that will display a clinical and biological (CRP) response in the following year. Further prospective studies will clarify if applying treatment algorithms based on therapeutic drug monitoring will reveal as cost-effective in IBD.
Disclosure of Interest: L. Guidi Lecture fee(s): MSD, AbbVie, Takeda, Zambon, Consultancy: MSD, AbbVie, Mundipharma, M. Marzo: None declared, B. Tolusso: None declared, D. Pugliese: None declared, G. Andrisani: None declared, C. Felice: None declared, R. Landi: None declared, S. Canestri: None declared, E. Gremese: None declared, I. De Vitis: None declared, A. Papa: None declared, G. L. Rapaccini: None declared, A. Armuzzi Financial support for research: MSD, Lecture fee(s): AbbVie, Astra-Zeneca, Chiesi, Ferring, Hospira, MSD, Otsuka, Takeda, Zambon, Consultancy: AbbVie, Hospira, Lilly, MSD, Mundipharma, Pfizer, Sofar, Takeda

P0953 PRESENCE OF PRIMARY SCLEROSING CHOLANGITIS DOES NOT CHANGE LEVELS OF GUT BARRIER FAILURE BIOMARKERS (I – FABP AND CCK18) IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Primary sclerosing cholangitis (PSC) is a progressive disease of the biliary tree characterised by inflammation, fibrosis and stenoses, and often associated with ulcerative colitis (UC); condition characterized by leaky gut. However, UC associated with PSC (''PSC – UC'' or ''PSC – IBD'') is described as a phenotype distinct from the conventional UC. Our aim was to compare serum levels of biomarkers of gut barrier damage in PSC-UC, UC and healthy subjects.
Aims & Methods: We used ELISA to analyze intestinal fatty acids binding protein (I-FABP) and caspase-cleaved keratin 18 (ccK18) in 74 individuals (38 with PSC, 19 with UC, 17 healthy controls) and 38 individuals (23 with PSC, 9 with UC, 6 healthy controls), respectively. Furthermore, we compared the levels of either biomarker with standard clinical (e.g. colitis extent and severity) and laboratory parameters (CRP, AST, ALT, ALP, GGT, INR).
Results: There is no significant difference between PSC-UC, UC and healthy subjects in I-FABP [median (IQR)] 503.9 (0.0 - 1548.0), 454.1 (0.0 - 747.3), 769.3 (220.9 - 1027.0) or ccK18 [median (IQR)] 174.1 (99.93 - 423.0), 90.08 (67.46 - 205.9), 98.7 (51.05 - 174.7). When the liver involvement is disregarded, I-FABP have a tendency to be higher in patients with pancolitis as compared with patients with partial colon involvement ($p = 0.07$). There is no statistically significant difference in serum I-FABP or ccK18 depending on colitis severity (without colitis, remission, mild, moderate and severe).
Conclusion: Neither I-FABP, nor ccK18 differs between PSC-UC and UC. In patients with pancolitis, I-FABP has a tendency to be higher compared to patients with smaller extent of colitis.
Disclosure of Interest: None declared

P0954 EFFICACY OF LOW DOSE CT FOR EVALUATION OF DISEASE ACTIVITY IN ULCERATIVE COLITIS

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Introduction: It is important to assess the disease activity and extent of involvement in ulcerative colitis patient. Endoscopic examination, however, carries a risk of perforation of the colon often requiring surgery because of mucosal vulnerability, especially in patients with ulcerative colitis relapsing. Recently, it has been reported that cross-sectional imaging techniques can be used as a diagnostic tool for the evaluation of inflammatory bowel disease, nevertheless, there have been few reports on the efficacy of low dose CT for ulcerative colitis. We report here the efficacy of low-dose CT for ulcerative colitis during active period.
Aims & Methods: The purpose of this study is to investigate the diagnostic performance of low-dose CT for evaluation of disease activity in ulcerative colitis patient. The patients with relapsing ulcerative colitis between July 2013 and April 2014 were included in this study. All patients had undergone sigmoidoscopy and low-dose CT scan with the weight-based intravenous contrast protocol. The colon CT image was divided into six segments: rectum, sigmoid colon, descending colon, transverse colon, ascending colon, and caecum, then we evaluated wall thickening, stratification, contrast enhancement and mesenteric vascular

engorgement, assigning a CT score to each segment. Further, we calculate a total CT score by the sum of CT scores of 6 segments. To assess endoscopic severity, Ulcerative Colitis Colonoscopic Index of Severity (UCCIS) was used. All patients were interviewed before examination to calculate Mayo partial score to assess the clinical severity. We investigated the correlation between those CT scores and UCCIS. The correlation between partial Mayo score and total CT score also investigated. For the correlation analysis, the Spearman rank correlation analysis was used. For comparison between two groups we used the Mann-Whitney U test.
Results: Twenty three cases of ulcerative colitis were included in this study. We achieved a 62.3 % reduction of radiation exposure by adjusting the scan conditions and reconstruction conditions ($P < 0.00326$). The average partial Mayo score of the cases was 4.4 ± 2.0. We observed a high degree of correlation between the sum of the CT scores of the rectum and sigmoid colon and the sum of the UCCIS of the rectum and sigmoid colon ($\rho = 0.629$). Although the UCCIS of the rectum and sigmoid colon segment calculated by sigmoidoscopy and partial Mayo scores did correlate ($\rho = 0.456$), the correlation between the total CT score showed better correlation with the partial Mayo score ($\rho = 0.643$).
Conclusion: The endoscopic examination is important for evaluate disease severity in ulcerative colitis relapsing; however, it is often difficult to perform total colonoscopy due to mucosal vulnerability. On the other hand, CT can provide diagnostic images without preparation or invasiveness. This study suggested that low-dose CT could provide more effective images to assess the disease activity of ulcerative colitis compared with sigmoidoscopy.
Disclosure of Interest: None declared

P0955 ASSESSMENT OF BACTEROIDETES GENOTYPES IN BIOPSIES OF INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS. A CASE-CONTROL STUDY

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Introduction: The exact role of gut microbiota on the etiopathogenesis of IBD, both Crohn's disease (CD) and ulcerative colitis (UC), is not well known. Most studies of human gut microbiota rely on the non-invasive collection of stool samples. However, the analysis of the fecal microbiota may not reflect the role of the mucosa-associated microbes which live in close proximity to the intestinal epithelium and that are in contact with the cells of the innate immune system directly involved in the inflammatory response.
Aims & Methods: The aim of this study was to investigate the genotypes of Bacteroidetes microbiota from colon biopsies of IBD patients and to determine their relationship with the endoscopic activity of the disease.
Methods: A prospective case-control study was designed. Colon biopsies from consecutive IBD patients and healthy controls (HC) (healthy subjects undergoing colonoscopy for colon cancer screening and having a healthy colon mucosa) were included. Inactive UC was defined as a Mayo endoscopic subscore of 0. Inactive CD was defined as a SES-CD score ≤ 2. Microbiota was characterized by using a restriction fragment length polymorphism (RFLP) analysis on PCR products targeting the 16SrRNA genes of Bacteroidetes digested with *Hinf*I, *Pci*I, *Dpn*II and *Aci*I. RFLP and sequencing analysis indicated that a a total of 8 genotypes of Bacteroidetes called N1 and C1-C7 (of which N1 genotype is probably a strain of *Bacteroides dorei* and C1, and maybe C2, strains of *B. vulgatus*) were detected in all the biopsy samples analyzed. Results are shown as percentages.
Results: 53 consecutive IBD patients (24 UC and 29 CD) and 20 HC were included. 8 patients presented inactive UC (iUC) and 16 active UC (aUC). In addition, 21 CD patients presented active CD (aCD) and 8 inactive CD (iCD). The number of genotypes present in biopsies from IBD patients was higher than in HC, in whom only the N1 (58%) and C1 (42%) genotypes appear. While the presence of N1 genotypes was relatively constant in patients with active CD and active/inactive UC, the percentage of C1 genotype in these patients was low (between 20% and 26%) compared to HC and iUC (51%). The C4 genotype never appeared in control samples and it was present in only 4% of iUC and iCD biopsies, whereas it was present in 13% and 14% of patients with aUC and aCD respectively. Moreover, C3 genotype was higher in iUC (8%) than with aUC (3%) and CD (3% with active and inactive patients). The C2, C3, C5, C6 and C7 genotypes appeared sporadically in biopsies of IBD but never in HC.
Conclusion: Bacteroidetes genotypes in colon biopsies differ between IBD patients and HC. These genotypes, and especially the C4 genotype, may be used as biomarkers for improving the diagnosis of CD and UC, as well as to investigate their potential role in pathogenesis.
Disclosure of Interest: None declared

P0956 REDISCOVERY OF THE ANTI-PANCREATIC ANTIBODIES AND EVALUATION OF THEIR PROGNOSTIC VALUE IN A PROSPECTIVE CLINICAL COHORT OF CROHN'S PATIENTS: THE IMPORTANCE OF SPECIFIC TARGET ANTIGENS (GP2 AND CUZD1)

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Introduction: Glycoprotein 2 (GP2) and CUB zona pellucida-like domain 1 (CUZD1) belong to protein families involved in gut innate immunity processes and have recently been identified as a specific target of anti-pancreatic autoantibodies (PAbs) in Crohn's disease(CD). The aim of the present study was to determine the predictive potential of novel target specific PAbs regarding determination of disease phenotype, therapeutic strategy and long-term disease course in a prospective referral adult CD patient cohort.
Aims & Methods: Sera of 458 consecutive well-characterized IBD patients (CD: 271 and UC: 187) from a single referral IBD center and 100 healthy subjects were tested by enzyme-linked immunosorbent assay (ELISA) with isoform 4 of recombinant GP2 (anti-MZGP2 and anti-GP2 IgA/IgG) and indirect immunofluorescence test (IIFT) system with GP2 or CUZD1 expressing transfected HEK 293 cells (anti-rPAg2 and rPAg1 IgA/IgG). Clinical data were available on evolvement of complicated disease or surgical interventions as well as disease activity and medical treatment during the prospective follow-up (median, [IQR]: 108 months [65-178]).
Results: 12.4% and 20.8% of CD patients were positive for IgA/IgG type of anti-GP2 and anti-CUZD1, respectively, with a significant difference compared to UC and controls ($p < 0.01$ for both). PAb status was not associated with actual disease activity and showed long-term stability. Agreement among three different anti-GP2 assays was good (kappa: 0.44-0.70). At diagnosis, 45% of the patients had ileocolonic disease and 79.7% had inflammatory behavior, while 52% had complicated disease behavior, 35.1% had perianal disease and 41.1% had at least one resective surgery at last follow-up. Clinical associations were different for anti-GP2 and anti-CUZD1 antibodies. Presence of different anti-GP2 antibodies was associated with pediatric onset ($p = 0.012$), ileal involvement ($p = 0.032$), stenosing ($p = 0.017$) and penetrating ($p = 0.028$) disease behavior at diagnosis and PSC ($p = 0.038$). In contrast, presence of anti-CUZD1 was associated with colonic involvement ($p = 0.041$) and cutaneous manifestations ($p = 0.044$). In a group of patients with pure inflammatory luminal disease at time of the diagnosis, positivity for PAbs, mainly IgA subtypes, predicted a faster progression towards complicated disease course in time-dependent models. In Kaplan-Meier analysis, time to surgery or development of perianal disease was associated with anti-GP2 IgA ($pLogRank < 0.01$) or anti-CUZD1 IgA ($pLogRank < 0.001$) positivity, respectively. Anti-CUZD1 IgA remained an independent predictor in multivariate Cox-regression model including age at diagnosis, sex, disease location and behavior and frequent relapse as potential confounders (HR: 3.43, 95%CI: 1.68–7.02, $p < 0.001$).
Conclusion: The present prospective follow-up study has shown that specific PAbs (especially IgA subtype) are predicting complicated disease course including the development of perianal disease in CD.
Disclosure of Interest: None declared

P0957 RISK MATRIX FOR PREDICTION OF DISEASE PROGRESSION IN A REFERRAL COHORT OF PATIENTS WITH CROHN'S DISEASE

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Introduction: Early identification of patients with Crohn's disease (CD) at risk for subsequent complications is essential for adapting treatment strategy. The aim of the present study was to develop a prediction model including clinical and serology markers for assessing the probability of developing advanced disease 3, 5 and 7 years after diagnosis in a prospective referral CD cohort.
Aims & Methods: 271 consecutive CD patients (42.4% males, median follow-up: 10.9 years) were included. ASCA IgA and IgG and anti-OMP Plus™ IgA antibodies were determined by QUANTA Lite® ELISA (Inova Diagnostics, San Diego, CA), cut-off 25 U/ml. Detailed clinical phenotypes were determined prospectively from diagnosis during the follow-up by reviewing the patients' medical charts. The analysis was limited to patients with inflammatory disease behaviour at diagnosis. Total exposure to steroids, azathioprine or anti-TNFs were 88.2%, 73.8% and 41.7%, respectively. At diagnosis, 45% had ileocolonic disease and 79.7% had inflammatory behaviour, while 52% had complicated disease behaviour and 41.1% had at least one resective surgery at last follow-up. Two definitions were used for advanced disease: 1.) having intestinal resection or progression in disease behaviour and 2.) having intestinal resection, progression in disease behaviour, or need for thiopurines (IBSEN definition).

Results: ASCA IgA and/or IgG (but not anti-OMP Plus IgA status), disease location, and need for early azathioprine were included in the 5-year prediction matrix. The probabilities of advanced disease during this period varied from 6.2% to 55% depending on the combination of predictors. The 3- and 7-year ASCA-based model resulted in probabilities of advanced disease ranging from 0 to 45.5% and from 11.1% to 64.7%. In addition, the model including ASCA, disease location, and early need for steroids but not age at onset, was only predictive for the outcome at 5-years if the IBSEN definition was used. In contrast, the association was lost if the need for azathioprine was excluded from the advanced disease definition. Similar findings were obtained from in a Cox regression analysis, the combination of ASCA, location and early azathioprine was associated with the probability to develop advanced disease (pLogRank < 0.001), while the original model combining ASCA, early steroids and location failed to predict disease progression.

Probability of developing advanced disease 5-years after the diagnosis in patients with initial inflammatory disease based on association between ASCA IgA and IgG positivity, disease location and need for early azathioprine (AZA).

B1 behavior at diagnosis		colon only	ileal
ASCA positive	early AZA YES	50.0%	55.0%
	early AZA NO	30.8%	29.0%
ASCA negative	early AZA YES	11.1%	22.2%
	early AZA NO	6.2%	18.8%

Conclusion: Our prediction models identified substantial differences in the probability of developing advanced disease in the short and intermediate course of CD. Markers identified in this referral cohort were different from those previously published in the population-based cohort suggesting that different prediction models should be used in referral setting.
Disclosure of Interest: None declared

P0958 ON THE ORIGIN OF CRP IN CROHN'S DISEASE: ROLE OF THE EXTRAMURAL COMPONENT

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Introduction: Due to the full thickness involvement of the bowel wall or complications, Crohn's disease (CD) evaluation is the result of an integration of endoscopy (the gold standard) with clinical, laboratory and radiological data. The role of MRI, which excels in identyfing extramural signs of inflammation, is still unclear in CD follow-up. Moreover it is still debated whether CRP serum levels increase is due to mucosal or mural/extramural inflammation, not only via liver production but also from extrahepatic sources such as hypertrophy of the mesenteric fat, a CD common feature.Increased mesenteric fat density assessed by CT was found to correlate with plasma CRP levels in CD patients[1].
Aims & Methods: Aim of this study was to correlate enteric and extraenteric inflammatory MRI findings with endoscopic severity and CRP in a group of CD patients.
52 consecutive patients with endoscopically proven CD underwent MRI enterography for the staging at diagnosis or activity assessment (68/32%). Endoscopic activity was scored through the SES-CD (range 0-40) with active mild, moderate ad severe disease defined as 4-10,11-19 and >20 respectively. MRI activity was scored through the Magnetic Resonance Enterography Global Score (MEGS, range 0-296), which integrates both mural and extramural items, namely lymph node, fistula, abscess and comb sign, with active disease defined as ≥ 1 score. For all participants CDAI was completed and CRP and fecal calprotectin (FC) were also measured (positivity cut-off respectively >0.50mg/dl and >150µg/gr). Fibrofatty proliferation (creeping fat) of the mesentery was qualitatively defined a bowel loop separation ≥ 3 cm.
Results: We enrolled 20M/32F mean age 38 ± 15 ys, mean CD duration 5 ± 5 ys.SES-CD and MEGS correlated well between them and with clinical and biological activity(table). According to SES-CD 62% of patients had mild disease, 19% moderate and 5% severe.Increasing severity at endoscopy was significantly correlated with trasmural/extramural involvement, only with CRP positivity ($p = 0.007$). MRI did not show ability to distinguish endoscopic severity ($p = 0.14$), but revealed trasmural/extramural signs of inflammation in 60% of patients in remission, 84% mild and 100% with moderate and severe disease, mostly with CRP positivity. Moreover CRP positivity was associated with the presence of extraintestinal($p = 0.006$; lymph nodes $p = 0.009$, combsign $p = 0.001$ and abscess $p = 0.005$), not of mural involvement ($p = 0.4$). Mean CRP levels increased according to the number of extramural signs of inflammation (from absence to 4 signs $p = 0.01$), while no correlation was seen with SES-CD severity ($p = 0.7$), phenotype ($p = 0.4$) or mural inflammation ($p = 0.7$). Patients with hypertrophy of mesenteric adipose tissue showed higher levels of CRP than those without (4.2 ± 4 mg/dl vs 1.9 ± 3.2 $p = 0.005$).

	SES-CD	CDAI	CRP	FC
MEGS	$r = 0.42$ $p < 0.001$	$r = 0.59$, $p < 0.001$	$r = 0.43$ $p < 0.005$	$r = 0.27$, $p < 0.01$
SES-CD		$r = 0.51$, $p < 0.001$	$r = 0.39$ $p < 0.005$	$r = 0.35$, $p < 0.01$

Conclusions: Transmural inflammation, which is more frequent in severe disease, may still be present regardless of endoscopical activity.Positive CRP is significantly correlated to extramural activity in CD patients, thus suggesting the need of MRI for the staging of the disease independently from endoscopic severity. Moreover these data suggest that mesenteric fat may contribute to the increased CRP production.

Reference

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Disclosure of Interest: None declared

P0959 IS MONITORING ANTI TNFA TROUGH LEVELS IN THE CLINICAL PRACTICE COST-EFFECTIVE? THERAPEUTIC IMPLICATIONS AND COST: A PRELIMINARY AND RETROSPECTIVE STUDY OF TWO NON TERTIARY SPANISH HOSPITALS

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Introduction: The loss of response to antiTNFa treatment occurs in about 13-18% of the patients/year. The cost and adverse events of these drugs drugs can make therapeutic monitoring of antiTNFa trough levels an adequate strategy for treatment optimization
Aims & Methods: This is a retrospective multicentric study with 40 IBD patients(pts) -77.5% Crohn disease (CD), 17.5% ulcerative colitis (UC) and 5% of undetermined colitis (IC)- treated with antiTNFa (IFX 52.5% or ADA 47.5%), and 72.5% of pts were also on immunomudulator therapy (IMM). The mean age was 42.5(22-76) with a 50% of female. AntiTNFa trough levels were measured by an **ELISA assays** (Sanquin).The consideration of supratherapeutic levels was made in relation with the range of the Elisa assay. Patients were included in: **Group 1 (57.5%) 23** out of 40 pts with secondary loss of response (**SLR**) to IFX (20pts) or ADA (3pts). **Group 2:** (40%) 16 out of 40 clinically asymptomatic pts on ADA treatment had ADA trough levels monitored per protocol during the follow up, **Group 3** (2.5%,1/40 pts) with mucosal healing.
Results: Group 1: 17.5% pts(4/23) had normal levels, **30%** of pts (7/23) **had supratherapeutic** levels and **52.5**% (12/23) **had low** levels and 25 % of them (3pts) had also detectable antiTNFa antibodies. 78.7% of pts (18 out of 23) of **Group 1** were on **IMM**. 8 out of 23 pts of **Group 1** with **SLR** had not worsening of inflammatory analytical markers 3 out of these 8 pts (37.5%) had low therapeutic levels without intensification of treatment, 2 out of those 8 (25%) had supratherapeutic levels.
Group 2: 31.2 % of pts (5/16) treated with ADA and clinically asymptomatic had supratherapeutic levels, 1 out of those 16 pts was on intensified treatment, 25% of pts (4/16) had low therapeutic levels with 2 pts on intensified therapy and 43.7% (7/16) had normal levels.Therefore we had to perform changes in 28 pts. In order to calculate the treatment-cost we use the standard cost of the different antiTNFa therapies at our hospital, considering if it is the case the price of the induction and the maintenance therapy. The cost of treatment optimization by taking into account the results of antiTNFa trough levels measurement and antibodies to antiTNFa (dose escalation if low levels, switching to another antiTNFa or switching to a different class of biologic agent if therapeutic or supratherapeutic levels) would have been 467127 euro per year for these 28 pts. Had we treated in the classic way without monitoring levels the cost would have been 530369€, So there is a 63000 euro/pt/year of savings (2250 euro per pts/year).
Conclusion: 1º Hardly 17.5 of pts with SLR had normal antiTNFa levels and 30% had high levels that should be changed to a different class of biologic agent. **2 º** Monitoring ADA trough levels during their normal F-U found a 25% of patients over-treated. **3º** 37.5 % of Pts with SLR but without inflammatory analytical markers could be treated with dose escalation until new endoscopic or radiologic studies are performed. **4º** The cost analysis show that monitoring antiTNFa levels is not only an effective way of pts management but also cost effective.
Disclosure of Interest: None declared

P0960 CONTRAST ENHANCED ENDOSCOPIC ULTRASOUND OF THE COLON IS A MARKER OF EARLY THERAPY RESPONSE FOLLOWING ANTI-TNF-THERAPY IN PATIENTS WITH ACUTE ULCERATIVE COLITIS

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Introduction: Though colonoscopy is an important tool in the evaluation of acute ulcerative colitis (aUC), it is limited to the mucosal surface and therefore exhibits a significant interobserver variability. As shown by our group, endoscopic ultrasound (EUS) of the colonic wall allows exact quantification gut wall with differentiation of the different layers and can therefore accurately quantify the grade of inflammation.

Aims & Methods

Aim: To evaluate EUS in sigmoid colon in patients with aUC undergoing treatment with Anti-TNF-α (adalimumab,(ADA)) for possible detection of early therapy response.

Methods: 36 patients (22m) with aUC and 20 healthy controls (HC)(12m) were examined prior and 1, 4 and 12 weeks after initiation of ADA therapy using a forward-viewing radial echoendoscope (Pentax-Hitachi, Japan). Mucosal, submucosal and total wall-thickness (TWT) were measured by EUS in the mid sigmoid. Vascularity of the gut wall was evaluated by dynamic contrast enhanced EUS (dCEUS) (contrast agent SonoVue). Contrast kinetics were quantified as Time to peak intensity (TTP). Results were compared to 20 healthy controls (HC) undergoing screening colonoscopy. The examiners were blinded to the macroscopic inflammation scores. EUS-results were correlated to the Mayo-score and histological inflammation scores (HIS).

Results: HC showed a TWT of 1.8 ± 0.03mm with clear differentiation of the different layers; TWT increased to 3.91 ± 0.21mm($p < 0.001$) in patients with aUC. In patients with clinical response to ADA therapy (n = 26; 72.2%) TWT was reduced by 27.7% ($TWT_{7d} = 2.5 \pm 0.2$mm; $p = 0.007$) within one week when compared to baseline levels with further reduction after 4 weeks ($TWT_{28d} = 2.2 \pm 0.2$mm).

In patients with non-response to ADA therapy no significant changes of TWT were observed compared to baseline after 7 (TWT7d = 3.7 ± 0.4mm; $p = 0.8$) and 28 days ($TWT_{28d} = 2.9 \pm 0.3$mm; $p = 0.4$) of therapy.

TTP in HC was 13.1 ± 1.3s; in aUC TTP was accelerated to 6.8 ± 0.7s ($p = 0.0005$). In case of response TTP normalized within 1 week ($TTP_{d7} = 9.9 \pm 0.8$s) with $p = 0.008$ compared to baseline. In contrast, hypervascularity remained unchanged in patient without response to ADA therapy ($TTP = 6.6 \pm 0.5$s;$p = 0.9$).

Prior to therapy there was a strong correlation of TWT and Mayo-scores. In contrast, no correlation was observed 1 week after ADA therapy ($p > 0.05$). During the entire course of ADA, a positive relation between TWT and HIS ($r = 0.65$; $p < 0.001$) was seen.

Conclusion: TWT of the sigmoid measured by EUS precisely quantifies the level of inflammation in patients with aUC and proved reliability for the evaluation of early therapy response. It may become an important diagnostic tool for the judgement of mucosal healing in ADA therapy.

Disclosure of Interest: None declared

P0961 LONG-TERM OUTCOME OF INFLIXIMAB MAINTENANCE TREATMENT FOR JAPANESE PATIENTS WITH CROHN'S DISEASE

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Introduction: Maintenance treatment with infliximab has enabled achievement of long-term remission in patients with Crohn's disease (CD). However, very few studies have reported on Japanese patients.

Aims & Methods: The aim of this study was to evaluate infliximab maintenance treatment for Japanese patients with CD based on long-term outcomes and related prognostic factors. Retrospective data were collected from luminal CD patients who received the standard treatment of 5 mg/kg infliximab for ≥ 14 weeks between May 2002 and August 2012 at the IBD Center, Sapporo Kosei General Hospital. The effectiveness of infliximab maintenance treatment was evaluated using sustained treatment success rates, which were estimated using the Kaplan–Meier method. Sustained treatment success was defined as a lack of treatment failure. Treatment failure was defined as follows: 1) the discontinuation of infliximab due to loss of response or side effects; 2) the need for dose escalation due to loss of response or 3) the need for abdominal surgery due to CD. Prognostic factors related to sustained treatment success rates were evaluated using log-rank tests and a multivariate Cox regression analysis.

Results: Of the 276 patients included in this study (mean age, 31.2 years), 72 were females. The mean duration of the disease was 7.5 years and the mean C-reactive protein (CRP) level at the first infliximab administration was 2.18 mg/dl. One hundred fifty-two patients had ileocolitis, 68 had ileitis and 56 had colitis. In addition, 111 patients had structuring disease, 36 had intra-abdominal fistulas and 114 had perianal disease. Concomitant treatment with immunomodulators (azathioprine or 6-mercaptopurine), 5-aminosalicylic acid, elemental diet therapy and prednisolone were administered in 197, 245, 194 and 28 patients, respectively. Before initiating infliximab therapy, 96 patients had undergone at least 1 intestinal resection and no patient had had prior use of any other anti-tumour necrosis factor antibodies. The 2-, 4-, 6-, 8- and 10-year sustained treatment success rates were 62%, 50%, 40%, 30% and 30%, respectively. In the univariate analyses, a lower CRP level at the first infliximab administration (<1.00 mg/dl; $P = 0.011$) and concomitant treatment with immunomodulators ($P = 0.016$) were significant prognostic factors for higher sustained treatment success rates. The multivariate Cox regression analysis, both of these factors identified as independent predictors of said success rate.

Conclusion: Among Japanese patients with CD receiving infliximab maintenance treatment over a period of ten years, the treatment failure rate was 70% but could be decreased by combination therapy of infliximab with immunomodulators. Conversely, a higher CRP level at the time of first infliximab administration was a prognostic factor for a poor long-term outcome.

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P0962 TREATMENT WITH MESNA AND N-3 POLYUNSATURATED FATTY ACIDS AMELIORATES EXPERIMENTAL ULCERATIVE COLITIS IN RATS

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Introduction: Oxidative damage is a central feature of ulcerative colitis. Here we tested whether the antioxidant Mesna, when administered alone or in combination with n-3 polyunsaturated fatty acids (n-3 PUFAs), affects the outcome of Dextran Sodium Sulfate (DSS)-induced ulcerative colitis in rats.

Aims & Methods: After the induction of colitis, DSS-treated rats were further treated orally (p.o), intraperitoneally (i.p) or intrarectally (i.r) for either 7 or 14 days with Mesna, n-3 PUFAs or both. Rats were euthanized at the end of each treatment period. Clinical disease activity index was recorded throughout the experiment. At necropsy, colorectal gross lesions were scored. Colitis was scored histologically and the expression of myeloperoxidase (MPO), caspase-3, inducible nitric oxide synthase (iNOS) and nuclear factor κB (NF-$\kappa\beta$) in colonic tissue, was assessed by immunohistochemistry.

Results: Mesna alone was sufficient to significantly reduce colorectal tissue damage, when administered orally or intraperitoneally. Orally coadministered n-3 PUFAs enhanced this effect resulting in significant suppression of DSS colitis after 7 days and a remarkable recovery of colorectal mucosa was evident after 14 days of treatment. The amelioration of colon pathology co-existed with a significant decrease of MPO expression, overexpression of iNOS and reduction of nuclear NF-κB p65 in inflammatory cells, and the suppression of apoptosis in colonic epithelial cells.

Conclusion: The simultaneous administration of Mesna and n-3 PUFAs is particularly effective in ameliorating DSS colitis in rats, by reducing oxidative stress, inflammation and apoptosis, probably through a mechanism that involves inhibition of NF-κB and overexpression of iNOS.

Disclosure of Interest: None declared

P0963 A MULTINATIONAL STUDY TO DETERMINE INDICATORS OF SUBOPTIMAL THERAPY AMONG ULCERATIVE COLITIS PATIENTS TREATED WITH TUMOR NECROSIS FACTOR ANTAGONISTS

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Table. I: ndicators of suboptimal anti-TNF therapy among UC patients during 2-year follow up

Indicators of suboptimal anti-TNF therapy N = 51	Canada N = 81 % of patients	France N = 149	Germany N = 132	Italy N = 80	Spain N = 45	UK N = 538	Overall
≥1 of the following Indicators:	70.6	66.7	53.0	59.1	61.3	71.1	61.0
Anti-TNF Dose escalation	39.2	35.8	12.1	33.3	28.8	11.1	25.8
Augmentation with non-biologic therapy	29.4	27.2	20.1	16.7	20.0	17.8	21.0
UC-related Surgery	<5%	8.6	8.1	5.3	10.0	26.7	8.9
Discontinuation of index anti-TNF	35.3	27.2	30.9	22.7	27.5	40.0	29.0
Switching to another anti-TNF	21.6	24.7	18.1	6.8	22.5	13.3	16.9

Abstract number: P0964 Table 1: Safety Profile of Adalimumab in Adult CD and UC Patients

AE	All CD Trials as of 6 Nov 2009 N = 3603 PY = 4088E (E/100PY)	31 Dec 2014 N = 3689 PY = 4178.7E (E/100PY)	All UC Trials as of 15 Apr 2012 N = 1010 PY = 2007E (E/100PY)	31 Dec 2014 N = 1789 PY = 3371.9E (E/100PY)
Any AE	24.875 (608.4)	25.247 (604.2)	7.508(374.0)	12.281 (364.2)
Serious AE	1473 (36.0)	1521 (36.4)	374 (18.6)	643 (19.1)
AE leading to discontinuation	695 (17.0)	712 (17.0)	235 (11.7)	397 (11.8)
Serious infection	270 (6.6)	281 (6.7)	68 (3.4)	116 (3.4)
Opportunistic infection (excluding TB)*	82 (2.0)*	14 (0.3)	29 (1.4)*	8 (0.2)
Injection site pain	321 (7.9)	322 (7.7)	22 (1.1)	31 (0.9)
Any malignancy	54 (1.3)	50 (1.2)	21 (1.0)	33 (1.0)
AE leading to death	6 (0.1)	6 (0.1)	2 (0.1)	5 (0.1)

*Rates in 2009 and 2012 included events of oral Candidiasis, while rates from 2014 did not.

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Introduction: Ulcerative Colitis (UC) patients treated with tumor necrosis factor antagonists (anti-TNFs) may require therapy changes over time, which may be considered as indicators of suboptimal therapy.

Aims & Methods: A multinational, multicentre, retrospective, chart review study was conducted to assess the indicators of suboptimal therapy among adult UC patients receiving their first anti-TNF [infliximab (IFX) or adalimumab (ADA)] between June 2009 and June 2013 (index therapy).

The indicators of suboptimal therapy during 2-year follow up included: anti-TNF dose-escalation (assessed >4 months after index to allow for initial dose adjustments), augmentation with non-biologic therapy, UC-related surgery, discontinuation of first anti-TNF and switching to second anti-TNF. Dose escalation was defined as any increase in either dose, frequency, or both of the index anti-TNF therapy. Augmentation was defined as starting a new non-biologic drug or increase in dose/frequency of the concurrent non-biological drugs with anti-TNF therapy. Discontinuation of index anti-TNF was based on entry in patients' charts and excluded patients who discontinued anti-TNF because it was effective during the follow-up period. Switch was defined as a subset of discontinuation patients who initiated another anti-TNF therapy over the follow-up period. The number and percentage of patients with each indicator and ≥1 indicator was summarized descriptively by country.

Results: The study included 538 UC patients with mean age (SD) of 41.6 (14.3) years. 47% of patients were females and 73% reported moderate to severe UC at index. The percentages of patients on ADA and IFX as first anti-TNF were 8% and 92% respectively. Overall, within 2 years, 61% of UC patients had ≥1 indicator of suboptimal therapy, 26% had anti-TNF dose escalation, 21% needed augmentation with non-biologic therapy, 9% underwent UC-related surgery and 29% discontinued their index anti-TNF. Of those who discontinued index anti-TNF (N = 156), 58% switched to another anti-TNF therapy. Patients with indicators of suboptimal anti-TNF therapy by each country are shown in the table.

Conclusion: In this large multinational cohort, more than 60% of UC patients had ≥1 indicator of suboptimal anti-TNF therapy. Predominant indicators included dose escalation and discontinuation of anti-TNF therapy.

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P0964 LONG-TERM SAFETY OF ADALIMUMAB IN CLINICAL TRIALS IN ADULT PATIENTS WITH CROHN'S DISEASE OR ULCERATIVE COLITIS

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Introduction: Adalimumab (ADA) is a fully human anti–tumor necrosis factor (TNF) monoclonal antibody used for the treatment of moderate to severe Crohn's disease (CD) and ulcerative colitis (UC) in patients who have inadequately responded to conventional therapies. Safety from ongoing ADA trials continues to be collected, allowing assessment of long-term safety as the number of patients and the amount of exposure to ADA increase.

Aims & Methods: The aim is to provide an update on the long-term safety profile of ADA in CD and UC patients. Safety data were evaluated for adult patients with CD or UC treated with ADA in randomized, placebo-controlled, phase 3 and 3b trials as well as their open-label extension studies. Treatment-emergent adverse events (AEs) were coded using the Medical Dictionary for Regulatory Activities, version 17.1(2014), and collected from the first dose to up to 70 days after the last dose or through the cutoff date of 31 Dec 2014. AE rates were assessed as events (E) per 100 patient-years (PYs) of exposure to ADA.

Results: As of 31 Dec 2014, the ADA clinical safety database contained data for 3689 CD patients and 1789 UC patients, representing 4178.7 and 3371.9 PYs of ADA exposure, respectively. Overall, AE, SAE, and malignancy rates per PYs exposure were similar between the prior and the most recent data cutoffs for each disease state **(Table)**. The type of infections in the Opportunistic infections (excluding TB) category changed in 2014 resulting in an apparent decreased rate **(Table)**.

Conclusion: ADA continues to be well tolerated in patients with moderately to severely active CD and UC. No new safety signals were identified with prolonged ADA use in these patient groups.

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P0965 VALIDITY AND SAFETY OF IRON SUPPLEMENTATION FOR THE TREATMENT OF MODERATE IRON DEFICIENCY ANEMIA IN PATIENTS WITH CROHN'S DISEASE—A RANDOMIZED, CONTROLLED, OPEN-LABEL, SINGLE CENTER STUDY

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Introduction: The necessity and optimal route for iron supplementation to improve anemia in Crohn's disease (CD) has not been determined so far. We therefore performed a randomized, controlled, open label, single center study to evaluate the necessity, efficacy and safety of iron supplementation for the treatment of iron deficiency anemia (IDA) in patients with CD.

Aims & Methods: 49 patients with moderate anemia(hemoglobin(Hb):60-90g/l), transferrin saturation $\leq 20\%$ and/or serum ferritin concentrations $\leq 20\mu g/L$ were enrolled in this study. All patients were divided into three groups. Intravenous group received iron sucrose injection of 200 mg two or three times per wk until reached a total dose according to Ganzoni's Formula. Oral group received polysaccharide iron complex 150 mg per day for 12 wks. The other patients didn't received any iron supplementation. Response to anemia therapy was defined as Hgb $\geq$ 110 g/L in women, Hgb $\geq$ 120 g/L in men and/or Hgb rise $\geq$ 20g/l.

Results: 47 patients completed the study while 2 patients quitted because of surgery. At 12wks, Hgb and response rate (RR) of intravenous group (Hgb: 110.2 ± 16.2g/l, RR: 75.0%(15/20)) were superior to oral group (Hgb: 101.9 ± 17.9g/l, RR: 54.5% (6/11)) and no iron supplement group (Hgb: 99.1 ± 15.7g/l, RR: 25%(4/16)) ($P = 0.02$, $P < 0.01$). No matter received iron supplement therapy or not, Hgb in patients in remission (CDAI < 150) was remarkable higher than in patient in active phase at 12wks (101.0 ± 6.2g/l vs 81.0 ± 12.5g/l, $t = -2.2$, $P = 0.03$). Multiple logistic analysis showed that no iron supplement, active disease, complication were independent risk factors for no response to anemia therapy. 3 patient in oral group could not tolerate side effects and re-divided into intravenous group. However, no statistical difference on side effect was found between intravenous and oral group.

Conclusion: Iron supplementation therapy could significantly improve IDA in CD. Intravenous therapy was more effective than oral supplement. Iron supplementation will be more effective when disease activity under control.

Disclosure of Interest: None declared

P0966 ANTIBODIES TO INFLIXIMAB, BODY WEIGHT AND LOW SERUM ALBUMIN LEVELS INCREASE CLEARANCE OF INFLIXIMAB, A POPULATION PHARMACOKINETIC STUDY IN 332 IBD PATIENTS

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Introduction: Factors suggested to influence the pharmacokinetics (PK) of infliximab (IFX) in patients with inflammatory bowel disease (IBD) have mainly been derived from clinical trials or computer modelling, clinical data are scarce.

Aims & Methods: We aimed to study the real-life PK of IFX in a large cohort of IBD patients and to identify patient, disease and treatment characteristics that influence serum concentrations and clearance of IFX. All measurements (November 2004 - August 2014) of IFX serum concentrations in IBD patients collected at a tertiary referral center were identified. Medical charts of these patients were reviewed for patient, disease and treatment characteristics (gender, age, body weight, location and behaviour of disease, dose, co-immunomodulators, serum albumin, CRP). IFX serum concentrations and antibodies to IFX (ATI) were measured using an ELISA and antigen binding test (radioimmunoassay, Sanquin Laboratories, Amsterdam, The Netherlands). PK was analysed by nonlinear mixed-effects modelling and described using a 2-compartiment PK model. All influential covariates were combined into a full model.

Results: A total of 997 distinct IFX concentrations measurements were included, comprising data from 332 IBD patients (54% male, mean age 39 years, 3 measurements/patient). Disease extent was scored by the Montreal classification for 253 Crohn's disease patients (L1: 55/253, L2: 80/253, L3: 118/253) and 79 ulcerative colitis patients (E1: 6/79, E2: 30/79, E3: 43/79). 264/332 (80%) of patients were anti-TNF naïve at start of IFX and 144/332 (43%) were receiving concomitant immunomodulation, with a mean IFX dose of 5.2 mg/kg, at time of measurement. ATIs were detected in 75/332 (23%) patients, resulting in unmeasurable serum IFX concentrations in 83% of their samples. All samples with ATI titers higher than 30 AU/mL were associated with unmeasurable IFX concentrations. The mean (inter individual variability) values for clearance, central and peripheral volume of distribution were 0.38 L/day (50%), 5.07 L (30%) and 3.59 L (32%). PK characteristics were similar for Crohn's disease and ulcerative colitis. The presence of ATIs, low body weight and serum albumin were identified as covariates independently ($P < 0.001$) affecting clearance. The presence of ATIs corresponded with an mean (SE) 4.40 (11.1) fold increased clearance. For body weight, range from 50 to 120kg resulted in a 1.31 fold increase over a 2.4 fold weight increase. Serum albumin had a -1.65 (8.4) fold inverse impact on clearance. Because serum CRP values tended to change rapidly after initiation of treatment, and use of concomitant immunomodulators was often intermittent, these factors could not be evaluated as independent covariates although the administration of continuous concomitant immunomodulators was associated with a decrease in clearance. Line of treatment was predictive of clearance, with anti-TNF naive patients exhibiting lower clearance than the previously exposed patients.

Conclusion: Antibodies to infliximab, low body weight and low serum albumin levels increase clearance of infliximab.
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P0967 COMPARATIVE STRUCTURAL, FUNCTIONAL, NONCLINICAL, AND PHASE 1 SIMILARITY ASSESSMENTS OF PF-06438179, A POTENTIAL BIOSIMILAR TO INFLIXIMAB, AND MARKETED REFERENCE PRODUCTS

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Introduction: PF-06438179 is being developed as a potential biosimilar to Remicade® (infliximab), which is a chimeric mouse/human monoclonal antibody that binds to the tumour necrosis factor (TNF) protein, in a stepwise approach following globally accepted regulatory guidelines. The similarity of PF-06438179 to infliximab reference products sourced from the United States (infliximab-US) and from the European Union (infliximab-EU) was assessed in structural, functional, in vivo nonclinical pharmacokinetic (PK)/tolerability and clinical PK studies.
Aims & Methods: Structural similarity was assessed using chromatographic peptide mapping. Functional similarity was assessed in vitro using an inhibition of soluble TNF-induced cell apoptosis assay. PK, tolerability and anti-drug antibody (ADA) response were evaluated in rats administered a single IV dose (0, 10 or 50 mg/kg) of PF06438179 or infliximab-EU. In a phase 1 study (NCT01844804), 146 healthy volunteers received a single 10 mg/kg IV dose of PF06438179 (n = 49), infliximab-US (n = 48), or infliximabEU (n = 49). All subjects provided informed consent. PK was evaluated over 8 weeks; safety and ADA were assessed up to 12 weeks. PK similarity in humans was considered to be demonstrated if the 90% confidence interval (CI) of the test-to-reference ratio of maximum concentration (C_{max}) and area under the concentration time curve (AUC) were within the 80.00%–125.00% bioequivalence (BE) acceptance window.
Results: Peptide mapping showed superimposable chromatographic profiles of PF-06438179, infliximab-US and infliximab-EU, demonstrating structural similarity. The dose-response curves of inhibition of cell apoptosis induced by all three study drugs were also superimposable, demonstrating functional similarity. In rats, PF-06438179 and infliximabEU were well-tolerated. Systemic exposures (assessed by C_{max} and AUC) in dosed animals appeared similar, with mean exposure ratios of PF06438179 relative to infliximab-EU ranging from 0.88 to 1.16. None of the rats developed detectable levels of ADA following administration of PF06438179. In healthy volunteers, the three study drugs exhibited a similar PK profile, and the 90% CI for the ratios of C_{max} and AUC were within the BE acceptance window of 80.00%–125.00% for each, individual three-way comparison. Overall safety and ADA profiles were comparable among the treatment groups.
Conclusion: Comparative studies demonstrated structural, functional, and nonclinical and clinical PK profiles of PF-06438179 to be similar to infliximab-US and/or infliximab-EU. A global, comparative clinical study is ongoing to assess efficacy and safety of PF06438179 and infliximab-EU in combination with methotrexate in subjects with active rheumatoid arthritis.
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P0969 STW 5, A MULTI-COMPONENT HERBAL PREPARATION, MODERATES MOTILITY AND INFLAMMATION CHALLENGES IN THE ENTERIC NERVOUS SYSTEM (ENS)

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Introduction: The enteric nervous system is responsible for the undisturbed regulation of gut motiliy, secretion or resorption. Whenever the gastrointestinal tract is affect by diseases, the ENS is also part of the problem. Especially during inflammation, the ENS can be stimulated and challenged by inflammatory signaling molecules such as cytokines or hormones.
Aims & Methods: respectively the enteric nervous system. Gut segments were kept in an organ bath under perfusion conditions and motility increased by neostigmin application. STW-5 was added after the stimulation. To investigate whether the ENS was the target for the compound, we also performed electrophysiological measurements of enteric neuronal networks on microelectrode arrays. Inflammation was simulated in isolated ENS tissue. Myenteric plexus from adult mice from both jejunum and colon was isolated and either stimulated with a cytokine cocktail of Interferon-gamma, IL-1ß and TNF-alpha alone, or in combination with the multi-component herbal preparation STW-5.
The plexus tissues were kept for 24 hrs in tissue culture medium and supernatant was collected the following day. Cytokine liberation was measured using Multiplex-ELISA.
Results: The application of STW-5 reduced significantly the neostigmin-induced motility in a dose dependent manner. The electrical activity of the neuronal networks could also be increased by neostigmine and was reduced to basal activity by additional STW-5. In the inflammation approach, the supernatants from colonic and jejunal myenteric plexus showed different responses. While many cytokines were released after cytokine stimulation in both colonic and jejunal preparations, STW led to a complete downregulation of the release only in the colonic myenteric plexus.
Conclusion: The application of STW-5 reduced significantly the neostigmin-induced motility in a dose dependent manner. The electrical activity of the neuronal networks could also be increased by neostigmine and was reduced to basal activity by additional STW-5. In the inflammation approach, the supernatants from colonic and jejunal myenteric plexus showed different responses. While many cytokines were released after cytokine stimulation in both colonic and jejunal preparations, STW led to a complete downregulation of the release only in the colonic myenteric plexus.
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P0970 BIOSIMILAR INFLIXIMAB: EFFICACY AND SAFETY BASED ON INTERIM RESULTS FROM A PROSPECTIVE NATIONWIDE COHORT

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Introduction: Biosimilar infliximab CT-P13 received EMA approval in June 2013 for all indications of the originator product. Prospective data on the efficacy and safety of the biosimilar infliximab in IBD are lacking.
Aims & Methods: A prospective, nationwide, multicentre, observational cohort was designed to examine the efficacy and safety of CT-P13 infliximab biosimilar in the induction treatment of Crohn's disease (CD) and ulcerative colitis (UC). Demographic data were collected and a harmonized monitoring strategy was applied. Early clinical remission, response and early biochemical response was evaluated at week 14. None of the patients had received infliximab within 12 months prior to initiation of the biosimilar infliximab. Safety data was registered.
Results: 201 consecutive IBD patients (122 CD patients and 79 UC patients) were included in the present cohort. The age at disease onset was 24/29 years (median, IQR: 19-35 and 22-38) in CD and UC patients, respectively. 38/43% of CD patients had colonic/ileocolonic disease localization, 34% of patients had perianal disease and 26% of the patients had gone through previous surgery. 5/38/57% of UC patients had proctitis/left-sided colitis/extensive colitis. 27/19% of patients had received previous anti-TNF therapy in CD and UC, respectively. 60/58% of CD/UC patients received concomitant immunosuppressives at baseline. 54/82% and 61%/90% of the CD (n = 94/64) patients and 72%/77% and 65%/80% of the UC (n = 60/40) patients reached clinical remission/response by week 6 and 14. There was no significant difference in the remission and response rates between patients with or without previous anti-TNF exposure. Additionally, there was a decrease in biomarkers by week 14 (mean CRP level decreased from 20.8 mg/L to W6: 11.4mg/L and W14: 6.7mg/L in CD and from 32.1mg/L to W6: 11.2mg/L and W14: 9.9 mg/L in UC). 8 patients had allergic reactions, 8 patients infections and 1 death occurred.
Conclusion: This prospective nationwide cohort shows that CT-P13 is safe and effective in the induction of clinical remission and response in both CD and UC.
Disclosure of Interest: None declared

P0971 INFLIXIMAB AND ADALIMUMAB IN CROHN'S DISEASE: A COMPARATIVE ANALYSIS OF EFFICACY, SAFETY AND MANAGEMENT OF SECONDARY LOSS OF RESPONSE IN A COHORT ROMANIAN STUDY

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Introduction: Adalimumab(ADA) and Infliximab(IFX), are an effective induction and maintenance therapy for moderate to severe Crohn's disease. The aim of this study was to evaluate their efficacy in a large Romanian population and to identify predictor factors of response.

Aims & Methods: We performed a national retrospective cohort study including 265 patients (136 ADA, 129 IFX) between 2008 and 2014, all naive to biologics. Binary logistic regression was performed with the statistical program Minitab, to identify predictors of response.

Results: Patients were half women, with a median age of 36 years, a median disease duration of 2.5 years, most of them (80%) received Azathioprine before biologic therapy, 70% aged 17- 40 years at diagnosis, almost 50% with ileocolonic involvement, 60% non-obstructive non-fistulising disease, and 20% suffered surgery (intestinal resection) before the biologic therapy. Mean therapy duration was 20 months in ADA group and 36 months in IFX group. 67% of patients had moderate flare of the disease, while 16% had mild disease activity. Complete response to ADA was recorded in 77%, secondary loss of response in 18%, while to IFX the rate of complete response was 65%, and secondary loss of response 28%, statistically comparable. With most patients with secondary loss of response to ADA (79.2%), the dose was escaladated, which reinduced response in 84.2%. 12.5% were switched to Infliximab, with a significantly lower rate of response: 33%. In 26/37 (70%) patients that lost response to IFX, the dose was increased, which resulted in regaining response in approximately 40% of patients. 12/38 subjects (30%) were switched to Adalimumab, with a better result: 83% regained response. Regarding surgical interventions, 74.5% of resected patients achieved complete response, comparable to non-resected patients (70%). Secondary loss of response was found in 20% of resected patients compared to 24.5% of the non-resected, while primary non-response was recorded in 4% versus 2%. 9 of the 23 resected patients treated with IFX suffered re-resection for POR, compared to 4 of the 28 treated with ADA, but p-value was not statistically significant 0.16. 13 of 216 non-resected subjects suffered surgical interventions on biologic therapy (6%).

Predictors of loss of response to ADA were: severe disease (CDAI >450): OR 5.67 (95% CI 0.17,185.65), presence of perianal fistulae: OR 5.87(95% CI 0.26,131.15), fistulising disease OR 3.71(95% CI 0.18,73.72). Predictors of loss of response to IFX were: age $>$ 40y: OR 63.71(95% CI 2.93, 1384.62), severe disease: OR 8.25 (95%CI 0.38,177.8), perianal fistulae OR 3.71 (95% CI0.65, 30.63).

Conclusion: In a real-life cohort, Adalimumab and Infliximab are equally effective in Crohn's disease, with a complete response rate of ~70%. Predictors of poor response to biologics were: severe active disease, perianal disease and fistulising behaviour. In case of secondary loss of response to IFX, the best solution is to switch to ADA, with 83% chance of regaining response, while in case of secondary loss of response to ADA, increasing the dose leads to 84 % chance of regaining response.

Disclosure of Interest: None declared

P0972 A REAL WORD REVIEW OF PATIENT COMORBIDITIES IN CROHN'S DISEASE AND THEIR IMPACT ON TREATMENT STRATEGIES AND PATIENT OUTCOMES

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Introduction: Several studies have evaluated the increased prevalence of comorbid diseases and risk factors in Crohn's disease (CD) patients and understanding the overlapping pathogenesis of comorbidities may be key to effectively managing and treating those with this complex disorder.

Aims & Methods: We used patient data collected as part of an online treatment survey conducted among a panel of gastroenterologists between April 2010 and December 2013 in France, Germany, Italy, Spain and the UK. We analysed 11,730 records of patients suffering from moderate to severe CD and classified them according to their comorbidities into 4 groups. Group 1 patients were reported as suffering from no comorbid conditions; group 2 patients suffered from cardiovascular or metabolic comorbidities including hypertension, metabolic syndrome and diabetes (CVD); group 3 consisted of patients who suffered from anxiety and/or depression and group 4 included all patients with an autoimmune disease, including rheumatoid arthritis, psoriasis, ulcerative colitis, uveitis and multiple sclerosis.

Results: Patients with CVD were on average significantly older than those from the other groups (50 years, $p < 0.05$). They were also significantly heavier (74kg) and more likely to be male (62% of patients). These patients had a greater number of comorbidities (1.3) and had been diagnosed for longer (9 years). They were more likely to have moderate CD at diagnosis but had the lowest level of biologic use (53%) with the greatest delay from diagnosis to 1st ever biologic (7 years).

Patient suffering from depression/anxiety were significantly more likely to currently have moderate or severe CD (46% and 17%, respectively) and more commonly suffered from fistulising disease (29%). A greater proportion of these patients were currently experiencing fistulae (33%) and had their upper GI tract (5%), rectum (26%) and anus (21%) affected by their disease vs. other groups. They reported the highest average CDAI score (167) and the highest proportion of patients having undergone ≥ 3 surgical interventions for their disease (5%). Rapid disease progression (55%) and frequency of relapse (26%) were more frequently chosen as reasons for initiating biologics among these patients.

Patient with autoimmune comorbidities were most likely to be receiving anti-inflammatories (13%) and biologics (72%) with the latter more commonly chosen due to patients' extra intestinal manifestations (46%). Although this group reported the highest proportion of patients having experienced remission over the course of their disease (45%) there were no significant differences in the frequency or duration of remission between the groups.

We saw no clear correlation between biologic use and improved patient outcomes and little correlation between individual disease attributes and patients' psychological status.

Conclusion: Our data confirm that CD is a heterogeneous disease with clear differences in patient profiles across the main comorbidity groups we covered. These differences appear to lead to different treatment approaches which in turn may lead to varying patient outcomes. Our results do not show a correlation between biologic therapy and patient outcomes but suggest that patients with uncontrolled disease (flaring, fistulae and high CDAI) are more likely to suffer from depression and anxiety, highlighting the impact that tight disease control can have on patients' quality of life.

Disclosure of Interest: None declared

P0973 IDENTIFICATION OF A CUT-OFF FOR PERSISTENT ANTI-INFLIXIMAB ANTIBODIES AS A PREDICTOR OF RESPONSE TO INFLIXIMAB MONOTHERAPY

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Introduction: The clinical and predictive role of anti-Infliximab antibodies (AIA) presence and concentration are still debated, both in Crohn's disease (CD) and ulcerative colitis (UC) patients. However, there is increasing evidence of their usefulness in order to improve the management of patients on biological treatment who experience a loss of response (LOR). AIA can be subdivided into 2 types, persistent and transient, on the basis of their occurrence on multiple samples and capability of interfering with infliximab trough levels (TL), and therefore persistent AIA seem to play a major role on treatment outcome.

Aims & Methods: The aim of our retrospective study was to evaluate the clinical relevance of persistent AIA in a single-center cohort of inflammatory bowel disease (IBD) patients. We selected from our cohort of 56 IBD patients treated with IFX mono-therapy who achieved clinical and biochemical remission after induction (IFX schedule: 5 mg/kg at week 0, week 2, and week 6), 18 patients (32.1%) who developed persistent AIA during 48 weeks follow-up. Blood samples were drawn at standardized time points (i.e., baseline, 2 weeks, 6 weeks, and every 8 weeks) before IFX infusion. TL and AIA were measured using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). Clinical disease activity was assessed both at week 14 (i.e. after induction) and week 48 by the Harvey-Bradshaw Index (HBI, remission defined by HBI < 5) in CD patients and by the Mayo score for UC patients (remission defined by Mayo score <2). Also, protein-C reactive and erythrocyte sedimentation rate (ESR) were measured.

Results: Eighteen patients (11 CD and 7 UC, 10M/8F, median age 39.5 years, range 18-69) developed persistent AIA at a median of 2 weeks during 48 weeks follow-up. Among these patients, 12 (66.7%) experienced LOR during the follow-up period. Median AIA were significantly higher in patients who showed LOR as compared to patients who maintained remission (8.29 U/ml, range 0.62-30.52 U/ml, versus 1.41 U/ml, range 0.77-9.94 U/ml; $P = 0.04$). ROC curve identified a persistent AIA cut-off of 3.91 U/mL as the threshold with the highest accuracy for the identification of relapsers (AUROC $= 0.799$, specificity $= 75.0\%$, sensitivity $= 83.3\%$).

Conclusion: The early occurrence of elevated persistent AIA serum concentrations during IFX mono-therapy treatment is associated with high risk of LOR. Furthermore, the use of an AIA concentration cut-off of 3.91 U/mL can be useful to accurately identify patients with LOR, although these results need to be confirmed in larger series.

Disclosure of Interest: None declared

P0974 ANTI-TNF THERAPY IN ULCERATIVE COLITIS. SHOULD WE REMOVE 5-ASA?

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Introduction: 5-aminosalicylates (5-ASA) are effective drugs for induction and maintenance treatment in ulcerative colitis (UC) patients. However, their usefulness as concomitant treatment with Anti-TNF drugs remains uncertain.

Aims & Methods: The aim of this study was to evaluate the efficacy of this therapeutic combination in patients with moderate to severe UC. **Methods:** A

retrospective observational single-centre study was designed. Inclusion criteria were all moderate to severe UC patients that were treated with anti-TNF drugs (Infliximab or Adalimumab) between January 2007 and December 2013. Only anti-TNF naïve patients were included. Patients with pouchitis or having received previous anti-TNF treatment were excluded. Clinical and demographic characteristics were recorded as well as the number of months in which all patients were treated with anti-TNF agents. Efficacy was defined as sustained remission and measured as the duration of clinical remission in months until treatment failure (defined as the need for intensification, a switch to another anti-TNF or colectomy). The presence of significant adverse events was also evaluated. The concomitant use of 5-ASA was also assessed. The data is shown as percentages and Hazard Ratio after Cox regression analysis was performed.
Results: 55 patients were consecutively included. 31 women (56.3%) and 24 men (44.7%) with a mean age of 44.2 years. 49 patients started treatment with Infliximab (89.1%) and 6 with Adalimumab (10.9%). Regarding smoking habits, only 1 patient was smoker (1.8%) and 6 were former smokers (10.9%). 25 patients received concomitant treatment with 5-ASA (45.4%) and 30 patients received concomitant treatment with azathioprine (54.5%). Treatment failure was observed in 26 patients (47.3%), those of which 19 needed treatment intensification (73.1%). The average time of sustained clinical remission was 10.1 months, being higher in women (14.5 months) than in men (4.9 months). Regarding 5-ASA concomitant therapy, despite the fact that patients with 5-ASA maintained remission for more time (12 months) than those without 5-ASA (8.4 months), statistically significant differences were not discovered. 3 patients (5.4%) presented adverse events and had to be withdrawn from treatment, all of whom were not receiving concomitant 5-ASA. After multivariable analysis the only factor independently associated with maintaining remission was female gender HR 4.33 (95% CI, 1.35 to 13.90). No perceptible influence of concomitant treatment with 5-ASA was found.
Conclusion: Roughly half of patients with UC maintained remission with anti-TNF therapy. The concomitant use of 5-ASA did not have any influence in maintaining remission in patients with moderate to severe UC. Female gender was associated with higher rate of response in this study.
Disclosure of Interest: None declared

P0975 FACTORS ASSOCIATED WITH ANTI-TNF THERAPY FAILURE IN PATIENTS WITH CROHN'S DISEASE (CD). DOES THE TYPE OF DRUG HAVE ANY INFLUENCE?

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Introduction: Anti-TNF monoclonal antibodies are effective drugs for induction and maintenance of remission in Crohn's disease (CD). However a significant portion of patients do not respond or lose the response during the treatment and predictive factors are not well known. There is no direct data comparing the efficacy between different anti-TNF drugs.
Aims & Methods: The aim of this study was to evaluate the factors associated with anti-TNF therapy failure in Anti-TNF naive patients with CD. **Methods:** A retrospective, observational single-centre study was designed. Inclusion criteria were all naïve patients older than 17 years old who started treatment with anti-TNF drugs, either Infliximab or Adalimumab, for moderate to severe CD between January 2007 and December 2013. Patients who had been previously treated with another anti-TNF were excluded. Patients who started anti-TNF for different indications like prevention of recurrence or refractory extraintestinal manifestations, were not included. Treatment failure was defined as the need for dose intensification due to loss of response, surgery resection, or therapy removal for ineffectiveness. The influence of demographic and clinical variables (gender, age, smoking history and type of biological agent used) on treatment failure was also evaluated. Results are shown as OR and95% CI and analyzed by the Chi square test and multivariable logistic regression analysis.
Results: 129 CD patients were consecutively included: 72 women (55.8%) and 57 men (44.2%) with a mean age of 35.9 years. 64 treatments with Infliximab (49.6%) and 65(50.4%) with Adalimumab. 52 smokers (40.3%) and 12 former smokers (9.3%). Mean Treatment failure was observed in 51 patients (39.5%): 36 due to dose intensification (27.9%), 11 due to surgery (8.5%) and 4 primary failures after anti TNF induction therapy (3.1%). No factors associated with treatment failure were identified in the multivariant analysis. Similar rates of treatment failure were found between infliximab and adalimumab($p = 0.802$).
Conclusion: More than 60% of CD patients maintained response to anti-TNF therapy, and 27% of patients required treatment intensification. No differences were found between Infliximab and Adalimumab in terms of treatment failure in patients with CD.
Disclosure of Interest: None declared

P0976 PROSPECTIVE, RANDOMIZED CLINICAL TRIAL COMPARING THE EFFICACY OF TWO VACCINES AGAINST HEPATITIS B VIRUS (HBV) IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS

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Introduction: .
Aims & Methods: To compare the success rate between 2 HBV vaccines in IBD patients: the traditional (Engerix®) and a new vaccine with an adjuvant (Fendrix®). To identify predictive factors of response to the vaccine
IBD patients with negative HBV serology and without previous vaccination against HBV were included (EUDRA CT number: 2010-023947-14), and randomized 1:1 to receive Fendrix® or double doses of Engerix® at months 0, 1, 2 and 6. Anti-HBs concentration was measured 2 months after the 3rd and 4th vaccine doses
Results: 173 patients were included. 54% of patients received Engerix® and 46% Fendrix®. Overall, 43% of patients had response (pre-defined as anti-HBs $\geq$ 100 IU/L) after the first 3 doses (165 patients have received 3 doses up to now), and 71% after the completion of the vaccination (161 have completed the vaccination). 47% of patients that did not respond after the 3th dose, responded to the 4th vaccine administration ($p < 0.0001$). The response rate after the 4 doses was 75% (95%CI, 63-84%) with Fendrix® vs. 67% (56-77%) with Engerix® ($p = 0.3$; however, the statistical power for this comparison was only 30%); considering anti-HBs^{3}10 IU/L (the standard threshold to define response), the success rate was marginally higher with Fendrix® than with Engerix® (88% [78-94%) vs. 77% [66-85%], $p = 0.06$). In patients under anti-TNF treatment, the response rate (anti-HBs^{3}100 IU/L) after the 4 doses was 67% (47-83%) with Fendrix® vs. 45% (27-64%) with Engerix® ($p = 0.09$); and considering anti-HBs^{3}10 IU/l, the success rate was 80% (61-82%) with Fendrix® and 58% (39-75%) with Engerix® ($p = 0.06$). In the multivariate analysis, older age ($OR = 0.9$, $p < 0.0001$), and the treatment with immunosuppressants ($OR = 0.12$, $p < 0.01$) or anti-TNFs ($OR = 0.09$, $p < 0.0001$) were associated with a lower response rate to the vaccination. The type of vaccine ¾Engerix® or Fendrix®¾ was not associated with the response to the vaccination ($OR = 1.8$, 95%CI = 0.8-4). The frequencies of IBD relapses during the study period were similar in patients receiving Fendrix® and Engerix® (17% vs. 22%)
Conclusion: We could not demonstrate a statistically significant higher response rate of Fendrix® (conventional dose) over Engerix® (double dose) in IBD patients, although a *beta* error cannot be excluded. A 4-dose vaccine schedule significantly increases the response compared with a 3-dose regimen. Older age and immunosuppressive and anti-TNF treatment impaired the success rate of the vaccine. The risk of clinical relapse of the disease is not increased with either vaccine
Disclosure of Interest: None declared

P0977 NUTRITIONAL ASSESSMENT IN ULCERATIVE COLITIS PATIENTS UNDER REMISSION: IS THERE A SINGLE RELIABLE TEST?

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Introduction: The nutritional aspect of patients with UC has been poorly studied. The best nutritional assessment method has not been established. In the last years it has been seen a trend towards overweight and obesity among those patients, although some individuals, especially those with severe disease could be suffering from malnutrition
Aims & Methods: The aim of this study was to evaluate the nutritional status of patients with UC in clinical remission using different methods. Protocol approved by local IRB (number 130392). **Methods**: 80 individuals from a single center of southern Brazil from January 2014 to February 2015 were evaluated. Demographic data and assessment of high, weigh, body mass index (BMI), triceps skin fold (TSF) mid-arm circumference (MAC), mid-arm muscle circumference (MAMC), Subjective Nutritional Global Assessment (SGA), bioelectrical impedance (BIA), serum albumin and transferrin were performed. Statistical analysis was performed using chi-square, Wilcoxon-Mann-Whitney, Cochran and Kappa tests, assuming a 95% CI and statistic $p < 0.05$.
Results: Eighty individuals were included: 62% woman; mean age 45 ± 11.7 years and 96% Caucasian. Less then 5% were taking steroids. Malnutrition prevalence through different methods is shown on table 1. There was no association between malnutrition and disease duration and neither with extent of disease. None of the variables had any correlation when Kappa evaluation was applied. Laboratorial tests performed showed that only 1 subject had low albumin value and 28 (35%) showed low transferrin value. Considering BIA results 26.3% were considered body fat percentage above normal. Thirty seven percent were overweight and 16% obese by BMI.**Table 1:** Malnutrition Prevalence (anthropometry)

Method	N: 80
BMI < 18,5 e 22 (elderly) (%) [a]	2 (2.5%)
TSF < 50 percentile (%) [b]	58 (72.5%)
MAC < 50 percentile (%) [b]	44 (55%)
MAMC < 50 percentile (%) [b]	22 (27.5%)
SGA – mildly or significantly malnourished [d]	3 (3.8%)

Reference Range: [a] World Health Organization 1998; Lipchitz, 1994. [b] Frisancho 1981; 1990. [c]Schüssel et al, 2008. [d] Detsky et al.1987

Conclusion: Applying only one method is neither advisable nor reliable when assessing nutritional status. Our results show that a single patient could be considered malnourished by one and overweight by another. This study found a high percentage of overweight and obese UC patients in remission. However there are different frequencies depending upon the evaluation method that is used, BIA, anthropometric or BMI.
Disclosure of Interest: None declared

P0978 BEYOND MUCOSAL HEALING: TRANSMURAL AND EXTRAMURAL HEALING AFTER ONE-YEAR ANTI-TNFA THERAPY IN CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is characterized by transmural (full-thickness) inflammation, frequently with extramural complications beyond to the mesentery and adjacent organs. The capability of anti-TNFα therapies in achieving and maintaining both clinical remission and mucosal healing (MH) has repeatedly been described, while only one study was designed to assess prospectively their role in transmural healing[1].
Aims & Methods: Aim of this study was to analyze transmural healing (TH) in consecutive CD patients after a one-year treatment with anti-TNFα and to correlate TH with endoscopic and clinical activity (CDAI) as well as biological markers (CRP and fecal calprotectin).
13 patients with moderate to severe ileocolic CD were enrolled. All underwent ileocolonoscopy and MRI-enterography before and after one-year treatment with anti-TNFα; clinical remission was defined as CDAI < 150, response as a 70-point reduction from baseline. CRP and fecal calprotectin (FC) (positivity cut-off respectively > 0.50 mg/dl and > 150 μg/gr) were also measured. Endoscopic activity was assessed by SES-CD, range 0-40, with mucosal healing defined as score < 3 and response as a 50% decrease from baseline. MRI activity was measured by MRI-enterography global score (MEGS), range 0-296, a score which takes into account transmural and extramural features, with active disease defined as a score ≥1, and response as above.
Results: We enrolled 6M/7F, mean age 36 ± 12 ys, mean disease duration 7 ± 5 ys. According to the Montreal classification the phenotype was L1 in 31%, L2 in 7% and L3 in 62%; the behaviour was B1 in 8%, B2 in 69% and B3 in 23%. Resectional surgery related to CD was observed in 15%. Signs of mesenteric inflammation were only lymph node enlargement or comb-sign. 3 patients were treated with IFX, 10 with ADA (all naive to anti TNFα). Mean SES-CD, MEGS, CDAI, CRP and FC values significantly decreased at one year (table). 53% had clinical remission, 77% clinical response. Biological remission was achieved in 69% and 53% according to FC and CRP respectively. MH was achieved 38%, endoscopic response in 46%. Normalization of MRI finding was achieved in 15%, 31% had transmural improvement; before therapy 85% showed at least one extramural sign of inflammation, after one year at least one sign persisted in 54% (p = ns). MEGS score after one year didn't change significantly between patients with endoscopic remission/improvement and those without (p = 0.7). CRP positivity at one year was correlated with presence of extramural involvement only (p = 0.02) and mean CRP level were higher (2.3 ± 2.4 vs 0.30 ± 0.50 mg/dl) in the presence of comb-sign (p = 0.03).

	Baseline	After one year	p value
SES-CD	10 ± 4	6 ± 4	p = 0.002
MEGS	29 ± 13	17 ± 12	p = 0.001
Transmural	22 ± 11	12 ± 9	p = 0.001
Extramural	85% (at least one sign)	54% (at least one sign)	p = ns
CDAI	227 ± 88	147 ± 103	p = 0.03
PCR	3,7 ± 4,1	1,2 ± 1,8	p = 0.03
FC	388 ± 277	177 ± 148	p = 0.03

Conclusion: Biological therapy is effective in inducing clinical, biochemical and endoscopical remission of CD while transmural inflammation may persist longer than one year. Transmural, mainly extramural, healing probably needs longer therapy to be achieved, and his activity was unrelated to endoscopic improvement while closely relates to CRP positivity and levels.

Reference

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Disclosure of Interest: None declared

P0979 EFFICACY OF TUMOUR NECROSIS FACTOR ANTAGONISTS IN STRICTURING CROHN'S DISEASE: A TERTIARY CENTER REAL-LIFE EXPERIENCE

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Introduction: Stenosis is the most common complication in Crohn's disease (CD). However, there are only limited data on the resolution of strictures induced by tumour necrosis factor antagonists in patients with stricturing CD.
Aims & Methods: 43 CD patients followed-up in a tertiary IBD Center between July 2006 and March 2015 were enrolled. All of them had stricturing CD (Ileal = 40, colonic = 3), diagnosed by colonoscopy and/or MRI enterography. Twenty-five subjects (58%) were given adalimumab, 18 (42%) infliximab. The primary outcome was to assess the rate of surgery due to stricturing CD. Statistical analysis included descriptive analysis, logistic regression with univariate analysis for risk factors, and Kaplan-Meier survival curve and Cox proportional hazards-regression analysis for estimation of efficacy of anti-TNFs in avoiding surgical resection. All differences were considered statistically significant for $p < 0.05$.
Results: 43 CD patients were analysed (20 males, median age 36 years, range 20-72). Median duration of disease was 3.92 years (range 0.26-29.52). After a median follow-up period of 41 months (range 7-105), 18/43 patients (41.86%) underwent abdominal surgery; 7/43 (38.8%) through the first year, 6/43 (33.3%) through the second year, 1/43 (5.5%) through the third year, 3/43 (16.6%) through the fourth year, and 1/43 (5.5%) through the fifth year. Patients treated with infliximab were more likely to delay or avoid surgery in the follow-up period (median survival time 67.47 months for infliximab vs. 49.03 months for adalimumab, HR 2.97; CI 95% 1.37 -11.10; p = 0.01). Based on univariate analysis, only penetrating behavior at baseline was more likely to be associated with the risk of surgery (OR 3.96; CI 95% 1.0.7 to 14.6; p = 0.039). Twenty patients over 43 (46.51%) continued anti-TNF therapy, 5/43 (11.62%) stopped treatment (1 for secondary loss of response, 2 psoriasis, 1 for pregnancy and 1 for recurrent tonsillitis). Patients treated with infliximab were more likely to avoid surgery than adalimumab (OR 2.80; CI 95% 0.05-2.0; SE 0.50; p = 0.0393).
Conclusion: Although in a small cohort, anti-TNF are effective in avoiding surgery in the long-term. Penetrating phenotype at baseline is associated with the risk of surgery. Patients treated with infliximab remained free of surgery longer than patients treated with adalimumab.
Disclosure of Interest: None declared

P0980 AZATHIOPRINE VERSUS AZATHIOPRINE-ALLOPURINOL TREATMENT IN INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE TRIAL EVALUATING CLINICAL REMISSION AND ADVERSE EVENTS

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Introduction: Low dose of Azathioprine (AZA) in combination with Allopurinol (ALLO) can be used in patients with inflammatory bowel disease (IBD) failing AZA therapy due to intolerance or to lack of efficacy. Combination of AZA-ALLO leads to increased levels of the active metabolite 6-Thioguanine-nucleotide (6-TGN) and simultaneously decreases the level of methylmercaptopurine (MeMP). Retrospective studies have shown that this combination therapy increases remission rates and eliminates some of the adverse events. Gaining experience with the combination therapy raises the question whether it is preferable to start patients on primary combination therapy instead of ordinary AZA therapy, thereby theoretically reducing intolerance and increase remission rates.
Aims & Methods: A prospective, single center, open label, randomized trial comparing efficacy and safety in AZA naïve IBD patients with normal thiopurine methyltransferase (TPMT) randomized to receive either standard weight-based dosing of AZA or combination therapy with AZA-ALLO.
Primary outcome was steroid and anti-TNFα free clinical remission (partial Mayo score ≤ 2 in UC or a Harvey-Bradshaw Index < 5 in CD) at week 24 without adverse events.
Results: 23 IBD-patients were randomized to each treatment group. 16 patients (69.6%) in the AZA-ALLO-group compared to eight patients (34.7%) from the AZA-group achieved steroid and anti-TNFα free clinical remission at week 24 without experiencing adverse events. The difference in clinical remission between the two groups was statistic significant with RR = 2.10 [CI:1.07-4.11]. Intolerance to treatment was observed in seven (30.4%) patients in the AZA-ALLO group compared to 11 (47.8%) patients in the AZA-group. Four patients in the AZA-group, otherwise tolerant to the treatment, failed to reach steroid and anti-TNFα clinical remission at week 24.
Only a single severe adverse event (severe anemia) was seen in a patient from the AZA-group. Three patients in the AZA-group and a single patient in the AZA-ALLO group had an infection. All 4 patients completed the study.
Seven patients that were withdrawn from the study from the AZA group due to intolerance or lack of efficacy accepted a trial of combination therapy with AZA-ALLO or 6-mercaptopurine (6-MP)-ALLO. Five of these patients tolerated the treatment with good clinical response. Five patients that were intolerant to AZA-ALLO treatment accepted a trial of 6-MP-ALLO, but only 2 patients tolerated this and had benefit of the treatment
Conclusion: Efficacy and tolerance rates are higher in patients treated with AZA-ALLO compared to standard therapy with AZA. These results could

imply that combination therapy with AZA-ALLO can be used in AZA naïve patients with normal TPMT, thereby achieving higher remission rates and reducing the risk of intolerance to the therapy.
Disclosure of Interest: None declared

P0981 INCREASED WEIGHT GAIN IN ANTI-TNF ALPHA ANTIBODY TREATED PATIENTS WITH INFLAMMATORY BOWEL DISEASE MAY BE ATTRIBUTED TO LEPTIN AND TNF ALPHA

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Introduction: It is well known that TNF α, a critical mediator of inflammation in inflammatory bowel disease (IBD) is related to inflammation- related cachexia and anorexia. Animal studies have shown that body weight is regulated by adipocyte derived leptin. On the other hand, remarkable weight increase was observed among patients with IBD during treatment with anti- TNFα treatment. The association between weight increase, leptin and TNF α levels is unknown.
Aims & Methods: We retrospectively analyzed 132 patients with IBD, 102 on anti-TNF α therapies [Infliximab (IFX), Adalimumab (ADA)] and 30 patients on immunomodulators (IMD) (azathioprine, 6 MP) in a single tertiary IBD center. Levels of leptin, apelin and TNFα were measured in the serum of IBD patients, after at least 6 month of treatment with TNFα blockers or thiopurines by ELISA.
Results: A total of 106/132 (80%) IBD patients in our cohort had Crohn's disease (CD), while 26/132 (20%) were diagnosed as Ulcerative Colitis (UC). No significant difference was found between initial body weights of the group on anti TNF-α therapy (65.96 $\pm$18.93 kg) and IMD group (68.09 $\pm$ 17.03 kg) ($p = 0.911$). 70% (72/102) of patients increased their body weight during the anti-TNF-α treatment (range 6–48 months) for median of 3.30 kg (range 0.0-40.0). Significantly higher levels of leptin (median 5.5 ng/ml, IQR 9) were found in the patient group on TNFα blockers compared to that on IMD therapies (median 2.5 ng/ml, IQR 6) ($p = 0.049$). Considerably lower levels of TNFα (median 6 ng/ml, IQR 14) were observed among patients on anti-TNFα therapies compared to IMD group (median 14.5 ng/ml, IQR 7) ($p = 0.02$). No difference of apelin levels between two groups was detected ($p = 0.791$). No significant correlation between leptin serum levels and the increase of body weight was detected (Spearman coefficient $r = 0.041$, $p = 0.684$) as well as between the levels of TNFα and the body weight escalation (Spearman coefficient $r = 0.036$, $p = 0.741$).
Conclusion: The increase of weight gain in anti-TNF treated IBD patients may be attributed to elevated levels of leptin caused by the anti-TNF α treatment. A further mechanism is the reduction of TNFα itself.
Disclosure of Interest: None declared

P0982 ANTI-TNFA TREATMENT EFFICACY IN PREVENTION OF POSTOPERATIVE RECURRENCE IN CROHN'S DISEASE DEPENDS ON PREVIOUS EXPOSURE TO ANTI-TNFA AGENTS

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Introduction: At least 50% of Crohn's disease (CD) patients will need surgical resection during their follow-up. Infliximab and adalimumab are effective to prevent postoperative recurrence in CD patient naïve from anti-TNFα antibodies (anti-TNFα). The effect of previous exposure to one or more anti-TNFα before surgery on prevention of post-operative recurrence by these agents is still unknown.
Aims & Methods: The aim of our study was to investigate the efficacy of anti-TNFα to prevent CD post-operative recurrence according to previous exposure to these drugs.
We performed a retrospective analysis of CD patients, followed in a tertiary referral centre, who underwent surgical bowel resection and prophylactic treatment with anti-TNFα between January 2005 and June 2012. Infliximab, adalimumab and certolizumab pegol were considered as prophylactic treatments if started within three months after surgery. Endoscopic recurrence defined as a Rutgeerts score $\geq$ i2 and clinical recurrence defined as physician judgment. We assessed those endpoints one year after surgery and also during the follow-up.
Results: Fifty-seven consecutive CD patients with bowel resection, anastomosis and prophylactic treatment with anti-TNFα were included in the study. Twenty two patients (39%) had prior intestinal resection for CD and a majority (45, 79%) were treated with at least one anti-TNFα before surgery. Twenty-four (42%) received two or more anti-TNF before surgery and 12 (21%) patients were naïve from anti-TNFα. Thirty-nine (67%) patients had a surveillance colonoscopy one year after surgery. At one year, the global endoscopic and clinical postoperative recurrence rates were 42% (17/39) and 19% (11/57), respectively. According to previous exposure to anti-TNFα, patients with two or more anti-TNF before surgery had a higher one-year endoscopic recurrence rate compared with patients that received one or zero anti-TNFα before surgery (62%, $n = 13/21$ vs. 31%, $n = 4/13$ vs. 20%, $n = 1/5$). Also, patients with two or more anti-TNFα before surgery had a higher rate of clinical recurrence compared with patients receiving less than two anti-TNFα before surgery (37%, $n = 9/24$ vs. 12%, $n = 4/33$, $p = 0.05$). In multivariate analysis, smoking ($HR = 3.2$; IC 95%: 1.2-7.8) and previous exposure to two or more anti-TNFα ($HR = 4.3$; IC 95%: 1.3-14.0) were significantly associated to the risk of clinical postoperative recurrence in CD patients.
Conclusion: Previous exposure to two or more anti-TNFα agents was associated to a higher risk of postoperative recurrence in CD patients receiving prophylactic treatment with anti-TNFα.
This study suggested that previous exposure to anti-TNFα should be taken into account when managing prevention of post-operative recurrence in CD patients.
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P0983 THE ROLE OF DIFFUSE NEUROENDOCRINE SYSTEM OF STOMACH AND INTESTINES IN THE OCCURRENCE OF IRRITABLE BOWEL SYNDROME WITH DIARRHEA IN CONJUNCTION WITH FUNCTIONAL DYSPEPSIA: THERAPY OPTIMIZATION

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Introduction: Endocrine cells (EC) of the gastric and intestinal mucosa secrete somatostatin (SS), vasoactive intestinal peptide (VIP) and motilin (MLN). The purpose of this study was to define the role of EC in the occurrence of irritable bowel syndrome with diarrhea (IBSd) in combination with functional dyspepsia (FD) and to optimize management of his comorbidity.
Aims & Methods: The study involved 45 patients with IBSd combined with FD. Inclusion criteria were age between 18 and 55 years; compatible with the Rome criteria III (2006) diagnosis of IBS and FD. The biopsy was taken during gastroscopy and colonoscopy from the antral mucosa and middle thirds of the sigmoid colon. Immunohistochemical examination was based on the use of murine monoclonal antibodies to SS, VIP and MLN (1: 100, Novocastra). All patients were randomized in a 1:1 ratio, depending on the nature of ongoing therapy. 22 patients (group 1) received therapy comprising proton pump inhibitors (PPI) in a dose of 40 mg per day, mebeverine (400 mg daily) and loperamide (until stool normalization). 23 patients (group 2) received dioctahedral smectite (1-3 sachets per day until stool normalization) instead of loperamide. Dynamic immunomorphological study was carried out at the manifestation of IBS and in remission after one month. The comparison group consisted of 20 healthy subjects.
Results: We defined increased number of EC, producing MLN and VIP, end reduced number of EC, synthesizing SS in mucous membrane of the antrum and colon in patients with IBSd in period of exacerbation, unlike the comparison group of persons. In the period of remission normalization of EC producing M, SS and VIP in the majority of patients was observed. In some patients the number of EC did not normalize, accompanied by the presence of residual symptoms. In group 1 stool normalization and epigastric pain disappearance were achieved in 20 patients at Day 4. In group 2 disappearance of the main clinical symptoms of FD and IBS was observed in 22 patients after 3 days of initiating therapy.
Conclusion: The obtained results suggest an important role of the diffuse neuroendocrine system in the occurrence of IBS with FD. Revealed changes in quantitative characteristic of EC in different parts of the digestive tract can explain the frequent combination of IBS with FD. Inclusion of dioctahedral smectite in drug therapy leads to an earlier clinical disappearance of disease but does not affect the quantitative characteristic of EC producing MLN, SS and VIP.
Disclosure of Interest: None declared

P0984 PREDICTORS OF DISEASE RELAPSE OF PATIENTS WITH CROHN'S DISEASE IN DEEP REMISSION: WHO AND WHEN CAN WITHDRAW THIOPURINE MAINTENANCE THERAPY?

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Introduction: Few data are available on the disease course of cessation of thiopurine (TP) therapy for Crohn's disease (CD) with deep remission (DR) in routine clinical practice.
Aims & Methods: We aimed to evaluate clinical outcomes and factors associated with relapse in CD patients with DR. 109 CD patients in clinical, endoscopic remission following formal disease assessment and elective TP withdrawal were included. Prognostic factors of relapse were looked for through a proportional hazards model.
Results: After a median follow-up period of 46 months (interquartile range, 27.5-67.6 months), 50 (45.87%) patients had ER and 41 (37.61%) patients had flare, 18 (16.51%) patients undergone operation, and 25 (22.94%) patients hospitalized. The cumulative probabilities of maintaining clinical ($P = 0.48$) or endoscopic remission ($P = 0.67$), and free of bowel surgery ($P = 0.62$) or hospitalization ($P = 0.72$) at 5 years did not differ between patients maintaining TP or withdraw TP.
A scoring system based on age, CRP, disease duration and incidence of bowel complications was developed which can predict a mild prognosis after the achievement of DR, giving patients the chance of therapy de-escalation. In

selective CD patients in DR without defined risk factors, up to 70% remained in clinical remission during the 60-month follow-up after the cessation of TP therapy. Importantly, 78% of these patients sustained endoscopic remission, 93.3% also free of bowel surgery.
Conclusion: No significant difference regarding the long-term outcomes of patients with DR maintaining TP or withdraw TP. Furthermore, a group of low-risked patients among whom therapy de-escalation maybe reasonably considered has been identified.
Disclosure of Interest: None declared

P0985 IMPACT OF LONG-TERM TREATMENT WITH AZATHIOPRINE ON DISEASE PROGRESSION IN PATIENTS WITH EARLY CROHN'S DISEASE

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Introduction: The impact of azathioprine (AZA) on the damage-based long-term outcome of early Crohn's disease (CD) still controversial. We aimed to evaluate the efficacy of AZA in patients with early CD.
Aims & Methods: To identify predictive factors associated with the long-term outcome of disease.
This longitudinal cohort study examined patients from a university-based IBD referral centre (2000 to 2013 year). Cox regression analysis was performed to identify potential predictive factors of CD progression.
Results: 190 Patients with early CD were followed- up prospectively for a total of 893 patient-years on AZA. After a median follow-up of 57 months (interquartile range, 31.3-76.2 months), 29 patients underwent abdominal surgery, 48 patients hospitalized, and 68 patients experienced clinical flare. The cumulative rate of free of CD- related bowel surgery, hospitalization and flare at 5-year on AZA treatment was 0.65, 0.59 and 0.39, respectively. The median CD-related bowel surgery-free survival, CD-related hospitalization-free survival and flare-free survival were 67.9 months (95% confidence interval (CI), 60.0-75.7), 67.9 months (95%CI 55.8-88.0), and 49.3 months (95%CI 34.9-63.7), respectively. Four independently predictors of Crohn's related operations were identified: prior bowel resection (hazard ratio (HR), 9.91; 95%CI 3.74-26.24), smoking (HR, 4.79; 95%CI 1.75-13.17), an AZA treatment duration < 40 months (HR, 8.3; 95%CI 2.19-31.47) and a baseline hemoglobin < 110 g/L (HR, 5.46; 95%CI 2.21-13.48). Prolonged use ($\geq$40 months) of AZA also independently predictive of free of CD- related hospitalization (HR 3.02) but not increase risk of adverse events ($P = 0.23$).
Conclusion: Prolonged use ($\geq$ 40 months) of AZA was associated with a more favourable course of early CD (lower risk of CD- related bowel surgery and hospitalization) without increasing the risk of adverse events.
Disclosure of Interest: None declared

P0986 PREDICTING CHANGE TREATMENT IN CROHN'S DISEASE: A MEASUREMENT OF RISK SCORE

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Introduction: Several independent predictors for complicated, severe or aggressive Crohn' disease (CD) have been so far identified with a wide variation across studies (1). However progression disease predictors are not still clearly identified and it is not known whether the degree of bowel damage is a risk factor for disease progression. Intestinal ultrasound after the ingestion of oral contrast (SICUS) accurately measures CD small bowel intestinal lesions and complications (2).
Aims & Methods: To assess among demographic, clinical, laboratory factors and SICUS findings, those that may predict the modality of CD progression to identify with a easily used risk score patients requiring a more intensive monitoring and preventive treatments. This prospective cohort study includes 160 CD patients (93 M, median age 31 yrs; B1 25%, B2 56%, B3 19%; L1 61%, L3 32%, L2 6%; PD 29%) seen at regular 6-12 month interval, irrespective of clinical recurrence. During a median follow-up of 7.9 yrs, mean lag-time between visits 7.2 months, a total of 1464 visits (on average 9 per patient, range: 2-23), each assessing clinical, laboratory, endoscopic, and SICUS findings, were performed. By Poisson models we evaluated the predictors at each visit of having, within the next visit the need to change treatment starting azathioprine or biologics. Visit to visit interval was considered as exposure time. Independent predictors were: gender, age at diagnosis, CD duration, location and behavior, perianal disease, CDAI, GI symptoms, inflammatory markers, BMI, smoking, family history, SICUS findings, systemic symptoms, steroids at first flare, use of steroids, azathioprine and biologics, previous surgeries. Continuous variables were categorized based on the quartile values. The predictors included in the final model were chosen by a backward selection including at each step only variables with an adjusted p-value < 0.15. Standard errors of the Poisson parameter models were adjusted for visits clustering within the same patient. Risk scores were realized taking for each predictor the integer part of each model coefficient (i.e., the logarithm of the estimated incidence rate ratio (IRR)) (2) and then summing all those present at each visit, being zero the lowest possible score. Finally goodness-of-fit test was performed.
Results: Four independent factors predict the need to start biologics within the next visit: at SICUS the presence of 1) CD complications or 2) small bowel CD lesion > 20 cm in absence of CD complications, 3) presence of specific intestinal symptoms; 4) the presence of inflammatory markers. The calculated integer risk score ranged from 0 to 5 points. Three independent factors predicts the need to start azathioprine within the next visit: 1) female gender; 2) BMI value < 21; 3) CDAI at visit > 50. The calculated integer risk score ranged from 0 to 4 points.
Conclusion: In CD patients a readily available risk score allows to identify those patients in need of more intensive monitoring and therapy

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Disclosure of Interest: None declared

P0987 COMPARATIVE SHORT-TERM EFFICACY OF CYCLOSPORIN, TACROLIMUS, INFLIXIMAB AND ADALIMUMAB AS RESCUE THERAPY IN HOSPITALIZED PATIENTS WITH SEVERE CORTICOSTEROID REFRACTORY ULCERATIVE COLITIS: A RETROSPECTIVE INVESTIGATION

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Introduction: The optimum therapeutic strategy for patients with severe steroid refractory ulcerative colitis (UC) is still a challenging clinical issue. Currently, cyclosporin A (CsA), tacrolimus (Tac), infliximab (IFX), and adalimumab (ADA) have been administered as rescue therapy for severe steroid refractory UC. However, there is inadequate evidence for clinical efficacy difference between these 4 medications.
Aims & Methods: We were interested to evaluate the short-term efficacy and safety of CsA, Tac, IFX, and ADA as rescue therapy to avoid colectomy in patients with severe UC after failure of corticosteroids. This was a single-centre retrospective investigation involving 213 consecutive corticosteroid (iv, up to 60mg/day) refractory inpatients with acute severe to fulminant UC. Lichtiger's clinical activity index (CAI) ≤ 16 meant severe UC, while CAI ≥ 17 meant fulminant UC. Patients received one of the following medications, iv CsA (initially 3mg/kg/day, aiming for blood levels of 400-600ng/ml, n = 92), oral Tac (initially 0.05mg/kg twice a day, aiming for blood trough levels of 10-15ng/ml, n = 46), IFX (5mg/kg at weeks 0, 2, n = 47), or ADA (160mg at week 0, 80mg at week 2; n = 28). Patients who did not improve after the first rescue therapy could switch to one of the other 3 medications as the 2nd rescue therapy or undergo colectomy. The primary clinical efficacy was evaluated at week 4 after the first rescue therapy. Further, at week 6, the efficacy of the 2nd rescue therapy was assessed. Clinical remission was defined as CAI ≤ 4. Additionally, patients received regular evaluations for adverse effects.
Results: Within 4 weeks, 156 of the 213 patients (73.2%) achieved remission with the first rescue therapy including 132 of 160 (82.5%) with severe UC and 24 of 53 (45.3%) with fulminant UC ($P < 0.05$). In the CsA group, 69 of 92 patients (75.0%) achieved remission vs 33 of 46 (71.7%) with Tac, 34 of 47 (72.4%) with IFX, and 20 of 28 (71.4%) with ADA (difference not significant). Further, for remission rate vs UC severity, with CsA, 49 of 58 (84.5%) patients with severe UC and 20 of 34 with fulminant UC (58.8%) achieved remission vs 31 of 38 (81.6%), and 2 of 8 (25.0%) for Tac, 32 of 40 (80.0%), and 2 of 7 (28.6%) for IFX, 20 of 24 (83.3%), and 0 of 4 for ADA ($P < 0.05$ for CsA vs Tac, IFX or ADA with respect to fulminant UC). After 6 weeks, 29 of 57 patients (50.9%) who had failed to respond to the first rescue therapy could avoid colectomy by switching to the 2nd rescue therapy. No patients experienced serious adverse events and there was no mortality.
Conclusion: In the first rescue therapy, the efficacy and safety of CsA, Tac, IFX and ADA were not significant different. In patients with fulminant UC, the efficacy of CsA was better than the other 3 medications for avoiding colectomy. Therefore, a 2nd rescue therapy should further reduce colectomy rate.
Disclosure of Interest: None declared

P0988 SHORTENING INTERVAL INJECTION OF ADALIMUMAB IS MORE EFFICIENT THAN DOUBLING DOSE IN CROHN'S DISEASE PATIENTS WITH LOSS OF RESPONSE

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Introduction: Adalimumab (ADA) is effective for the management of Crohn's disease (CD), but relevant proportion of patients treated will experience a loss of response after a primary response. Response to dose escalation to ADA is a major concern in clinical practice as only few therapeutics agents have shown their efficacy in CD. The aim of the present study was to evaluate early and sustained response to ADA dose escalation for CD patients with secondary loss of response and to identify predictors of clinical response.
Aims & Methods: We conducted a retrospective observational study, including all patients who underwent a dose escalation of ADA after a secondary loss of response from 2007 to 2015. Main outcome was clinical response to dose escalation at weeks 12 (defined by continuation of ADA with no new dose escalation, no introduction of corticosteroids or immunosuppressors, and no surgery). Kaplan–Meier analysis was used to describe duration of sustained response after dose escalation over time. Univariate and multivariate logistic

regression analyses were performed to identify predictors of response to ADA dose escalation at weeks 12 and 52.
Results: One hundred and twenty four patients were included. Among them, 81/124 (65%) had non-penetrating non-structuring disease, 31/124 (25%) structuring disease, and 12/124 (9%) penetrating disease. Fifty (40%) patients underwent previous intestinal resection. Sixty-seven (54%) patients received previous infliximab treatment. Median time to dose escalation was 44 weeks (IQR 18-117). At ADA dose escalation, 26/124 (20%) patients received concomitant immunosuppressors and 20/124 (12%) received concomitant corticosteroids. ADA dose escalation was achieved by shortening interval to 40 mg every week (ew) in 100/124 (80%) patients, and by increasing dose to 80 mg every other week (eow) for in 24/124 (19%) patients. Clinical response at weeks 12 was observed for 99/124 (79%) patients. In multivariate analysis, factors predicting response to ADA dose escalation at week 12 were a stricturing behavior (OR 2.55, 95% CI : 1.00-6.45 ; p = 0.048) and duration of ADA therapy more than 44 weeks before ADA loss of response (OR 9.83, 95% CI : 1.25-76.81 ; p = 0.029). In patients with initial response to ADA dose escalation at week 12, cumulative probabilities of sustained response were 91%, 76% and 58% at 6, 12 and 24 month, respectively. In multivariate analysis, shortening interval injection of ADA to 40 mg ew was the sole predictive factor of sustained clinical response at week 52 (OR 4.91, 95% CI : 1.00-24.24 ; p = 0.05). Among all the patients, ADA was stop after dose escalation in 2 patients because of side effect (one for myocarditis and one for paradoxical psoriasiform skin lesions).
Conclusion: ADA dose escalation can recapture clinical response at week 12 in most CD patients who experienced a secondary loss of response to ADA; the majority of patients with initial response maintained clinical response over time. Importantly, shortening interval injection to 40 mg ew (compared to increasing dose to 80 eow) was the sole predictive factor for a sustained response to ADA dose escalation.
Disclosure of Interest: None declared

P0989 ENDOSCOPIC DILATATION OF CROHN'S ANASTOMOTIC STRICTURES IS EFFECTIVE IN THE LONG-TERM AND ESCALATION OF MEDICAL THERAPY IMPROVES OUTCOMES

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Introduction: A clinically relevant stricture is usually defined as a luminal narrowing with pre-stenotic dilatation and obstructive symptoms. Surgical resection is an effective treatment for Crohn's anastomotic strictures, however disease recurrence after 15 years is more than 50%, often with the need for a further resection[1]. The long-term outcome of endoscopic balloon dilatation is unclear as most cohorts have a follow-up time of less than 3 years.
Aims & Methods: All endoscopic balloon dilatations performed at a single centre for patients with anastomotic Crohn's strictures between 2004-2009 were retrospectively reviewed with the aim of collecting long-term follow-up data. The stricture length, signs of disease activity and evidence of upstream dilatation were assessed from imaging. Clinical data on medical therapy and escalation to anti-TNF or thiopurines was obtained. Endoscopic data including disease activity, balloon size and therapeutic success, along with histological reports were recorded with images graded by an experienced endoscopist.
Results: A total of 54 patients were identified with a median age of 52 years (46-62). 21/54(39%) were male. The median follow-up period was 6 years(5-7) with a median disease duration of 28 years(19-32). Stricture length at cross-sectional imaging was described in all cases with a median of 20mm(10-30), features of active mucosal inflammation were described at the anastomosis in 38/54(70%) and upstream dilatation in 25/54(46%). At endoscopy, active disease was reported in 50/54(92%) of cases and a median balloon dilatation of 15mmHg was used to achieve therapeutic success in 48/54 (89%). The median number of dilatations was 2(IQR 1-9) with a time to repeat dilatation of 23months (7.2-56.9) with 31/44 (70%) of patients being managed endoscopically requiring repeat dilatations. There was one perforation which resulted in a resection of the anastomosis and temporary ileostomy.
Rutgeert's grading of endoscopic images was possible in 50/54 cases with a median of i2 (range 1-4). 10 (18%) patients had anastomotic resection with a Rutgeert's score of $\geq$i2 being positively associated with this outcome (p = 0.048). Female gender (OR 1.604 95%CI 1.093-2.352 p = 0.028), active disease at time of first endoscopy (OR 2.45 95% CI 1.145-5.234 p = 0.021) and length of stricture > 20mm (p = 0.015) predicted need for repeat dilatation. Furthermore, escalation of medical therapy to either azathioprine or anti-TNF resulted in a delay in time to repeat dilatation in Cox-regression analysis.
Conclusion: At long-term follow-up only 18% of patients required surgical resection. Of the remaining patients 32% were well with no further endoscopic intervention required. 68% required intercurrent endoscopic dilatation. This is the longest follow-up period in the literature and demonstrates that endoscopic dilatation is effective and appropriate escalation of medical therapy appears to delay the need for further interventions.

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Disclosure of Interest: None declared

P0990 PERSONALISING THERAPY: CLINICAL, HISTOLOGIC AND ENDOSCOPIC PREDICTORS OF ANTI-TNF OUTCOME IN CROHN'S DISEASE

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Introduction: Primary non-response (PNR) and secondary loss of response (LOR) are major issues affecting ongoing use of biological therapy in Crohn's disease. Mucosal healing is currently the endpoint of many clinical trials and has been shown to improve outcomes. However, clinical or biochemical biomarkers of prediction for anti-TNF therapy are currently lacking.
Aims & Methods: We aim to determine factors using endoscopy and histology to predict PNR and secondary LOR with anti-TNF therapy in patients with Crohn's disease.
Patients who were commenced on anti-TNF therapy (adalimumab or infliximab) from Jan 2007- June 2014 were identified along with clinical data, including demographics and phenotype. Patients with a colonoscopy and biopsies taken within 6 months of commencement of an anti-TNF and a further group with histology obtained within 12 months of their first dose were included. Each colonic segment of the colonoscopy was evaluated for activity of disease. Histology was assessed by a gastrointestinal pathologist who was blinded to the clinical data. PNR was defined by global assessment (clinical and biochemical) of lack of improvement within 6 months of commencement of anti-TNF therapy. Secondary LOR was defined as cessation of their anti-TNF in view of clinical deterioration as assessed by their gastroenterologist. Variables influencing PNR, secondary LOR and surgery were examined using the chi-square test, Wilcoxon rank-sum test and Cox-squared logistic regression
Results: 237 patients were identified; with 91 (38%) having ileal involvement (Table 1). There was no difference between PNR and secondary LOR in patients on combination therapy versus secondary LOR (p = 0.12). PNR occurred in 36 (15%) patients and secondary LOR in 58 (24%) with 122 (51%) having ongoing anti-TNF therapy. Crypt architecture distortion was found in 64 (34%), lymphoid aggregates in 14% and granuloma(s) in 8%.
On univariate analysis, PNR was associated with smoking (p = 0.048), > 5 segments of disease at colonoscopy (p = 0.012) and granuloma(s) (p = 0.045) in a biopsy specimen. Ileal disease was associated with a greater likelihood of response (p = 0.046). On univariate analysis, secondary LOR was associated with smoking (HR 2.53 p = 0.018) and presence of lymphoid aggregates (HR 1.78 p = 0.038). Multivariate analysis for PNR was significant for smoking and > 5 diseased segments at colonoscopy. Multivariate analysis for secondary LOR factors was smoking. Cryptitis and crypt abcesses were not significant in either univariate or multivariate analyses.

Table 1: Baseline characteristics of patients

Characteristics (n = 237)	Median (IQR)
Age	30 (18-45)
Gender	45% male
Disease phenotype	Ileal involvement (38%)Stricturing disease (25%)
Duration of anti-TNF therapy	19 months (10-36).

Conclusion: Smoking is associated with PNR and secondary LOR. Extent of involvement (> 5 segments of disease at colonoscopy) was associated with PNR. Histologic factors such as granuloma and lymphoid aggregates may contribute to prediction for PNR and secondary LOR respectively.
Disclosure of Interest: None declared

P0991 THE EFFECTIVENESS AND SAFENESS OF ALLOGENEIC MESENCHYMAL STROMAL CELLS IN PATIENTS WITH REFRACTORY CROHN'S DISEASE - 5 YEARS OF OBSERVATION

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Introduction: Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract with recurrent nature of the flow. The frequency of exacerbations is approximately 20-25% at 1 year and 75% for 3 years. If the remission lasted less than 12 months, there is a 65% chance that the aggravation comes in the next 18 months. Aim. To evaluate the influence of culture of allogeneic mesenchymal stromal cells (MSCs) of bone marrow for the duration of remission in patients with refractory CD.
Aims & Methods: The 1-st group of patients with CD (n = 30) received MSCs, the dose of prednisone was not more than 20 mg/day. The second group of patients (n = 30) received standard anti-inflammatory drug therapy of 5-aminosalicylic acid (5-ASA) and glucocorticosteroids (GCS). Age of patients ranged from 19 to 49 years (Me-36 years). The disease was of moderate and high activity, length of damage - ileokolit, ileitis and colitis, the observation time ranged from 42 to 68 months. Clinical activity was assessed by the Crohn's disease activity index (CDAI). The culture of allogeneic MSCs injected drip at 2.5 million per 1 kg of body weight (0-1-26 weeks).
Results: CDAI in the 1st group was 242.6 ± 11.7 points, in the 2nd 240.9 ± 12.9 points (p = 0.83), CRP levels in 1st group was 29.3 ± 6.4 mg/l, the 2nd - 27.8 ± 4.8 (p = 0.47). After 1 year of follow-CDAI in 1st group was 70.0 ± 11.0 points, in the

2nd - 133.8 ± 22.2 points ($p < 0.001$), CRP levels in 1st group was 6.36 ± 1.5 mg/l, in the 2nd - 12.2 ± 2.9 ($p < 0.001$). After 2 years CDAI 1st group was 99.6 ± 19.3 points, in the 2nd - 147.1 ± 22.1 points ($p < 0.001$), CRP levels in 1-st group was 16.0 ± 6.0 mg/l, in the 2nd - 18.8 ± 4.4 ($p = 0.156$). After 3 years, the CDAI in 1st group was 110.5 ± 21.9 points, in the 2nd - 180.6 ± 20.3 points ($p < 0.001$), CRP levels in 1st group was 10.9 ± 2.6 mg/l, in the 2nd - 16.9 ± 3.0 ($p < 0.001$). After 4 years - the CDAI in 1st group was 120.0 ± 22.3 points, in the 2nd - 208.7 ± 17.6 points ($p < 0.001$), CRP levels in 1st group was 11.3 ± 2.6 mg/l, in the 2nd - 15.5 ± 2.4 ($p < 0.001$). After 5 years - the CDAI in 1st group was 126.0 ± 23.8 points, in the 2nd - 248.7 ± 14.6 points ($p < 0.001$), CRP levels in 1st group was 12, 3 ± 2.8 mg/l, in the 2nd - 19.5 ± 3.1 ($p < 0.001$). In the first group of patients in remission after 1, 2, 3, 4, and 5 years was kept at 70%, 56.6%, 50%, 46.7% and 33.3%, respectively. In the second group of patients at 1, 2, 3, 4, and 5-year remission was maintained at 36.6%, 26.6%, 13.3%, 6.67% and 6.67%, respectively. Complete healing of the intestinal mucosa in 60% of patients in the first group during the 1st year of observation, after 5 years - 26.7%. Over the entire period of observation never there were no malignant transformation, life-threatening infectious complications and death.

Conclusion: Transplantation of MSCs contributes to longer-term clinical and endoscopic remission in patients with refractory Crohn's disease compared with therapy with corticosteroids

Disclosure of Interest: None declared

P0992 CHANGES OF COLONIC MICROBIOTA AND EFFICACY OF ORAL PROBIOTIC THERAPY IN IBD

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Introduction: The mechanisms explaining complex relationship between the commensal colonic microbiota and inflammatory bowel disease (IBD) have a common outcome, a violation of bacterial antigens exposure to effector T-cells and innate immune cells residing in the intestinal mucosa and/or alteration of the host immune response to bacteria. While the role of gut microbiota and respective immune changes has become more evident in recent years there is no sufficient database explaining the character of microbiota changes in IBD. Expanding this idea, probiotics have been the subject of intensive research, mainly focusing on bifidobacteria and lactobacteria. However, existing reports of probiotic use in IBD are contradictory.

Aims & Methods: The aim of this study was to find relation between changes of colonic microbiota and IBD, introduce rarely used probiotic, and understand whether oral probiotic therapy with *P. Shermani* has any therapeutic significance in IBD. Totally 104 individuals participate in the study. Colonic resistance studied in mucosal bioptates. Standard aerobic and anaerobic microbiology techniques with nosology identification and quantity composition of microbiota were used. Specially designed strain of *P. Shermani* (T73) with high antagonistic potential was orally given twice on a daily basis during 150-180 days in a form of suspension containing 10^{12}-10^{14} bacteria. Patients without probiotic treatment formed control. Both groups' patients received mesalazine 1500-3000 mg daily as a basis therapy. Treatment efficacy evaluated according to WGO Global Guidelines and included CDAI, SF-36 and IBDQ scores.

Results: Major autochthonic species (14 in total) were present in all samples: among them Lactobacteria, Bifidobacteria, *E. coli*, several other anaerobic species were dominating. However, Lacto- and Bifidobacteria were found in significantly lower levels compared to healthy subjects ($p = 0.02$-0.0031). The general tendency for colonic resistance in IBD was decrease of autochthonic anaerobes (Bifido-, Lactobacteria, Bacteroides spp, Clostridia spp, Bacillae spp.) and significant growth of allochtonic aerobes and facultative anaerobes (*E.coli* Hly+, Pseudomonas, Serratia, Hafniae, *P. mirrabilis* and other conditionally pathogenic Enterobacteriaceae). Enterococci were present in 60.0% of healthy and 7.14-20.69% of IBD patients. Staphylococci were present only in IBD group (17.24-31.58%). There were 16.67% and 22.22% recurrences requiring hospitalization during the study period. CDAI score at the end of study was 49.37 ± 3.14 points lower in study group ($p < 0.05$). SF-36 score difference between groups became 11.8 ± 0.84 %. Abdominal pain, stool, and drug use for symptomatic therapies improved in study group, too. However, probiotic treatment did not influence anemia and other extraabdominal symptoms. Endoscopic picture and biopsies presented no specific differences between groups after treatment.

Conclusion: Our data suggest that morbid changes of colonic mucosal microbiota, e.g. abnormal ratio of autochtonic and allochtonic species, may be considered as a strong characteristic feature of IBD. We hypothesized that results of existing studies of probiotic use in IBD are confusing due to improper selection of probiotic agent. *P. Shermani* T73 is comparatively rare and understudied probiotic, showing its usefulness for use in IBD.

Disclosure of Interest: None declared

P0993 6-THIOGUANINE AS AN ALTERNATIVE THERAPY IN INFLAMMATORY BOWEL DISEASE - EXPERIENCE IN A LONDON DISTRICT GENERAL HOSPITAL

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Introduction: Conventional thiopurines (Azathioprine/6-Mercaptopurine) remain the cornerstone of maintaining remission in steroid-dependent inflammatory bowel disease (IBD). Despite the well-documented efficacy of these drugs, more than 50% of patients discontinue treatment due to adverse events or therapy resistance. Over the past decade, there has been renewed interest in the use of 6-thioguanine (TG), an agent historically used in haematological malignancy. With a shorter metabolic pathway, TG possesses a favourable side effect profile and it's use as an alternative thiopurine in IBD is growing. We report our experience in tolerability, safety and efficacy of TG use in a London district general hospital.

Aims & Methods: A retrospective review of electronic patient records including clinic letters, blood tests and endoscopic findings were carried out on patients commenced on TG between 2012 and 2015. Data was collected on patient demographics, indication and duration of therapy, response rates and reasons for treatment failure.

Results: A total of 28 patients received TG and median treatment duration was 14 months (range 1-40). Therapy was equally distributed amongst males and females (14:14), and mean age was 44 years (range 19-67). 14 (50%) patients had Ulcerative colitis (UC), 13 (46%) Crohn's disease (CD) and 1 (4%) Indeterminate colitis. 24 patients (86%) received TG due to adverse reactions to conventional thiopurines vs. 3 patients (11%) who were non-responders. Treatment with TG resulted in clinical remission in 86% (19/22) patients at 6 months and 75% (12/16) at 12 months. In total, 6 patients (21%) discontinued TG. 4 patients failed treatment (2 continued alternative medical therapy and 2 had surgery) and 2 suffered adverse events (headaches and confusion). Tolerability and efficacy rates were similar in both UC and CD groups. All patients underwent blood monitoring and no abnormalities in liver function tests were detected. Of those who underwent MRI liver there was no evidence of nodular regenerative hyperplasia.

Conclusion: TG was well tolerated with comparable remission rates to conventional thiopurine therapy. We advocate the use of TG therapy in selected cases where conventional thiopurine therapy has failed or resulted in adverse reactions. Larger prospective trials are required to further evaluate the efficacy and safety of TG, with a view to potentially incorporate it's use into clinical guidelines.

Disclosure of Interest: None declared

P0994 IMPACT OF ANTIBIOTIC TREATMENT BEFORE FAECAL MICROBIOTA TRANSPLANTATION (FMT) IN CHRONIC ACTIVE ULCERATIVE COLITIS

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Introduction: Faecal microbiota transplantation (FMT) is investigated as a new therapeutic tool in chronic active ulcerative colitis (UC). The efficacy however, varies among distinct study protocols for FMT administration. The aim of this study was to investigate the impact of antibiotic treatment before FMT for therapy refractory chronic active UC.

Aims & Methods: 27 patients with chronic active UC were treated with an antibiotic triple therapy for 10 days. Afterwards 17/27 patients received FMT via colonoscopy into the right colon, which was repeated in 14 days intervals by sigmoidoscopy for a total of 5 applications (FMT group). 10/27 patients received antibiotic triple therapy without subsequent FMT and any other therapy (AB group). Clinical efficacy was assessed by total mayo score. Furthermore disease activity was also measured by faecal calprotectin and endoscopy. The follow up of the patients were 90 days and end of follow up to 30 weeks respectively.

Results: Antibiotic treatment led to an overall reduction of the Mayo score from 8.4 to 6.8 in all patients (9.0 to 7.3 in the FMT group; 7.5 to 5.9 in the AB group) within 10 days. In contrast to sole antibiotic therapy, FMT showed an additional benefit in the follow-up period of 30 weeks (total Mayo score FMT group 9.0 to 4.7 points vs 7.5 to 6.3 in the AB group). Adherence to therapy during follow up in the AB group was low (5/10; 50%) due to *Clostridium difficile* infection (3/10), acute UC flare (1/10) and antibiotic-associated diarrhea (n = 1/10) vs. 100% in the FMT group. Overall, at day 90 clinical remission was assessed in 4/17 patients (total Mayo score $\leq$ 2), partial responders in 6/17 patients (reduction of total Mayo score $\geq$ 3 points) in the FMT group, versus partial response in 2/5 patients in the AB group.

Conclusion: Our data demonstrate a clinical benefit of antibiotic treatment before FMT in chronic active UC, whereas antibiotic therapy without consecutive FMT in chronic active UC is poorly tolerated.

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Disclosure of Interest: None declared

P0995 USTEKINUMAB EFFICACY AND SAFETY IN CROHN'S DISEASE PATIENTS REFRACTORY TO CONVENTIONAL AND ANTI-TNF THERAPY: A MULTICENTER RETROSPECTIVE EXPERIENCE

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Introduction: Ustekinumab, a human monoclonal antibody against the p40 subunit of interleukin (IL)-12 and IL-23, has been shown to be effective in Crohn's disease (CD) patients refractory to anti-tumor necrosis factor (TNF) in a phase-2 trial.
Aims & Methods: The aim of the present study was to assess benefit and safety of subcutaneous (SC) ustekinumab in a multicenter cohort of anti-TNF refractory CD patients. A retrospective observational study was conducted in tertiary centers from the GETAID, including all consecutive active CD patients refractory to anti-TNF treatment, who received at least one SC injection of ustekinumab and had a follow-up of at least 3 months. The primary outcome was ustekinumab clinical benefit at 3 months, defined by a significant improvement as judged by the physician leading to continue the treatment with complete steroids weaning if given at inclusion. Ustekinumab safety and clinical benefit at 6 and 12 months were also recorded.
Results: One hundred twenty-two patients (87 females, median age: 38.8 years, IQR: 27.5-43.9) received at least one SC ustekinumab injection in 20 centers from France and Switzerland. At baseline, median disease duration was 12.9 years (IQR: 6.9-17.1); 119 (97.5%) patients experienced previous failure or intolerance to thiopurines or methotrexate and 122 (100%) patients have failed to at least one anti-TNF agent (infliximab or adalimumab, with 112 (91.8%) subjects who received both anti-TNFs) and 75 (61.5%) patients underwent prior intestinal resection. Ustekinumab was given for luminal CD to 110 (90.2%) patients and for perianal disease to 12 (9.8%). At inclusion, 18 (14.7%) patients received immunosuppressant (IS) and 19 (15.6%) steroids. Clinical benefit of ustekinumab at 3 months was observed in 79/122 (64.7%) patients in the whole population and in 8/12 (67%) patients treated for perianal disease. Concomitant IS at inclusion was the sole predictive factor of clinical benefit to ustekinumab at 3 months with an odds ratio of 5.43 (95% CI: 1.14- 25.77; $p = 0.03$). With a median follow-up duration of 9.8 months (IQR: 4.9-14.5 months), cumulative probability of maintained clinical benefit (without surgery, steroids or IS introduction) at 6 and 12 months was 92.8% and 68.2%, respectively. Twenty patients (16.4%) developed an adverse event with only one severe adverse event.
Conclusion: Clinical benefit of a SC ustekinumab induction was observed in two out of three CD patients and was maintained in majority of patients for up to 12 months. Pending results from ongoing trials, ustekinumab can be considered in CD patients refractory to anti-TNF agents.
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P0996 MAINTENANCE TREATMENT WITH GRANULOCYTE/MONOCYTE ADSORPTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND AN INITIAL RESPONSE TO TREATMENT. A SWEDISH LONG-TERM PROSPECTIVE REGISTRY STUDY

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Introduction: Inflammatory bowel diseases (IBD) are chronic with different character and intermittent or more rarely continuous inflammatory activity. The activity ranges from mild to severe. The response to treatment varies and the choice of treatment is still partly arbitrary. Some patients represent a particular problem due to lack of response or intolerance to conventional treatment. There is a lack of data on results from maintenance treatment with Granulocyte/Monocyte Adsorption (GMA) in patients with an initial response to treatment.
Aims & Methods: 136 patients, 54 with ulcerative colitis (UC), 81 with Crohńs disease (CD) and 1 with indeterminate colitis (IC) were included in a registry covering the majority of patients treated with GMA in Sweden. The disease activity was mainly mild or moderate. 49 IBD-patients initially achieving clinical response 3 month after a GMA course received maintenance treatment with GMA. The GMA maintenance treatments were scheduled with one of the following: one session monthly, every second month, every third month and every fourth month according to relapse rate and disease severity. Included patients were followed every third month for 12 months after induction GMA treatment. Monitoring includes symptoms (short health scale), activity indices (HBI, SCCAI) and fecal calprotectin.
Results: Overall, burden of symptoms, activity indices and fecal calprotectin levels remained at the same low level throughout the maintenance treatment period.
Conclusion: Maintenance treatment with GMA is effective in patients with an initial good response.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00–17:00
PAEDIATRIC: LOWER GI – HALL 7

P0997 METRONIDAZOL VERUS RIFAXIMIN IN THE TREATMENT OF CLOSTRIDIUM DIFFICILE INFECTION IN INFLAMMATORY BOWEL DISEASE CHILDREN: A RANDOMIZED STUDY

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Introduction: The aim of the study was to compare the effectiveness of metronidazole and rifaximin in the treatment of *Clostridium difficile* infection (CDI) in pediatric patients with inflammatory bowel disease (IBD).
Aims & Methods: We conducted a prospective, double-blinded, randomized trial with children age 12-18 years. Crohn's disease (CD) and ulcerative colitis (UC) were diagnosed according to Porto criteria. CDI diagnosis was based on a positive stool VIDAS® *Clostridium difficile* toxin A/B ELFA (bioMerieux, France) test. Patients were randomly assigned to receive metronidazole or rifaximin for 14 days; doses of drugs were weight-adjusted. Stool samples were collected before and 4 weeks after the end of treatment.
Results: In the present study, 26 patients were enrolled (mean age 14.3 years), including 9 with CD and 17 with UC. 14 received metronidazole and 12 received rifaximin. There were no statistically significant differences between study groups in age, gender and disease type. 4 weeks after the end of treatment *Clostridium difficile* toxins were found in 5/14 (36%) patients in metronidazole group and in 4/12 (33.3%) patients in rifaximin group (n = NS).
Conclusion: Metronidazole and rifaximin was equally effective in the treatment of CDI in pediatric patients with IBD.
Disclosure of Interest: None declared

P0999 ITEM GENERATION AND REDUCTION OF THE "TUMMY" INDEX, A NEWLY DERIVED PATIENT REPORTED OUTCOME (PRO) FOR PEDIATRIC ULCERATIVE COLITIS

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Introduction: The Pediatric Ulcerative Colitis Activity Index (PUCAI) is a non-invasive clinician-based index, proven to reflect well mucosal inflammation in pediatric ulcerative colitis (UC). Under the qualification program of the FDA and EMA, we aimed here to develop a Patient Reported Outcome (PRO) measure of signs and symptoms for pediatric UC (i.e. the TUMMY index) to complement the PUCAI, when used with endoscopic assessment. The derived questionnaire will enable calculating both the TUMMY and the PUCAI scores independently.
Aims & Methods: We performed qualitative interviews- 35 with UC children (age 12.3 ± 3.2, range 4-18 years; 50% males; 83% with extensive colitis; 25% with moderate-severe disease) and 25 with their caregivers, in Israel, England, Ireland, Canada and the USA, to ensure cultural diversity. Interviews were centered at exploring signs and symptoms reflecting the colitis and which are important to children. Items were rank ordered according to the frequency of endorsement and importance, graded on a 1-5 scale by the interviewees.
Results: There was a general agreement between the total scoring of the children and their caregivers. The following items were identified in decreasing order of weights (importance X frequency): abdominal pain (4), rectal bleeding (3.5), stool frequency (2.8), stool consistency (2.8), general well-being (2.8), urgency (1.8), and nocturnal stools (1.7). Two other items were scored low and are perceived as having low accuracy (lack of appetite (1) and weight loss (0.6)). Children 13-18 years comprehended adult vocabulary, 8-12 years simple vocabulary and younger children had poor understanding and thus their disease may be more accurately scored by a caregiver-reported questionnaire.
Conclusion: In this first report of the TUMMY development, items were generated and ranked by input purely from patients. These items are now being explored for optimal vocabulary and response options. The TUMMY index will supplement the PUCAI in clinical trial outcome assessment.
Disclosure of Interest: L. Marcovitch: None declared, A. Nissan: None declared, D. Mack: None declared, A. Otley: None declared, S. Hussey: None declared, M. Kappelman: None declared, B. Mclean: None declared, N. Croft: None declared, F. Barakat: None declared, A. Griffiths: None declared, D. Turner Financial support for research: This study was funded by a grant from Janssen, Conflict with: Royalties from SickKdis

Abstract number: P1000 Table: Concordance and discordance of PCDAI remission and CDAI remission in patients aged 13–17 yrs with CD treated with ADA in IMAgINE 1.

Week	PCDAI remission & CDAI remissionn (%)	No PCDAI remission & no CDAI remissionn (%)	Concordantn (%)	No PCDAI remission & CDAI remissionn (%)	PCDAI remission & no CDAI remissionn (%)	Discordantn (%)
26	44 (36.1)	59 (48.4)	103 (84.4)	18 (14.8)	1 (0.8)	19 (15.6)
52	37 (30.3)	77 (63.1)	114 (93.4)	7 (5.7)	1 (0.8)	8 (6.6)

P1000 RELATIONSHIP OF THE PEDIATRIC CROHN'S DISEASE ACTIVITY INDEX (PCDAI) AND CROHN'S DISEASE ACTIVITY INDEX (CDAI) IN IMAGINE 1

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Introduction: The Pediatric Crohn's Disease Activity Index (PCDAI) assesses disease activity in children and adolescents with Crohn's disease (CD), and was developed to take in account more objective measures than the Crohn's Disease Activity Index (CDAI). Although both indices have similar components, the PCDAI includes additional laboratory measures and disease features specific to children and adolescents with CD. In IMAgINE 1, a 52-week (wk), phase 3, multicenter, randomized open-label induction/double-blind maintenance trial of adalimumab (ADA) in 192 patients aged 6–17 yrs with CD, both PCDAI and CDAI were calculated for patients aged 13–17 yrs.[1]
Aims & Methods: This post-hoc analysis evaluated concordance of remission status based on PCDAI and CDAI. Patients in IMAgINE 1 had CD with a baseline PCDAI score >30 and were intolerant or resistant to conventional therapy. Patients received open-label ADA induction at weeks 0/2 based on body weight (≥40 kg, 160/80mg; <40 kg, 80/40 mg). At wk 4, patients were randomized to higher (≥40 kg, 40 mg every other wk [eow]; <40 kg, 20 mg eow) [HD] or lower dose (≥40 kg, 20 mg eow; <40 kg, 10 mg eow) ADA maintenance therapy. The agreement of PCDAI remission (PCDAI score ≤10) and CDAI remission (CDAI score <150) at wks 26 and 52 was evaluated in both dosing groups combined. Non-responder imputation was used for missing data.
Results: Of 188 patients who entered the double-blind maintenance period of IMAgINE 1, 122 were aged 13–17 yrs. PCDAI remission rates at weeks 26 and 52 were 37% (45/122) and 31% (38/122), respectively; CDAI remission rates at weeks 26 and 52 were 51% (62/122) and 36% (44/122), respectively. At wk 26, 36% (44/122) patients achieved both PCDAI and CDAI remission, and 48% (59/122) had neither PCDAI nor CDAI remission (**Table**); thus, the agreement between measures was 84% (Kappa = 0.6899; $p < 0.001$) At wk 52, 30% (37/122) patients achieved both PCDAI and CDAI remission, and 63% (77/122) had neither PCDAI nor CDAI remission (**Table**); thus, the agreement between measures was 93% (Kappa = 0.8535; $p < 0.001$).
Conclusion: Agreement among PCDAI and CDAI was moderate to substantial at weeks 26 and 52. However, CDAI may over estimate remission in pediatric CD given the higher overall rates of remission by this metric. The agreement of PCDAI and CDAI with other outcome measures requires further exploration.

Reference

1. Hyams JS, et al. *Gastroenterology* 2012; 143: 365–74.

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P1001 INCIDENCE AND PHENOTYPE AT DIAGNOSIS IN VERY EARLY COMPARED TO LATER-ONSET PEDIATRIC INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY (1988-2011)

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Introduction: Age at diagnosis of inflammatory bowel disease (IBD) in children has taken an important role and very early onset IBD (VEO-IBD; diagnosis < 6 years) seem to be a form of IBD distinct from that of older children.
Aims & Methods: We aimed to compare the incidence and phenotype at diagnosis of VEO-IBD and IBD in older children (6-17 years) from a French population-based study over a 24-year period. We extracted the pediatric IBD cohort through the population-based Registry from 1988 to 2011.
Results: In total, 1412 children (8% of all IBD) have been recorded including 42 (3%) with VEO-IBD. The incidence of overall IBD in children increased from $3.0/10^5$ in 1988-1990 to 6.3 in 2009-2011 (+110 %; $p < 10^{-3}$). The incidence remained stable among VEO-IBD children ($0.4/10^5$ from 1988-1990 to 2009-2011) while it increased from 1.6 to $3.5/10^5$ (+119%; $p < 10^{-3}$) among 6-9 years old, and from 6.1 to $13.1/10^5$ (+115%; $p < 10^{-3}$) among children ≥ 10 years old. The initial classification as ulcerative colitis (UC) or IBD unclassified (IBDU) was more common among the VEO-IBD group (40% *vs* 26%; p = 0.05). Differences in phenotype according to age at diagnosis are summarized in the Table.

Variables at diagnosis	< 6 years at diagnosis	6-17 years at diagnosis	P-value
All IBD	N = 42 (3%)	N = 1370 (97%)	
Crohn's Disease (CD)	N = 25 (60%)	N = 1007 (74%)	
UC	N = 14 (33%)	N = 329 (24%)	
Diagnosis at Hospital	**69%**	**42%**	**$< 10^{-3}$**
Male	52%	52%	0.92
Diarrhea	76%	66%	0.15
Rectal bleeding	**81%**	**45%**	**$< 10^{-4}$**
Mucous stools	**40%**	**21%**	**$< 10^{-2}$**
Abdominal pain	**43%**	**74%**	**$< 10^{-4}$**
Weight loss	**21%**	**49%**	**$< 10^{-3}$**
EIMs*	17%	17%	0.97
Growth failure (Z score weight/height < 2)	17%	10%	0.14
Diagnosis delay > 6 months	27%	30%	0.67
IBD family history	9%	15%	0.30
Complicated behavior in CD (B2 + B3**)	5%	17%	0.20
Anoperineal lesions in CD	8%	6%	0.65
Pure colonic location in CD (L2)**	**36%**	**13%**	**$< 10^{-2}$**
Proctitis in UC (E1**)	9%	30%	0.12
Extensive colitis in UC (E4**)	55%	43%	0.31

* Extra intestinal manifestations** According to Paris classification

Conclusion: According to the present retrospective population-based study, the incidence of VEO-IBD was low and remained stable from 1988 to 2011. Children diagnosed with VEO-IBD were more often diagnosed in hospital than those diagnosed after the age of 6. VEO-CD children presented more rectal symptoms, presumably in relation to a high prevalence of isolated colonic CD.
Disclosure of Interest: None declared

P1002 PREVENTION OF LOSS OF RESPONSE TO TNF-A BLOCKERS IN PAEDIATRIC AND ADULT IBD PATIENTS BY USING THE GRAZ ALGORITHM

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Introduction: Treatment in inflammatory bowel diseases (IBD; Crohn's disease [CD] and ulcerative colitis [UC]) has improved due to biologics. However, a problem is loss of response (LOR) maybe due to the formation of antibodies against these biologics. Our aim was to investigate antibody response against standard biologics infliximab (IFX) and adalimumab (ADA) in paediatric and adult patients with IBD and develop an algorithm to avoid a LOR.
Aims & Methods: We conducted a prospective, multi-center study assessing antibody levels in IBD patients with active disease by an enzyme-linked immunoassay (Immunodiagnostik AG, Bensheim, Germany) which is able to measure free and bound antibodies against IFX or ADA. We investigated a

Abstract number: P1003 Table: Demographics and baseline characteristics by disease severity (intent-to-treat population)

	Moderate CD (PCDAI < 40) (N = 80)	Severe CD (PCDAI ≥ 40) (N = 108)
Age, years, mean (SD)	14.0 (2.4)	13.4 (2.5)
Male, n (%)	41 (51.3)	64 (59.3)
CRP, mg/dL, median (range)	0.65 (0, 16.8)[a]	1.76 (0, 14.4)
Prior CD-related immunomodulator use, n (%)	73 (91.3)	96 (88.9)
Prior CD-related corticosteroid use, n (%)	59 (73.8)	86 (79.6)
Prior infliximab use, n (%)	32 (40.0)	51 (47.2)
Concomitant CD-related immunomodulator use, n (%)	51 (63.8)	66 (61.1)
Concomitant CD-related corticosteroid use, n (%)	26 (32.5)	45 (41.7)
Disease duration , year, mean (SD)	3.1 (2.3)	2.9 (2.2)
PCDAI, mean (SD)	34.8 (2.4)	45.7 (5.5)
CD location, n (%)		
-Anal/Perianal	20 (25.0)	34 (31.5)
-Colon	67 (83.8)	87 (80.6)
-Ileum	64 (80.0)	81 (75.0)
Draining fistulas, n (%)	12 (15.0)	24 (22.2)
IMPACT III score, mean (SD)	118.2 (16.1)[b]	112.0 (18.0)[c]

[a]N = 78, [b]N = 77, [c]N = 104

possible correlation between LOR during therapy and positive antibodies and furthermore linked clinics with antibody levels. LOR was defined as dose escalation, discontinuation of treatment or shortening of dosage interval.

Results: One-hundred-and-eighty-eight patients were included. 27/91 of CD patients (30%) and 12/45 (27%) of UC patients with IFX therapy showed positive antibody levels. In the ADA group in 3/46 (7%) with CD and 1/6 (17%) with UC antibodies were detected. 27% of antibody-positive CD patients and 100% of UC patients with IFX therapy had a LOR, whereas 67% of antibody-positive CD patients and 100% of UC patients had a LOR under ADA. Correlation with clinics showed that most of the patients with positive antibodies showed low IFX or ADA levels with 63% and 43%, respectively. Furthermore, an algorithm was developed including drug monitoring for dose optimization and antidrug monitoring to consider switch of medication.

Conclusion: Our study suggests that occurrence of antidrug antibodies is a frequent event associated with LOR. By using an algorithm antidrug and drug monitoring may support optimal treatment of paediatric and adult patients receiving biological therapies in IBD.

Disclosure of Interest: None declared

P1003 BURDEN OF DISEASE IN PAEDIATRIC PATIENTS WITH MODERATE VERSUS SEVERE CROHN'S DISEASE IN THE IMAGINE 1 TRIAL

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Introduction: Biologic therapy is generally reserved for children with moderate to severe Crohn's disease (CD), however, distinguishing moderate from severe disease by the Paediatric CD Activity Index (PCDAI) can be difficult.[1]

Aims & Methods: To compare disease burden in patients (pts) classified as moderate *vs* severe by PCDAI in IMAgINE 1,[2] a 52 week (wk) trial of adalimumab in which pts aged 6-17 years with CD and baseline (BL) PCDAI > 30 were enrolled. All pts had failed concurrent or prior corticosteroids (CS) and/or immunomodulators (IMM) therapy. Infliximab (IFX)-exposed pts could enroll. BL characteristics, demographics, and the proportion of pts with a BL score of 10 (worst score) for at least one of the PCDAI components of abdominal pain (AP), stool frequency (SF), and general well-being (GW) were assessed in pts with moderate (PCDAI < 40) and severe CD (PCDAI ≥ 40) as defined by the median PCDAI at BL.

Results: The intent-to-treat population included 188 of 192 pts enrolled. 43% (80) had moderate and 57% (108) had severe CD at BL. Demographics, CD activity, prior and concomitant CD-related IMM and CS use, prior IFX use, and IMPACT III scores at BL were similar for both groups (Table). Median CRP was numerically higher in pts with severe *vs* moderate CD (1.76 *vs* 0.65 mg/dL), but ranges largely overlapped. A similar proportion of pts with moderate and severe CD (83 *vs* 95%) had the most severe score of 10 at BL for at least one of the PCDAI components of AP, SF, or GW.

Conclusion: Clinical characteristics and treatments administered to pts with moderate or severe disease activity by PCDAI were similar. Overall, the disease burden in the moderate pts was similar to severe pts in IMAgINE 1.

References

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P1004 REDUCTION OF ANTI-INFLIXIMAB ANTIBODY FORMATION IN PAEDIATRIC CROHN'S PATIENTS ON CONCOMITANT IMMUNOMODULATORS

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Introduction: Combining thiopurines with infliximab might reduce antibody formation against infliximab, but no paediatric data supporting this assumption are available yet.

Aims & Methods: Evaluation of the effect of concomitant immunomodulator use on formation of antibodies to infliximab (ATI) in paediatric patients with Crohn's disease (CD) and the association of ATI appearance and loss of response. In this retrospective nationwide multicentre observational study we collected clinical and biochemical data of children diagnosed with CD treated with infliximab between 2009 and 2014. ATI formation was analysed with Chi-square test and time to ATI formation with Kaplan-Meier and log rank test. Loss of response was defined as need for either surgery or switch to other medical therapy than infliximab.

Results: In total, 229 children were identified (138 men, median 25 months on infliximab). Eighty-six patients (38%) received continuous combined immunosuppression (CCI) with infliximab, 115 patients (50%) early combined immunosuppression (ECI) (median 6.2 months), followed by infliximab monotherapy, and 28 patients (12%) infliximab monotherapy (IFX). Overall 25 of 229 patients (11%) developed ATIs: 6 on CCI (7%), 11 on ECI (10%) and 8 on IFX (29%)

after respectively 6, 25, and 11 months (median). Antibodies were measured in 162 patients (70.7%). The incidence of ATI formation was higher in patients receiving IFX compared to CCI (p = 0.006) and ECI (p = 0.01), while no significant difference was found between CCI and ECI (log rank overall 0.004). Sixteen out of 25 patients (64%) developing ATIs had loss of response, versus 32 of 204 patients (16%) without ATIs (p = 0.0001, log rank 0.01). When focusing on the group early combined immunosuppression, 10 out of 80 patients (12.5%) developed ATIs when receiving less than 12 months combination therapy, compared to 1of 35 (2.9%) patients receiving more than 12 months combination therapy.

	Concomitant immunomodulator use	
	< 12 months	> 12 months
ATI, n (%)	10 (12.5)	1 (2.9)
Non-ATI, n (%)	70 (87.5)	34 (97.1)
Total	80	35

Conclusion: Combination therapy is superior to infliximab monotherapy as it significantly reduces antibody formation and loss of response in children with CD. Concerns about the lymphoproliferative risk of long-term use of thiopurines make that early combined immunosuppression for at least 12 months, followed by infliximab monotherapy, might be a safer and equally effective alternative to continuous combined immunosuppression.
Disclosure of Interest: None declared

P1005 CLINICAL REMISSION INDUCED BY EXCLUSIVE ENTERAL NUTRITION (EEN) IN PEDIATRIC CROHN'S DISEASE IS ASSOCIATED WITH MICROBIOME METABOLIC CHANGES TOWARD INCREASED XENOBIOTIC BIODEGRADATION AND METABOLISM

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Introduction: The mode of action of exclusive enteral nutrition (EEN) as induction therapy in pediatric Crohn's disease (CD), is proposed to involve changes in gut microbiome structure and function. Characterization of the microbiome has largely focused on the assessment of diversity and the identification of protective and disease-associated species.
Aims & Methods: Our aims were to compare microbial community structure and function in pediatric CD patients before and after induction of remission by EEN treatment. Community structure was assessed in terms of phylotypes, and function was assessed in terms of metabolic pathways.
Stool metagenomic sequences of 5 pediatric CD patients who underwent EEN treatment were obtained (MiSeq). Sequences were searched against the green genes database to obtain microbial composition profiles (using 16S rRNA genes). To obtain functional assignment, sequences were searched against 28 representative KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways and HUMAnN to assign function. Samples collected prior to EEN treatment were compared to samples collected after 4, 8 or 12 weeks of EEN treatment. All participants achieved clinical remission (PCDAI < 10) after 12 weeks of EEN. Microbial composition profiles were analyzed using QIIME and STAMP, and functional profiles were inferred using STAMP and BiomeNet.
Results: Changes in CD patient microbial community structure before and during EEN were variable. However, functional profiling of CD patient microbiota before and during EEN treatment revealed a significant increase in metabolic functions related to biodegradation and metabolism of xenobiotics, such as benzoate ($p < 0.05$). BiomeNet uncovered changes during weeks 4 and 8 of treatment consistent with large-scale changes in metabolic interactions at the community level. We observed associated changes in community diversity: a decrease and then increase in diversity over the course of EEN treatment. Metabolic potential generally increased at the same time as diversity decreased. This could be due to the metabolic repertoire of those species that were present (as inferred from enzyme encoding gene sequences). Bayesian modeling of metabolic structures via BiomeNet revealed that the therapeutic effect of EEN might be predicted by monitoring the change in community level metabolic structures over the course of treatment.
Induction of clinical remission by EEN was characterized by a distinct cycle of change in community level metabolic structure, and the microbiome of the one patient that experienced several severe flare-ups did not complete this cycle of change. This finding suggests that community metabolic function could be monitored for the purpose of determining if the duration of EEN was sufficient to maintain a flare free state. Alternatively, patients who complete the cycle quickly might discontinue EEN early.
Conclusion: The microbiome of CD patients is functionally altered during EEN treatment. Metabolic potential for xenobiotic biodegradation and metabolism increases during treatment, but then, after 12 weeks, it returns to a state very similar to pre-treatment and controls.
Disclosure of Interest: None declared

P1006 EFFECT OF EARLY VERSUS LATE AZATHIOPRINE TREATMENT IN PEDIATRIC ULCERATIVE COLITIS: DATA FROM THE ITALIAN REGISTRY FOR PEDIATRIC IBD

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Introduction: Thiopurines, 6-mercaptopurine and azathioprine (AZA), are the mainstay in maintenance therapy of pediatric ulcerative colitis (UC).
Aims & Methods: We aimed at describing the efficacy of AZA in newly diagnosed pediatric UC, comparing the outcomes of "early" (0-6 months) versus "late" (6-12 months) initiation of therapy.
Data from all children with UC treated with AZA within 12 months after the diagnosis and included in the SIGENP prospective, multicenter registry, were included. Corticosteroid (CS) free remission at 12 months was the primary outcome evaluated. The 2 groups were also compared for mucosal healing, need for treatment escalation, therapy-related adverse events and need for surgery at a 24-month follow-up.
Results: Of 401 children with a diagnosis of UC, 166 were treated with AZA within the first year of diagnosis. Seventy-one patients were excluded because of a follow-up shorter than 1 year, thus 95 were included for efficacy analyses (mean age 10.7 ± 3.8 years, 59% females). Fifty-four patients (57%) started AZA between 0–6 months (early), 41 (43%) after 6–12 months (late). Twenty-seven (51%) of the "early" patients were in CS-free remission at 1 year, compared to 24 (61.5%) of the "late" ones (p = 0.39). Mucosal healing occurred in 26 (39%) of the 66 patients for whom data on mucosal inflammation at 1 year were available, no difference was found between the two groups (32% "early" versus 45% "late"; p = 0.45). Serious adverse events occurred in 3 patients (2 fungal pneumonia, 1 pancreatitis), 2 in the "early" and 1 in the "late" group. Overall, mild side effects were recorded in 16 patients (17%; 5 leucopenia, 11 pancreatic enzyme elevation):10 in the "early" and 6 in the "late" group (p = 0.78), 3 requiring AZA discontinuation. No difference was found for the need of treatment escalation, use of infliximab over time and rate of surgery.
Conclusion: Introduction of AZA within 6 months of diagnosis is not more effective than later treatment to achieve CS-free remission in pediatric UC. The rate of mucosal healing is not related to the timing of AZA initiation. Serious adverse events related to treatment are uncommon.
Disclosure of Interest: None declared

P1007 MONITORING MUCOSAL HEALING WITH FAECAL CALPROTECTIN IN CHILDREN WITH ULCERATIVE COLITIS

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Introduction: Faecal calprotectin (FC) is a good marker in monitoring mucosal healing in adults with ulcerative colitis. Its concentration in faeces is closely related to state of mucosa observed in endoscopy. There are a few studies concerning FC in mucosa status assessment in paediatrics population with inflammatory bowel disease.
Aims & Methods: The aim of the study was to assess the usefulness of FC as a biomarker of endoscopy proven mucosal healing in monitoring of children with UC. 81 patients with UC (F 43, M 38, ±14.04 years) were involved to the study and had elective colonoscopy performed, FC level and erythrocyte sedimentation rate (ESR) within a week before endoscopy measured. Each patient had also body mass index (BMI) and paediatric ulcerative colitis activity index (PUCAI) calculated. Mucosa status during endoscopy was assessed with Baron score. Full mucosal healing was defined as Baron score = 0. We have identified two subgroups: those with full mucosal healing, and patients with inflamed gut mucosa. The receiver operating characteristic curve (ROC) was used as a statistical method to establish cut-off points. The cut-off points are calprotectin threshold for simple model and posterior probability threshold for the linear discriminant analysis (LDA). The area under the curve (AUC) assesses the differentiation quality of the study group based on the model score. To increase sensitivity at high specificity the LDA with FC, ESR, BMI and PUCAI was taken.
Results: AUC for the simple model was 0.86. The selected cut-off level of discrimination between subgroup with full mucosal healing vs. subgroup with mucosal inflammation present was 274 μg/g with sensitivity 0.97 and specificity 0.62. When specificity was outweighed over sensitivity the cut-off point was 37 μg/g with sensitivity 0.32 and specificity 0.94. Due to the low sensitivity accompanying high specificity we used LDA with other parameters to increase sensitivity rate. With LDA used on FC, ESR, BMI and PUCAI the AUC was 0.88, and we could discriminate our patient with sensitivity 0.53 and specificity 0.96.
Conclusion: FC is a good marker of mucosal healing in monitoring of children with UC. FC above 274 μg/g enable to select 62% of patients with active inflammation in gut mucosa. LDA with FC, ESR, BMI and PUCAI let us

select 53% of patients with full mucosal healing. Using these two methods, step by step, we could discriminate patients with unknown mucosa status, that requires endoscopy.
Disclosure of Interest: None declared

P1008 REMISSION INDUCTION IN CORTICOSTEROID-NAÏVE CHILDREN AND ADOLESCENTS WITH ACTIVE ULCERATIVE COLITIS BY ADSORPTIVE LEUCOCYTAPHERESIS AS MONOTHERAPY OR IN COMBINATION WITH LOW-DOSE PREDNISOLONE AFTER FAILURE OF FIRST-LINE MEDICATIONS

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Introduction: Given that patients with active ulcerative colitis (UC) have elevated and activated myeloid lineage leucocytes including the CD14 + CD16+ monocyte phenotype known to release tumour necrosis factor-α, selective depletion of myeloid leucocytes by adsorptive granulocyte/monocyte apheresis (GMA, Adacolumn) should promote remission, or enhance drug efficacy. This strategy is most relevant in paediatrics and adolescents in whom corticosteroids raise safety concerns.
Aims & Methods: This study was to evaluate the efficacy of GMA in children and adolescents with active UC in whom conventional first-line medications had failed. In a single centre setting, between 2010 and 2014, a total of 28 consecutive children and adolescents, age 11-19 years, body weight 33-55kg were given mesalazine (n = 21) or sulphasalazine (n = 7) as a first-line medication. Twenty patients relapsed or did not respond and received GMA with the Adacolumn, 2 sessions in the first week, then weekly, up to 11 sessions. Patients who achieved a decrease of $\geq$5 in the clinical activity index (CAI) continued with GMA, while non-responders received 0.5 to 1.0 mg/kg/day prednisolone plus additional GMA sessions. At entry and week 12, patients were clinically and endoscopically evaluated, allowing each patient to serve as her (or his) own control.
Results: At entry, all 28 patients were corticosteroid naïve and none had deep colonic UC lesions together with extensive loss of the mucosal tissue at the affected sites. Eight patients achieved remission with the first-line medications and did not receive GMA. Six patients did not respond well to the first 5 GMA sessions and received prednisolone plus GMA, while 12 patients responded to the first 5 GMA sessions and received additional sessions and 2 withdrew. At entry, the average CAI was 14.2 ± 0.4, range 11-17, and the average endoscopic index was 9.2 ± 0.4, range 7-11. The corresponding values at week 12 were 2.1 ± 0.2, range 1-4 ($P < 0.001$) and 2.4 ± 0.2, range 1-4 ($P < 0.001$). Prednisolone was tapered to 0mg within 3 months. Therefore, at week 12, all 26 patients had achieved clinical remission, majority with mucosal healing (complete remission). No serious adverse event associated with GMA was observed.
Conclusion: GMA in patients with deep ulcers and extensive loss of the mucosal tissue (a major GMA non-responder feature) has not been associated with significant efficacy. In this study, GMA in young corticosteroid naïve patients with active UC refractory to the first-line medications was associated with clinical remission and mucosal healing, while in non-responders to GMA monotherapy, addition of a low dose prednisolone enhanced the efficacy of GMA and tapering of prednisolone was not associated with UC relapse. Therefore, the majority of young steroid-naïve UC patients who fail to respond to the first-line medications should respond well to GMA and avoid pharmacologicals.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00–17:00
OTHER LOWER GI DISORDERS II – HALL 7

P1010 CLOSTRIDIUM DIFFICILE INFECTION: COMPARISON OF DIAGNOSTIC TESTS AND CHARACTERIZATION OF STRAINS

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Introduction: *Clostridium difficile* is an anaerobic gram-positive, spore-forming, toxin-producing bacillus, which cause illnesses ranging from mild diarrhea to fulminant colitis. Laboratory diagnosis largely relies on rapid toxin detection kits through immunoenzymatic assays (ELISA), although this diagnostic approach has recently been called into question. The incidence of *C. difficile* infection has markedly increased in the last years, notably with the epidemic spread of the binary toxin producer ribotype 027.
Aims & Methods
Aims: to compare the performance of commercial ELISA kits versus cytotoxicity (CTA) and toxigenic culture (TC) assays for the diagnosis of CDI in Brazil. Furthermore, isolate and characterize, genotypically and phenotypically, the *C. difficile* strains.
Methods: Ninety six fecal samples were obtained and analyzed between January and November 2014 from inpatients admitted to Hospital das Clínicas of Universidade Federal de Minas Gerais in Belo Horizonte, Brazil. All patients were under broad-spectrum antibiotic therapy and the samples were collected during active diarrhea episodes. All samples were tested for the presence of toxins A/ B by the following commercial ELISA kits: *C. difficile* Tox A/B II (Techlab Inc., USA), Remel ProSpecT *C. difficile* Toxin A/B (Oxoid, UK), and Ridascreen *C. difficile* toxins A/B (R-Biopharm, Germany). Cytotoxicity assays were performed using Vero cells. Stool samples were also cultured and all colonies with suggestive morphologies were subjected to a multiplex-PCR protocol involving a housekeeping gene (tpi), toxins A (tcdA) and B (tcdB), and a binary toxin gene (cdtB). All strains positive for tcdA or/and tcdB were considered toxigenic. *C. difficile* isolates were analyzed by PCR-ribotyping. Minimal inhibitory concentration for metronidazole (MTZ) and vancomicyn (VAN) was determined.
Results: From the 96 sampled patients, 25 (26%) were positive according to CTA. C. difficile was isolated from 29 (30.2%) samples, of which six isolates were considered non-toxigenic and 23 (24%) were toxigenic according to PCR. The kappa concordance between TC and CTA was 0.71 (0.51-0.9). Of these patients, 15 (65.2%) were A + B + CDT-, six (26.1%) were A + B + CDT+, and two (8.7%) were A-B + CDT-. Nine PCR-ribotypes were identified among the isolates, three unpublished (SLO 197, 198 and 199). PCR-ribotype 027 was not detected. The three ELISAs exhibited sensitivities between 64 and 68% and specificities greater than 94%. All strains were susceptible to MTZ and VAN.
Conclusion: It is essential to have accurate laboratory diagnosis of *C. difficile* infection to ensure patients receive appropriate treatment. Furthermore, the detection and isolation of genes related to virulence factors in *C. difficile* strain can aid the understanding of risk factors and epidemiology of disease. Despite not having been detected the presence of ribotype 027, some strains, including those three not previously described, had the gene of the binary toxin, resulting in potential increased of the virulence. There were no strains resistant to conventional therapy, although the therapeutic success can also be influenced by other factors, such as the intestinal microbiota.
Disclosure of Interest: None declared

P1011 HEALTHY BUT NOT TUMOR TISSUE-DERIVED CELL-FREE DNA NEUTRALIZES THE ACTIVATION OF HUMAN MONOCYTES

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Introduction: Bacterial ligands (LPS) and self-DNA sequences are recognized by TLRs on human immune competent cells. Cell-free DNA sequences with unmethylated CpG dinucleotide motifs may be a possible non-specific immune system stimulants by the mechanism of supression the function of the Treg cells and the re-activation of anti-tumor immunity.
Aims & Methods: We compared the immunostimulatory effect of LPS (from *E.coli*) and cell free DNA originated from normal and tumor colonic tissue on isolated peripheral mononuclear cells (PBMCs) from healthy volunteers.
DNA isolation was performed from fresh-frozen surgically removed colonic samples. PBMC were donated by healthy volunteers and isolated by Ficoll-Hypaque (Sigma-Aldrich). The viability of PBMCs was determined by Trypane blue dying. PBMCs were incubated for 24 hours with 10 µg of DNA either from normal and tumor origin. After the incubation we performed the treatment with normal and tumor tissue derived DNA (TLR9 agonists) in or without the combination with LPS (TLR4 agonist) As a next step Affymetrix U133 2.0 whole-genome expression analysis was performed from the isolated total RNA.
Results: Affymetrix whole-genome microarray results reflect a massive monocyte activation of the LPS treatment through the overexpression an early phase pro-inflammatory cytokine IL-6, monocytic marker CD163, and other chemokines (CXCL1, CXCL5). We also observed an increased IFNG and IL-10 expression in PBMCs after LPS treatment. Dual activation of TLR4 and TLR9 (co-administration of tumor or healthy tissue tissue DNA and LPS) has resulted a different effect on the gene expression. Healthy tissue derived DNA and LPS co –treatment induced down-regulation of TLR4, IRG1 CXCL6, CXCL9 and CCL13.
Conclusion: LPS treatment induced a massive activation of monocytes, which could be neutralized by the co-administration of healthy tissue derived cell-free DNA through the down-regulation of the sensing receptor and response genes. We reflected the antagonism between TLRs and the possible non.-inducible effect of tumor tissue derived cell free DNA on immune competent cells through TLR9.

Abstract number: P1012 Table: Effects of inflammation and IMQ on EBF.

			Non inflamed		Inflamed	
	Vehicle	IMQ	Vehicle	IMQ		
In vitro Flux of FD4 (% in 60 min)		Basolateral vehicle/IMQ	0.0016 ± 0.0005	0.0009 ± 0.0004	0.0031 ± 0.0008*	0.0024 ± 0.0009
	Apical vehicle/IMQ	0.0018 ± 0.0005	0.0010 ± 0.0002	0.0041 ± 0.0010*	0.0019 ± 0.0005#	
In vivo		FD4 in serum (µg/mL)	2.03 ± 0.33	1.89 ± 0.17	15.88 ± 7.25*	7.89 ± 2.60*
	FD4 in urine (µg/mL)	8.68 ± 1.79	12.53 ± 1.51	155.80 ± 36.57**	84.12 ± 24.03*	

Data are mean ± sem, n = 4-10; #: $P < 0.05$ vs. Inflamed-vehicle; **: $P < 0.01$, *: $P < 0.05$ vs. non-inflamed vehicle, respectively.

Disclosure of Interest: None declared

P1012 STIMULATION OF TOLL-LIKE RECEPTOR 7 ATTENUATES EPITHELIAL BARRIER DYSFUNCTION DURING COLITIS IN MICE

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Introduction: Altered epithelial barrier function (EBF) and deregulation of mucosal immune responses are common in intestinal inflammatory disorders. Activation of innate immunity-dependent mechanisms, including those mediated by Toll-Like receptors (TLR), has immunomodulatory activity with beneficial effects in colitis.
Aims & Methods: We assessed if TLR7 participates in the modulation of EBF during states of intestinal inflammation. Colitis was induced in CD1 male mice by exposure to dextran sodium sulfate (DSS; 5 % in the drinking water, for 5 days). EBF was determined assessing the permeability to macromolecules (4 kDa fluorescein isothiocyanate–dextran, FD4) *in vitro* (apical-to-basolateral flux FD4 in an Ussing chamber system) and *in vivo* (passage of intracolonic FD4 to blood and urine). Potential modulatory role of colonic TLR7 on EBF was assessed by local stimulation of the receptor with the selective agonist imiquimod (IMQ). Changes in gene expression of tight junction-related proteins (occludin, claudin 2, claudin 3, Zona Occludens-1) and barrier-related markers (proglucagon and myosin light-chain kinase) were assessed by RT-qPCR.
Results: Exposure to DSS lead to a state of colitis, as evidenced macro and microscopically. In colitic animals the passage of FD4, as assessed either *in vitro* or *in vivo* was increased, thus indicating an altered EBF. In *in vitro* conditions, stimulation of TLR7 with IMQ in inflamed tissues (300 μg, apical or basolateral) restored the epithelial permeability to FD4 to basal levels (Table). Similarly, in *in vivo* conditions, intracolonic IMQ (300 μg/mice) attenuated the passage of FD4 to blood and urine in colitic mice, thus indicating a partial restoration of EBF (Table). In DSS-treated animals, expression of tight junction-related proteins and barrier related factors was down regulated (50-70% vs. non-inflamed animals). Local stimulation of TLR7 with IMQ did not revert these effects.
Conclusion: Stimulation of TLR7 leads to an improvement of inflammation-induced altered EBF. The mechanisms mediating these actions seem to be independent of the modulation of tight junction-related proteins and barrier modulators. TLR7-mediated innate immune responses might regulate EBF with a defensive function, preventing the passage of luminal factors and, therefore, reducing antigens exposure and the development of exacerbated immune responses and intestinal inflammation.
Disclosure of Interest: None declared

P1013 ABDOMINAL TUBERCULOSIS – 10 YEAR EXPERIENCE FROM A UK DISTRICT GENERAL HOSPITAL

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Introduction: The rate of tuberculosis has remained relatively stable over the past decade; however the proportion of cases with extra-pulmonary disease has increased from 40.9% to 47.9%. Multiple studies have shown that diagnosis of abdominal tuberculosis (ATB) is often delayed due to non-specific symptoms in patients. The aim of this study was to examine a selection of patients from a UK district general hospital with a diagnosis of ATB and the process in which that diagnosis was reached.
Aims & Methods: We performed a retrospective review of all patients at Russells Hall Hospital, Dudley, who had a diagnosis of ATB between 2004 and 2014. Demographic, clinical, laboratory and radiographical findings were collated including the time delay between hospital presentation and diagnosis.
Results: Sixteen cases of ATB were identified with a median age of 38.5 years at time of diagnosis (range 22-73 years) and a male/female split of 56% and 44% respectively. The majority (87.5%) were of non-white background; South Asian (69%), Afrocaribbean (19%) and White British (12%). The commonest features were abdominal pain (62.5%), weight loss (50%) and fevers (50%). The time between first presentation to hospital and diagnosis ranged from 2 days to 3 years. Basic investigations revealed mean haemoglobin of 11.9 g/dL (SD 1.70), CRP of 109 mg/L (SD 91.81), Alkaline phosphatase of 200 IU/L (SD 159.32), and albumin of 37.1 g/L (SD 6.54). The chest x-ray was normal in 11 patients and of the remaining abnormalities included consolidation in 3 patients, cavitating lesion in 1 patient, and the final patient did not have an x-ray. There was a wide range of sites of disease including small bowel (25%), peritoneum (25%), lymph nodes (18.75%), appendix (12.5%), liver (12.5%) and omentum (6.25%). Tuberculin test was only performed in three patients and all of which were positive. Diagnosis was based on either histology (43.75%), imaging (31.25%), microbiology (6.25%), or a combination of clinical suspicion and imaging or appearances at surgery (18.75%). The majority who received treatment (9/14) were given Rifater plus ethambutol. The remaining five patients all received a different combination of antituberculous treatment (Rifater alone, Rifinah ± Pyrazinamide and Ethambutol, Rifampicin/Isoniazid/Pyrazinamide ± Ethambutol). Two patients did not receive treatment as their diagnosis was made post-mortem. Of the sixteen patients, ten were treated and discharged, three died, two have on going review and one was lost to follow up.
Conclusion: ATB is a difficult diagnosis to make and there can be a significant time delay between symptom onset and diagnosis as the symptoms can be varied and insidious in nature. It is an easily treatable condition and a combination of abdominal pain, fevers and/or weight loss in a non-Caucasian patient should warrant further investigation.
Disclosure of Interest: None declared

P1014 TUMOUR BUDDING WITH AND WITHOUT ADMIXED INFLAMMATION: TWO DIFFERENT SIDES OF THE SAME COIN?

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Introduction: In colorectal cancer, the morphology at the invasive tumour margin is known to reflect the biology of disease, rendering important prognostic information. Tumour budding, defined as the presence of isolated single cells or small clusters of cells (composed of fewer than five cells), has been associated with adverse outcome. In contrast, peritumoural inflammation has been associated with favourable outcome. Of note, the antitumour activity of inflammation may lead to the destruction of tumour glands and, ultimately, the presence of small clusters of cells scattered in the tumour stroma (''pseudo-budding''). Our study aimed to analyse the relationship between tumour budding and inflammation and its possible prognostic significance in a large cohort of colorectal cancer patients.
Aims & Methods: Tumours of 381 randomly selected patients were retrospectively reviewed for the extent of tumour budding, with high-grade budding reflecting presence of 10 or more budding fociscattered at the invasive tumour margin. The intensity of the peritumoral inflammation was assessed using a four-degree scale according to Klintrup-Mäkinen criteria. Progression-free and cancer-specific survivals were determined using the Kaplan-Meier method.
Results: Overall, 221 (58%) tumours showed low grade, 160 (42%) tumours high-grade budding. 167 (44%) tumours showed no increase or only a mild and patchy increase of inflammatory cell sat the invasive tumour margin, but no destruction of invading cancer cell islets (scores 0-1), whereas in 214 (56%) tumours a band-like infiltrate of inflammatory cells with at least some destruction of cancer cell islets was seen (scores 2-3). When analysis was restricted to tumours with high-grade budding, 82 (51%) cases showed mild inflammation (scores 0-1) and 78 (49%) marked inflammation (scores 2-3). Tumour budding was significantly associated with both progression-free and cancer-specific survival in our cohort. Cases with high-grade budding and marked inflammation had a better outcome regarding progression-free ($p < 0.001$) and cancer-specific survival ($p < 0.001$) than high-grade cases with only mild inflammation. Outcome in these cases, however, was still worse compared to cases with low-grade budding, in which the extent of peritumoral inflammation had no further prognostic effect.
Conclusion: Though tumours with marked inflammation at the invasive tumour margin may showd estruction of cancer islands due to the anti-tumour effect of the inflammatory infiltrate(''pseudo-budding''), the presence of isolated tumour cells and small clusters of cells scattered in the stroma at the tumour margin does not *per se* imply favourable outcome in these cases. It is of note that tumours with high-grade budding and marked inflammation at the invasion front still bear a significantly poorer outcome than tumours with low-grade budding, in which the extent of peritumoural inflammation had no prognostic effect.
Disclosure of Interest: None declared

P1015 ADMINISTRATION OF ANTI-INTERLEUKIN-6 ANTIBODIES AMELIORATES CAECAL LIGATION AND PUNCTURE-INDUCED GASTROINTESTINAL MOTILITY DISTURBANCES AND COLONIC PERMEABILITY CHANGES

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Introduction: Sepsis represents a significant burden of disease and mortality in Intensive Care Units. Ileus, the inhibition of the propulsive motility of the gastrointestinal (GI) tract, together with mucosal barrier dysfunction, will maintain sepsis by the translocation of bacteria and luminal antigens. Interleukin-6 (IL-6) is a major proinflammatory cytokine that is secreted by

immune cells such as macrophages and T cells. In previous experiments, we observed a significant increase in systemic and colonic IL-6 levels that coincided with an increase in colonic permeability.
Aims & Methods: We aimed to investigate the effect of anti-IL-6-antibodies on ileus, colonic permeability and translocation of intestinal bacteria in blood in a septic mouse model. Sepsis was induced in Swiss-OF1 mice by caecal ligation and puncture (CLP). Sham-operated animals served as controls. Mice received either one injection of anti-IL-6 antibodies 1 mg/kg i.p. (anti-IL6) or the IgG isotype control (IgG) jointly with the CLP procedure (n = 8-12/group). Occurrence of ileus was confirmed 48h post-procedure by studying the geometric center (GC) of beads. In the permeability study, mice were anesthetized and underwent a laparotomy, during which the colon was ligated and injected with 100 µL of a 9% Evans blue (EB) solution. Mice were sacrificed 1h later via cardiac puncture, and serum samples as well as homogenized colon supernatants were analyzed for IL-6 levels. Colons were rinsed and incubated for 24h in formamide to extract the EB from the colon wall. Whole blood was plated directly onto agar plates and cultured for 24h to quantify bacterial translocation.
Results: CLP-induced sepsis significantly delayed GI transit and this effect was reversed by anti-IL-6 treatment (GC: sham + IgG 5.4 ± 0.4, sham + anti-IL6 5.8 ± 0.4, CLP + IgG 2.6 ± 0.4*, CLP + anti-IL6 4.3 ± 0.5). Serum and colonic IL-6 levels rose significantly following CLP, and anti-IL6 was able to reduce them (serum: sham + IgG 4.6 ± 2.5, sham + anti-IL6 2.0 ± 0.6, CLP + IgG 276.6 ± 71.6, CLP + anti-IL6 84.5 ± 18.3 pg/mL, $p < 0.05$ for the effect of CLP and of anti-IL6; colon: sham + IgG 3.8 ± 2.4, sham + anti-IL6 2.2 ± 0.8, CLP + IgG 209.8 ± 94.6, CLP + anti-IL6 52.3 ± 14.1 pg/100 mg colonic tissue, $p < 0.05$ for the effect of CLP). CLP-induced sepsis significantly increased colonic permeability. The impaired barrier was improved by anti-IL6 treatment (sham + IgG 22.6 ± 1.7, sham + anti-IL6 29.3 ± 2.2, CLP + IgG 52.9 ± 10.4*, CLP + anti-IL6 27.8 ± 5.5 µg EB/100 mg colon). Finally, anti-IL6 numerically reduced the number of positive blood cultures in septic animals (sham + IgG 0/6, sham + anti-IL6 0/8, CLP + IgG 7/9, CLP + anti-IL6 5/9 positive cultures, Pearson's Chi-squared test $p < 0.05$ for CLP + IgG or CLP + anti-IL6 versus sham + IgG).
Conclusion: CLP caused a marked delay in GI transit with an increased colonic permeability and subsequent increased risk of bacterial translocation. Anti-IL-6 treatment significantly ameliorated GI motility, suppressed inflammation and normalized the permeability of the colonic wall. We conclude that the proinflammatory cytokine IL-6 has a major influence on colonic permeability and GI motility disturbances following CLP-induced septic ileus.
Disclosure of Interest: None declared

P1016 CONTIUOUS STIMULATION WITH CYTOKINES LEADS TO IRREVERSIBLE ACTIVATION OF NF-ΚB SIGNALING IN COLONIC EPITHELIAL CELLS BY ORGANOID CULTURE

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Introduction: The patients with ulcerative colitis are at increased risk of developing colitis-associated cancer, suggesting that contiuous inflammation in colon leads to the development of carcinogenesis. However, the mechanism of the carcinogenesis in colitis-associated cancer remains unknown. Recently, 3-dimentional (3D) primary organoid culture of colonic epithelial cells has been established in our group (*Nature Medicine* 2012).
Aims & Methods: We therefore aimed to assess the influence of continuous stimulation with cytokines on colonic epithelial cells in vitro, using 3D primary organoid culture.
Colonic crypts were isolated from 8-week old female mouse and were cultured by TMDU method. To mimic chronic inflammation, the mixture of tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), lipopolysaccharide (LPS) and flagellin were added into the medium every other day. Microarray analysis was performed after 60 weeks of cytokines stimulation. Gene Set Enrichment Analysis (GSEA) was also performed for the detection of specific cell signaling pathway. The expression of NF-κB target genes IL-8, DUOXA2 was assessed by quantitative RT-PCR. For the analysis of accumulation of NF-κB p65 in nuclei, 3D immunohistochemistry of whole organoid was performed by stain with anti-NF-κB p65 antibody. To evaluate reactive oxygen species (ROS) in live organoids, CellROX® Deep Red Stress Reagents (Life technologies) was added to medium for one day. Organoids were visualized by confocal laser fluorescent microscopy.
Results: The stimulation with TNF-α, IL-1β, IL-6, LPS and flagellin showed the significant induction of NF-κB target genes in colonic organoids. Microarray analysis with GSEA analysis showed significant induction of NF-κB signaling after 60 weeks of cytokines stimulation. Interestingly, the expression of DUOXA2 gene, which was NF-κB target genes and upregulated in microarray analysis, was gradually increased by the continuous stimulation with cytokine mixtures, suggesting that NF-κB signaling might be accumulated by the stimulating time. 3D immunostaining analysis showed that NF-κB p65 was accumulated in nuclei by longer time of the stimulation, indicating that continuous stimulation with cytokines might lead to a stronger activation of NF-κB signaling. Interestingly, accumulated NF-κB signaling by long-term stimulation remained active after the removal of all cytokines, whereas NF-κB signaling induced by short-term stimulation was completely shut down by the removal of all cytokines. ROS analysis showed that ROS were induced by stimulation with cytokines. Moreover, ROS in the organoid with long-term stimulation remained at 11 weeks after the removal of cytokines, suggesting that oxidative stress in the organoid with long-term stimulation was also irreversible.
Conclusion: Persistent inflammation leads to irreversible NF-κB signaling activation in colonic epithelial cells, suggesting that "signal spiral" might be crucial for the carcinogenesis of colitis-associated cancer.
Disclosure of Interest: None declared

P1017 THE DISTURBANCE OF CENTRAL DOPAMINERGIC NEURONS IN RAT MODEL OF PARKINSON'S DISEASE INCREASES SUSCEPTIBILITY TO COLONIC INFLAMMATION

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Introduction: The development of colonic inflammation in experimental colitis is associated with increase of the blood-brain barrier permeability and the loss of central dopaminergic neurons [1]. From the other hand, the disturbance of central dopaminergic neurons during Parkinson's disease (PD) is characterized by colonic constipation [2]. Constipation might be associated with the growth of pathogenic microflora as a result of that the disruption of intestinal barrier integrity, inflammation development and further exacerbation of PD symptoms.
Aims & Methods: The aim of the present study was to check whether the colonic inflammation is primary associated with the early stages of PD pathogenesis or PD increases the susceptibility to colonic inflammation development. Study was done on male Wistar rats (180-250 g). Model of experimental PD was induced by single unilateral 6-hydroxydopamine (6-OHDA) administration, rats were enrolled in study 1 month after. Colonic inflammation was induced by 6% iodoacetamide enema. Levels of spontaneous and carbachol-stimulated colon motility was estimated by ballonographic method *in vivo*; the activity of Mg^{2+}, Ca^{2+}-ATPase and K^{+}-ATPase in colonic smooth muscles - by the release of inorganic phosphate; colonic levels of calmodulin – by Western blot; the parietal microflora - by bacteriological culture methods; colonic endothelial permeability - by Evans blue extravasation; levels of inflammation - by colon myeloperoxidase activity (MPO), levels of I?AM-1 and arginase activity in peritoneal macrophages.
Results: 6-OHDA lesioned-rats had decreased tonic indexes of spontaneous and stimulated colon motility by 11.3 ($p < 0.05$) and 22.5% ($p < 0.01$); increased frequency of contractions of spontaneous (by 31.6%, $p < 0.05$) but not stimulated motility; increased amplitude of contractions (by 31.16%, $p < 0.01$) and decreased motor-activity index of stimulated colon motility (19.9%, $p < 0.05$) *vs* sham-lesioned rats. Delayed in colon motility in 6-OHDA rats was associated with increased colon level of Mg2+, Ca2+-ATPase activity (39.7%, $p < 0.05$), decreased K+-ATPase activity (17.0%, $p < 0.05$) & level of calmodulin ($p < 0.05$). Colon and ileum parietal microflora composition were not changed between sham & 6-OHDA-lesioned rats. It was no difference in the colonic mucosa endothelial permeability & ICAM-1 levels as well. While 6-OHDA rats had 2.3-fold depleted peritoneal macrophages functional reserve ($p < 0.05$). 6-OHDA rats were more predisposed to iodoacetamide-induced colonic inflammation *vs* sham-lesioned rats: MPO activity was higher 2.6-folds ($p < 0.05$); colonic endothelial permeability – 1.5-folds and I?AM-1 levels 5.5-folds ($p < 0.05$).
Conclusion: The delayed colonic motility is an early feature of experimental PD which is associated with low grade systemic inflammation. We showed for the first time that disturbance of central dopaminergic neurons in rat model of PD increases susceptibility to colonic inflammation development.

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P1018 ADAPTIVE IMMUNE RESPONSES TRIGGERED BY HERPES SIMPLEX VIRUS TYPE 1 CAUSE ENTERIC NERVOUS SYSTEM DYSFUNCTION

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Introduction: Anomalies of the enteric nervous system (ENS) have been associated to motility and inflammatory disorders of the gut. Since enteric neuropathies are characterized by various histopathological pictures including loss of ganglion cells or infiltrating mononuclear cells an immune-mediated damage, possibly triggered by an infectious agent, has been postulated. Indeed, we have recently shown in rodents that following intragastric (IG) administration the neurotropic Herpes simplex virus (HSV)-1 can infect the ENS resulting in time-dependent intestinal neuromuscular abnormalities[1]. Therefore, we aimed to investigate whether adaptive immune responses are involved in the onset of ENS dysfunction following HSV-1 infection.

Aims & Methods: Male C57/Bl6 (WT) mice were inoculated intranasally with HSV-1 (10^2 pfu) and 4 weeks (W) later IG (10^7 pfu). Starting 4 W after viral IG inoculum a group of mice received anti-CD8 antibody. Six-ten W after viral IG inoculum we: a) determined gastrointestinal (GI) motility by measuring fluorescein-isothiocyanate dextran distribution; b) assessed ENS integrity by immunohistochemistry on ileal whole-mount preparations; c) characterized the lymphocytes infiltrating the longitudinal muscle myenteric plexus (LMMP) and their reactivity to HSV-1 antigens by FACS analysis; d) quantified changes in isometric muscle tension following electric field stimulation (EFS) of ileal segments. To verify the role of lymphocytes in HSV-1 induced ENS dysfunction, CD3+cells were isolated from the LMMP of mice 8-10 W after viral IG inoculum, *in vitro* pulsed with HSV-1, and injected in recipient mice. After one week the effects on isometric muscle tension following EFS stimulation of ileal segments were determined.
Results: At 8 and 10 W after IG inoculum, HSV-1 caused a significant delay in GI transit, impaired cholinergic neuromuscular transmission ($p<0.01$ vs control mice), altered expression and distribution of the neurofilaments peripherin and βIII-tubulin, whereas no anomalies were observed at 6 W after IG inoculum. In the LMMP, but not in the spleen, we observed an increase in CD3+lymphocytes starting at 6 W and persisting up to 10 W after viral IG inoculum. At 8 W after viral IG inoculum HSV-1 reactive $CD3^+CD4^+IL4^+$ and $CD3^+CD8^+INF\text{-}\gamma^+$ were demonstrated in LMMP, whereas at 10 W non-HSV-1 specifically activated CD8+ T-cells were present in LMMP. Depletion of CD8+ T-cells, by administration of monoclonal anti-CD8 antibody, abolished the ENS damage and the neuromuscular anomalies observed at 8 W after viral IG inoculum. Ileal muscle tension was significantly altered ($p<0.01$ vs control) in recipient mice receiving *in vitro* HSV-1 pulsed LMMP lymphocytes isolated at the 8th W post IG viral inoculum. Instead, the adoptive transfer of lymphocytes from 10 W infected mice resulted in dysmotility with or without *in vitro* exposure to viral antigens.
Conclusion: At different time points following infection of the ENS, HSV-1 activates lymphocyte subsets directly causing intestinal neuromuscular dysfunction. We speculate that HSV-1 infection of the ENS, as opposite to the central nervous system compartment, triggers adaptive immune responses that can alter the structure and the integrity of the neurons thus predisposing to bowel anomalies.

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P1019 NO ASSOCIATION BETWEEN LACTASE 13910 POLYMORPHISM AND COLORECTAL POLYPS ANDCARCINOMA

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Introduction: Primary lactase deficiency (PLD) affects more than the half of the world's population. LCT-13910 polymorphism was described and being widely used for diagnosis of PLD. The relationship between LCT-13910 polymorphism and risk for colorectal cancer is unclear.
Aims & Methods: We investigated the presence of a relationship between lactase deficiency and colon cancer and adenomatous polyps of the colon in our population. 166 patients (M:103; Mean Age: 60.7 ± 10.4), who had undergone total colonoscopy were included in the study. Anticoagulated blood was drawn from the patients following colonoscopy for genetic analyses (LCT-13910).
Results: The CC genotype in lactose gene 13910 locus, which was accepted as the genetic indicator of lactase deficiency, was determined as 83.7%. The CC genotype rate was determined as 89.1% in patients who had the history of milk intolerance and 81.5% in those with a history without milk intolerance (p = 0.236). No difference was detected between the patients who had colorectal polyp, cancer and normal colonoscopy findings with regard to lactase gene polymorphism. No difference was determined between groups when compared with regard to C or T allele and also for the number and location of the polyps, genetic polymorphism.
Conclusion: The presence of a negative relationship between lactase deficiency and milk consumption is inevitable. Therefore, a relationship should be expected between lactase deficiency and colorectal cancer; however, such a relationship could not be determined in our study.

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P1020 HIGH CARCINOEMBRYONIC ANTIGEN LEVEL MAY BE A DIAGNOSTIC MARKER FOR COLORECTAL ADENOMA IN KOREAN YOUNG MEN

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Introduction: Colon cancer is the 3rd most commonly diagnosed cancer in South Korea. Colorectal cancer screening is recommended for average-risk persons beginning at age 50 in South Korea. However, prevalence of adenoma in subjects aged 40-49 years men was higher than we expected.
Aims & Methods: The aim of this study to determine the prevalence and risk factors of colorectal adenoma in persons aged 40-49 years men. 1902 asymptomatic subjects (1330 men, 69.9%, mean age of 47.9 ± 6.7) who underwent screening colonoscopy in a health examination center of Myongji hospital from 2010 to 2013 were enrolled in this study. We conducted case-control study to determine the risk factor for adenoma. The subjects were classified into two groups (adenoma vs controls and 40 – 49 years vs ≥50 years group).
Results: At least 1 colorectal neoplasm was identified in 385 patients (20.2%). 372 patients were found to have a non-advanced adenoma, 13 individuals had an invasive adenoma and no patient had a cancer. Male, old age, smoking, metabolic syndrome and elevated carcinoembryonic antigen (CEA) level were significantly associated with colorectal adenoma in univariate analysis. According to multiple logistic regression, adenoma was significantly associated with male and tended to be associated with high CEA level (p value = 0.059). To validate the diagnostic values of CEA for adenoma, AUROC was calculated. Area under the curve of CEA for colorectal adenoma in non-smoking men (n = 585) under 50 years was 0.600 (0.543∼0.656). Area under the curve of CEA for colorectal adenoma in smoking men (n = 376) under 50 years was 0.615 (0.540∼0.690).
Conclusion: Male sex, metabolic syndrome, smoking and high CEA level seem to be associated with colorectal adenoma. High CEA level may be a diagnostic marker for any colorectal adenoma for 40 – 49 years Korean men. Further studies based on a large sample size will be needed to confirm the exact role of CEA for diagnostic marker of colorectal adenoma in Korean young men.

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P1021 COMPARATIVE STUDY OF CLINICAL MANIFESTATIONS ACCORDING TO THE RESULTS OF INTERFERON-Γ ASSAY IN PATIENTS WITH INTESTINAL TUBERCULOSIS

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Introduction: Intestinal tuberculosis (ITB) is still prevalent in Korea. Recently, the incidence of Crohn's disease (CD) is also increasing, therefore, differential diagnosis of CD from ITB is challenging. An INF-gamma assay (QuantiFERON-TB gold test, QFT) is regarded as a good supplementary tool for the diagnosis of ITB. However, the clinical implication of the positive results of QFT in ITB is uncertain. We investigated the clinical features of patients of ITB according to the results of QFT.

Aims & Methods: We enrolled the ITB patients who were tested for QFT in the initial diagnosis from April 2007 to July 2013. We retrospectively analyzed clinical features of ITB patients based on the results of QFT.

Results: A total of 109 patients with ITB were enrolled from 3 institutes and 82 patients (75.2%) showed positive results of QFT, whereas 27 patients (24.8%) showed negative results. In QFT-positive group, the mean age at the time of diagnosis as ITB is 44.1 ± 12 years, which is significantly higher than QFT-negative group (37.0 ± 14.8 years, $p = 0.0096$). C-reactive protein level at the time of diagnosis as ITB is significantly lower in QFT-positive group (1.3 ± 2.3 mg/dL) than QFT-negative group (6.4 ± 9.9 mg/dL, $P < 0.000$). However, no differences were found between groups regarding the presence of granuloma in colonic tissues ($P = 0.095$) or accompanying of extra-intestinal TB ($P = 0.592$).

Conclusion: QFT-positive results were gained in three-fourths patients with ITB and we confirmed that QFT is a good supplementary tool for the diagnosis of ITB. In QFT-positive group, the mean age is higher and has lower level of CRP than QFT-negative group. These results suggested the possibility that prior exposure to TB may cause mild inflammation in patients with ITB.

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P1022 ASSOCIATION OF VISCERAL OBESITY WITH COLORECTAL ADENOMATOUS POLYPS AND COLORECTAL CANCER: A PRELIMINARY REPORT

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Introduction: Obesity is a well-established risk factor for colorectal adenoma, but its association with colorectal cancer (CRC) is not clear.

Aims & Methods: The aim of this study was to examine whether visceral adipose tissue (VAT) serves as a risk factor for CRC as well as colorectal adenomas. A retrospective case-control study was conducted with 45 patients with CRC (2 rectal and 43 colon cancers), 50 patients with colorectal adenoma and 50 normal controls. All subjects underwent various laboratory tests, computed tomography (CT) scan available for abdominal fat measurement, and colonoscopy. All patients with CRC also had available abdominal CT scan 1-2 years before the diagnosis. VAT was defined as an intraabdominal adipose tissue area measured by CT scan. Adipose tissue areas were measured at the level of the umbilicus from CT scan.

Results: Body mass index, fasting blood glucose (FBS) and VAT areas were significantly increased in adenoma and CRC groups compared to controls (all $P < 0.01$). The mean ± standard deviation of VAT area was 92.4 ± 4.8 cm^2 in normal controls, 120.9 ± 5.2 cm^2 in adenoma group and 123.2 ± 5.9 cm^2 in CRC group ($P = 0.007$ by ANOVA). On the other hand, subcutaneous adipose tissue areas were not different between the 3 groups ($P > 0.05$). Serum total cholesterol levels were significantly lower in CRC group than control or adenoma groups ($P < 0.001$). Although there was no significant difference in VAT areas between adenoma and CRC groups, VAT areas in CRC patients from CT scan taken 1-2 years before the diagnosis of CRC were significantly higher than those in adenoma group ($P = 0.045$).

Conclusion: Our study showed that both visceral obesity and insulin resistance were significant risk factors for CRC in the Korean population. However, the effect of visceral fat might be limited to the early stage of adenoma-carcinoma sequence in colorectal carcinogenesis. Further studies are warranted in the future.

Disclosure of Interest: None declared

P1023 CUMULATIVE INCIDENCE OF ADVANCED NEOPLASIA AFTER RESECTION OF HIGH AND INTERMEDIATE RISK ADENOMAS IN COLORECTAL CANCER POPULATION SCREENING PROGRAMS: RETROSPECTIVE COHORT STUDY

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Introduction: European guidelines for quality in colorectal cancer (CRC) screening recommends different surveillance intervals in patients after adenoma resection. However, these recommendations have not been validated.

Aims & Methods

Aims: To assess whether the cumulative incidence of advanced neoplasia (AN) (advanced adenoma or CRC) and CRC in patients undergoing endoscopic surveillance differs between high-risk ($\geq$5 adenomas or $\geq$ 20mm) and intermediate groups (2-4 adenomas or 10 to 19 mm or villous histology or high-grade dysplasia) of the European guidelines for quality in the CRC screening.

Methods: Retrospective cohort study of national ambit. We included subjects with high or intermediate risk adenomas detected in CRC population screening programs and in COLONPREV study from its inception until June 2011. The main dependent variable was the cumulative incidence of AN. We compared follow-up time with the Student's t test. We analyzed the differences in endoscopic surveillance and the cumulative incidence of AN and CRC between both groups with the Mantel-Haenszel test. We performed a proportional hazards regression to control for confounding variables (sex, age, quality of baseline colonoscopy program and screening test). Differences between groups were expressed as risk ratio (RR) or hazard ratio (HR) and its confidence interval at 95% (95% CI).

Results: We included 5401 subjects, 3379 people with intermediate-risk adenomas and 2022 with high-risk adenomas (men = 70.1%, mean age = 60.9 ± 5.7 years, baseline number of colonoscopies = 1.2 ± 0.5, cecal intubation = 99.2%, adequate cleansing = 99.3%). A surveillance endoscopy was performed in 64.3% of subjects (high 68.2%, intermediate 62%; RR 1.3, 95% CI 1.2-1.5) at a mean interval of 2.8 ± 1 years (high = 2.7 ± 1.1, intermediate = 3 ± 0.9; $p < 0.001$). In subjects with endoscopic surveillance, the cumulative incidence of AN in high and intermediate risk cohorts was 15.8% (58.6 cases per 1000 person-years) and 12.4% (41.9 cases per 1,000 people-year) with a RR = 1.3 (95% CI 1.1-1.6); and CRC cumulative incidence was 0.5% and 0.6% respectively (1.9 cases per 1000 person-years) with a RR = 0.9 (95% CI 0.3 to 2.2). In the proportional hazards analysis, the cumulative incidence of AN was higher in the high-risk cohort (HR 1.6, 95% CI 1.3-1.9). However, we found no differences in the cumulative incidence of CRC (HR 1.1, 95% CI 0.4 to 2.9).

Conclusion: In subjects performing endoscopic surveillance, the AN cumulative incidence is higher in the European guideline high risk group. However, we detected no differences in the CRC cumulative incidence between both cohorts.

Disclosure of Interest: None declared

P1024 DIAGNOSTIC RISK FACTORS FOR COLORECTAL CANCER IN PATIENTS WITH SERRATED POLYPOSIS SYNDROME

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Introduction: Serrated polyposis syndrome (SPS) is characterized by multiple serrated polyps (SP) throughout the colon and accompanied by an increased

life-time risk of colorectal cancer (CRC). SPS is diagnosed based on clinical criteria, which includes a very heterogeneous group of patients with a wide variation in CRC risk.

Aims & Methods: We aimed to assess CRC risk factors in a large cohort of patients with SPS and to evaluate the risk of CRC during surveillance. Patients were retrospectively enrolled from 7 centers in the Netherlands and 2 in the UK. Data were retrieved from medical charts, pathology and endoscopy reports. Criteria from the World Health Organization of 2010 were used to diagnose SPS (WHO1: ≥5 SP proximal to rectosigmoid with ≥2 of ≥10mm; WHO2: ≥1 SP proximal to rectosigmoid and a first degree relative with SPS; WHO 3: ≥20 SP of any size, but distributed throughout the colon). Patients that only fulfilled WHO criterion 2, with inflammatory bowel disease and/or a known hereditary CRC syndrome were excluded from analysis. Multivariate logistic regression was used to calculate adjusted risk factors for CRC. Incidence rate was calculated to evaluate the risk of CRC during surveillance after the resection of all lesions > 5mm.

Results: In total 435 patients with SPS were included for analysis. The mean age at diagnosis was 58 years (SD 14), 49% were male and 57% of patients had a history of smoking. Of all patients, 27% fulfilled WHO criterion 1, 41% WHO criterion 3 and 32% WHO criteria 1&3. In total 128 (29%) patients were diagnosed with CRC. Patients with ≥1 SP with dysplasia (OR 2.05; 95%CI 1.26-3.31), ≥1 advanced adenoma (OR 2.31; CI 1.46-3.66) and patients that fulfilled WHO criteria 1&3 (OR 1.70; CI 1.10-2.57) were at increased risk of developing CRC, adjusted for age at SPS diagnosis (Table 1; only significant results shown). SPS patients with a history of smoking had a decreased risk of developing CRC (OR 0.35; CI 0.22-0.55). A total of 261 patients underwent surveillance after clearing of all lesions > 5mm with a median follow up of 3.2 years (IQR 1.6-5.7) and a median interval between colonoscopies of 1.2 years (IQR 1.0-1.6). In total 3 patients were diagnosed with CRC during surveillance (2.90 events/1000 person years (95%CI 0.74-7.89).

Risk factors for CRC

	Univariate OR(95% CI)	p-value	Multivariable OR(95% CI)	p-value
Age at diagnosis SPS (per year)	1.04 (1.02-1.06)	**<0.001**	1.03 (1.01-1.05)	**<0.001**
History of smoking	0.48 (0.30-0.78)	**<0.01**	0.35 (0.22-0.55)	**<0.001**
≥1 SP containing dysplasia	2.31 (1.47-3.65)	**<0.001**	2.05 (1.26-3.31)	**<0.01**
≥1 advanced adenoma	2.49 (1.62-3.85)	**<0.001**	2.31 (1.46-3.66)	**<0.001**
Fulfilling WHO criteria 1&3	1.65 (1.07-2.54)	**0.02**	1.70 (1.10-2.57	**0.02**

Conclusion: SPS patients with advanced adenomas, SPs containing dysplasia and/or a combined WHO 1&3 phenotype are at an increased risk of developing CRC. Patients with a history of smoking show a markedly lower risk of developing CRC, possibly due to the fact that the pathogenesis of disease is different in these patients. The risk of developing CRC during surveillance and after clearing of all relevant lesions is lower than earlier assessed in literature, which may reflect a more mature multi-centre cohort with less selection bias.

Disclosure of Interest: None declared

P1025 THE APC I1307K ALLELE CONVEYS DIFFERENT RISKS FOR CANCER IN MEN AND WOMEN

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Introduction: ***Background:*** The prevalence of the APC I1307K missense mutation is~6% in Ashkenazi Jews (AJ) and is associated with an increased risk of colorectal (CRC) neoplasia.

Aims & Methods

Aim: To examine the association of this variant with non-CRC in a large cohort.

M&M: 13,017 consecutive healthy subjects, undergoing annual screening at Integrated Cancer Prevention Center in the past decade. This population was enriched with **1,607** cancer patients recruited from Oncology, Surgery, Gastroenterology, Urology and Hematology services. Demographics, medical history, and pathological data were recorded. Mortality data was obtained from Israel's Ministry of Health registry. The APC I1307K analyses were performed using real-time PCR on DNA extracted from peripheral mononuclear cells. The detection rates of I1307K were compared using multiple variable logistic regression adjusted for age and sex. P-values for significance were adjusted to multiple testing by FDR methods.

Results: The I1307K was detected in 803/14,624 (5.5%) individuals (8.9% and 2.4% among Ashkenazi and Sephardic Jews). I1307K carriers showed a significantly increased risk for any type of cancer with an adjusted age and sex odds ratio (OR) of 2.53 (95% CI 2.11-3.04, P < 0.0001). In men increased risk for brain (OR 12.7), lung (7.3), urinary system (4.3), pancreas (3.7), BCC (3.2), and melanoma (3) was found. Female carriers showed a greater risk only for breast (2.8) and skin (4.8) cancers. A significantly increased CRC risk was found in men similar to previous studies: adenomatous polyps OR = 1.67 (95% CI 1.23-2.25, P = 0.001); CRC OR = 1.90 (95% CI 1.35-2.69, P < 0.0001). In women increased risk only for adenomatous polyps OR = 1.69 (95% CI 1.24-2.29 P < 0.001), but not for CRC. Carriers with one cancer were at significantly increased risk for developing at least one more cancer (OR 1.80 95% CI 1.14-2.8 P = 0.011). The increased risk for > 2 cancers was significant only in women.

Overall survival between carriers and non-carriers using revealed that female carriers died at a significantly older age than non-carriers (average age of death 78.8 years, SE 2.2 vs. 70.4, SE 0.67 p = 0.003). A Cox proportional hazard regression yielded a near significant HR of 0.69 (95% CI 0.47-1.01 p = 0.055). iCarrier female cancer patients also had higher survival rate (HR 0.58, 95% CI 0.36-0.93 p = 0.022).

Conclusion: 1. The I1307K allele of the APC gene is a reliable marker for overall cancer risk (OR – 2.53) in particular in men. 2. This risk was higher than the prior described association with CR neoplasia. 3. In women the I1307K allele is only associated with an increased risk for breast and skin cancers and no increase in risk for CRC. 4. Carriage of this allele is associated with an unexplained significant 8 year increase in longevity in women.

Disclosure of Interest: None declared

P1026 MISMATCH REPAIR DEFICIENCY IN RADIOTHERAPY- AND CHEMOTHERAPY-ASSOCIATED COLORECTAL CANCER

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Introduction: Hodgkin lymphoma (HL) survivors who were treated with infradiaphragmatic radiotherapy and/or high dose procarbazine have an approximately 5-fold increased risk to develop colorectal cancer (CRC) compared with the age-matched general population. The mechanism behind the transformation of normal colonic mucosa into CRC after exposure to radiotherapy or chemotherapy remains unknown. This study aims to provide insight into the development of treatment-induced CRC by evaluating the histopathological and molecular characteristics of treatment-induced CRC.

Aims & Methods: Formalin-fixed paraffin-embedded (FFPE) material from CRCs diagnosed in HL survivors was requested through the Nationwide Pathology Database (PALGA). Histopathological revision and immunohistochemical staining for mismatch repair (MMR) proteins were performed. Microsatellite stability status (pentaplex PCR) and CpG island methylator phenotype (CIMP, multiplex ligation-dependent probe amplification) status were assessed in all CRCs. Microsatellite instable (MSI) CRCs were additionally evaluated for promoter methylation of MMR genes.

Results: FFPE material of 51/64 (80%) cases was obtained, including 3 cases with 2 synchronous CRCs. The median age at CRC diagnosis was 57 years (range 30-79), 65% were male and the median latency between HL and CRC was 22 years (range 7-39). 13/54 (24%) CRCs were MSI and loss of staining was displayed for MLH1 and PMS2 (5/13) or MSH2 and MSH6 (7/13). One MSI tumor showed normal levels of all four MMR proteins. *MLH1* promoter methylation was found in 3 MSI CRCs that showed loss of MLH1 and PMS2 protein staining. One MSS tumor showed loss of PMS2 staining; all the other MSS tumors stained positive for the four MMR proteins. 21/53 CRCs were CIMP (Ogino 5/8 gene positivity). The incidences of MSI and CIMP did not vary between different treatment groups (RT alone, procarbazine alone or RT + procarbazine).

Conclusion: In this study we demonstrated a high frequency of MSI among radiotherapy- and chemotherapy-associated CRCs, which surprisingly cannot be explained by promoter hypermethylation. Normal tissue and tumor DNA sequencing of *MLH1*, *PMS2*, *MSH2* and *MSH6* is in progress.

Disclosure of Interest: None declared

P1027 ALTERED EXPRESSION OF ACETYLCHOLINE RELATED PROTEINS IN NORMAL COLONIC MUCOSA FROM PATIENTS WITH COLORECTAL NEOPLASIA

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Introduction: Studies suggest that acetylcholine (ACh) plays a role in development of colorectal neoplasia (CRN). Local level of several transporters and enzymes involved in epithelial synthesis of ACh[1], muscarinic M3-receptor[2] and ACh esterase[1,3] appear dysregulated and involved in neoplastic cell-proliferation.

Aims & Methods: The aim of this study was to investigate the expression of genes coding for proteins related to epithelial synthesis and metabolism of ACh in colonic mucosa from patients with and without CRN. Furthermore, functional role of ACh was investigated. Endoscopic biopsies (N = 25) from patients with CRN (CRN-pts) and controls were acquired from macroscopically normal mucosa in the sigmoid colon. qPCR was performed for the following 17 ACh-related genes: Choline transporter-like protein (CTL) 1-5, organic cation transporter 1-3, high-affinity choline transporter-1, vesicular ACh transporter, choline acetyltransferase, carnitine acetyltransferase, muscarinic receptor M1-3, ACh esterase and butyrylcholine esterase. All tests were run in triplicates and expression levels normalized with β-actin expression. Biopsies were mounted in micro-Ussing chambers and exposed to amiloride (20 μM) and subsequently

increasing doses of ACh (0.125–2048 μM). Transepithelial electrogenic transport was measured by short circuit current (SCC). Data are reported as mean ± SEM. Statistical significance was tested using Student's unpaired *t*-test and Mann-Whitney *U*-test for equal and unequal variances of the groups, respectively. Unequal qPCR-data were first log-transformed. For categorical data Chi-square was used.

Results: *qPCR:* CTL1 and CTL4 were significantly increased in CRN-pts compared to controls. Relative expression level for CTL1 was 0.95 ± 0.06 in CRN-pts vs 0.61 ± 0.06 in controls ($p = 0.002$). Relative expression level for CTL4 was 0.57 ± 0.04 in CRN-pts vs 0.42 ± 0.06 in controls ($p = 0.04$). *Ussing chamber:* ACh induced rapid biphasic change in SCC. First part (decrease in SCC) was observed in 36 % of CRN-pts vs 78 % of controls ($p = 0.049$). For the second part of SCC response (increase), double Michaelis-Menten analysis provided the best fit indicating activation of two receptors. For both parts of the biphasic response, the EC_{50} and maximal responses showed no significant difference between CRN-pts and controls.

Conclusion: Data demonstrate increased expression of choline transporter CTL1 and ACh transporter CTL4 in mucosa from CRN-pts, indicating increased absorption/excretion of choline/ACh. Further, functional data demonstrate altered response to ACh in CRN-pts as measured by electrogenic transepithelial transport.

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P1028 PERITONEAL DISSEMINATION IS MORE COMMON IN BRAF MUTATION THAN KRAS MUTATION OR KRAS/BRAF WILD TYPE IN COLORECTAL CANCER

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Introduction: Molecular alterations are well studied in colorectal cancer, however there is still need for an improved understanding of their clinicopathological features. This study aims to characterize colorectal cancer with regard to *KRAS* and *BRAF* mutations in connection with tumor distant metastasis and prognosis in patients with colorectal cancer.

Aims & Methods: We consecutively selected 96 stage IV colorectal cancer patients who underwent surgical resection at the Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital from January 2008 to December 2011 after obtaining their informed consent. All samples were analyzed to identify any *BRAF* (V600E) and *KRAS* (codons 12 and 13) mutations by direct sequencing. Patients with inflammatory bowel disease, a known history of familial adenomatous polyposis, Lynch syndrome or microsatellite instable were excluded.

Results: Of the 96 colorectal cancer patients, 25 (26.0%) were *KRAS* mutation, 7 (7.3%) were *BRAF* mutation and 64 (66.6%) were *KRAS*/*BRAF* wild type. In total, 73 (76.0%) were hematogenous metastasis, 22 (22.9%) were lymphogenous metastasis and 27 (28.1%) were peritoneal dissemination. In *KRAS* mutation patients, 8 (20%) were containing dissemination. In *BRAF* mutation patients, 5 (71%) were peritoneal dissemination and 14 (21.9%) in *KRAS*/*BRAF* wild type. Dissemination were significantly more common in *BRAF* gene mutation than in *KRAS*/*BRAF* wild type (Fisher's exact test, $p = 0.01$). Median survival time were 692 days in *KRAS* gene mutation, 470 in *BRAF* gene mutation and 1143 in wild type (logrank test, $p < 0.01$).

Conclusion: Peritoneal dissemination is more common in *BRAF* mutation than *KRAS* mutation or wild type in colorectal cancer.

Disclosure of Interest: None declared

P1029 IDENTIFICATION OF NORE1A AS A NEGATIVE FEEDBACK REGULATOR OF TNFA-NF-ΚB SIGNALING, WHICH DIRECTS APOPTOTIC SWITCH OF TNFA FUNCTION IN COLORECTAL TUMOR CELLS

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Introduction: NORE1A (RASSF5), a member of the Ras-association domain family (RASSF) of proteins, plays an important role in various cellular processes, including cell proliferation and apoptosis. NORE1A expression is commonly silenced or down-regulated in many human malignancies, including colorectal cancer. However, the mechanisms underlying its tumor suppressive functions have not been entirely defined.

Aims & Methods: To explore whether NORE1A inactivation is associated with colorectal tumor cell resistance to TNFα-induced apoptosis, we investigated TNFα effect on NORE1A expression using semi-quantitative RT-PCR and immunoblotting assay. NORE1A regulation of TNFα-NF-κB signaling and its cellular effects were defined by luciferase reporter and flow cytometric analyses and cell proliferation and apoptosis assays.

Results: NORE1A transcription was activated by TNFα and its induction strongly increased apoptotic response of colorectal tumor cells to TNFα. TNFα activation of NORE1A was disrupted when the RIPK1-IκBα-NF-κB signaling was blocked while it was further enhanced by p65/RelA transfection, indicating that NORE1A is a novel transcriptional target of TNFα-NF-κB signaling, which stimulates apoptosis-promoting function of TNFα. We also found that TNFα-induced NORE1A causes a rapid degradation of TNFα receptor type I (TNFRI) protein and subsequently suppresses NF-κB signaling, indicating the presence of a negative feedback regulatory loop between TNFα and NORE1A. Intriguingly, NORE1A degradation of TNFR1 was found to selectively impede TNFα-mediated RIPK1-IκBα-NF-κB signaling, thus blocking NF-κB-mediated cell growth and survival, whereas it facilitates TNFα-induced caspase activation and apoptosis. We finally observed that restoration of NORE1A expression in nonexpressing tumor cells strongly enhances apoptotic sensitivity of tumor cells to TNFα, suggesting that loss of its expression in tumorigenic process might be a key event that debilitates TNFα's proapoptotc effect.

Conclusion: Our data demonstrate first that NORE1A is a negative feedback regulator of TNFα, which directs apoptotic switch of TNFα function by selectively impeding TNFα-NF-κB signaling. These results strongly suggest that NORE1A inactivation might be a critical event that drives the oncogenic conversion of TNFα function in colorectal tumorigenesis.

Disclosure of Interest: None declared

P1030 THE ASSOCIATION OF GENETIC VARIATION WITHIN THE WNT SIGNALLING PATHWAY WITH COLORECTAL CANCER: A META-ANALYSIS

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Introduction: 35% of colorectal cancer (CRC) risk is attributable to heritable factors, of which a large proportion remains unexplained. Genome wide association studies have conclusively identified several risk variants in the TGF-beta pathway. Both TGF-beta and Wnt pathways are key regulators of colonic crypt homeostasis and colorectal carcinogenesis. The Wnt pathway is deregulated in 93% of CRCs, however the role of Wnt pathway genetic variation in CRC risk is uncertain.

Aims & Methods: The aim is to perform a systematic review and meta-analysis to assess the association of polymorphisms within the Wnt signalling pathway and the risk of CRC.

A systematic literature review of the Pubmed and HuGENet databases was conducted. Studies were included/excluded based on pre-specified criteria. In order to assess the risk attributed to each identified variant, the 'per allele' model was utilised to calculate pooled odds ratios. Heterogeneity was investigated by subgroup analyses for ethnicity, gender and tumour location. Publication bias was investigated using funnel plots and Egger's test. Statistical analysis was conducted using the R program (version 3.1.0).

Results: Forty-three polymorphisms across 18 different genes in the Wnt pathway were identified. Meta-analyses were conducted for 12 of these polymorphisms including between 831 to 31,427 cases per polymorphism. 6 polymorphisms were significantly associated with the risk of CRC. Rs1801155 within *APC* (OR = 1.79; 95% CI 1.27-2.52) and rs10505477 at the 8q24.21 locus (OR = 1.15; 95% CI 1.12-1.19) were associated with an increased risk of CRC. rs16260 (OR = 0.94; 95% CI 0.89-0.99) and rs9929218 (OR = 0.93; 95% CI 0.90-0.95) within *CDH1*; rs6983267 (OR = 0.85; 95% CI 0.83-0.87) within *MYC* and rs7014346 (OR = 0.87; 95% CI 0.81-0.94) at the 8q24.21 locus, were associated with a decreased risk of CRC. Subgroup analysis revealed gender, ethnicity and tumour location were not sources of heterogeneity.

Conclusion: Six polymorphisms associated with CRC risk account for a significant proportion of familial risk, although are unlikely to account completely for aberrant activation of the Wnt pathway. These polymorphisms are located within *APC, CDH1 and MYC* genes and the 8q24.21 locus. Further research into their precise role in colorectal carcinogenesis is warranted. Meta-association studies of all SNPs in the Wnt pathway should be conducted to identify further risk variants. Rare variants, copy number variations and epigenetic alterations may contribute to the remaining heritability and Wnt pathway activation.

Disclosure of Interest: None declared

P1031 IMMUNESURVEILLANCE IN NON INFLAMMATORY COLORECTAL CARCINOGENESIS: EPITHELIAL CELLS IN ADENOMA ENHANCE THEIR ANTIGEN PRESENTATION CAPABILITY WITHOUT ELICITING A STRONG IMMUNE RESPONSE

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Introduction: In non inflammatory colorectal cancer, T cell populations were demonstrated to play a significant role in the patients prognosis although it is not clear the trigger of this immune response and its efficiency in the preneoplastic lesions. Costimulatory interactions are decisive in sensitization of T cells by antigen presenting cells and important for the elicitation of the immune responses. Our previous studies demostrated that immunesurveillance mechanisms mediated by CD80-CD28 signalling may lead to dysplasia regression in ulcerative colitis.
Aims & Methods: The aim of this multicentric study was to explore the effect of CD80-CD28 signaling in human non inflammatory carcinogenesis and in a murine model of colonic carcinogenesis.
We prospectively enrolled 105 subjects who underwent screening colonoscopy or colectomy: 45 of them had an adenoma, 45 had an adenocarcinoma and 15 were healthy subjects. Biopsies were taken from their healthy mucosa and colonic lesions. Flow cytometry for CD8 + CD28+ or CD8 + CD38+, CD4 + CD25+ and CD25 + FoxP3+ lymphocytes and for CD80+ or HLA ABC+ epithelial cells were performed.
The azoxymethane (AOM)-induced colon carcinogenesis mouse model was used to block in vivo CD80 signaling by administration of neutralizing antibodies against CD80 or isotype control. Mice were euthanized 4 and 6 months after the first AOM injection. Colons were removed and examined. Flow cytometry was performed. Non parametric statistics was used.
Results: A higher rate of epithelial cells expressing CD80 or HLA-ABC was observed in colorectal adenoma compared to healthy colonic mucosa ($p = 0.036$ and $p = 0.022$, respectively) and colorectal adenocarcinoma ($p = 0.19$ and $p = 0.008$, respectively). The rate of CD8 + CD28+ and CD8 + CD38+ lymphocytes resulted higher in colorectal adenocarcinoma than in colorectal adenoma ($p = 0.001$ and $p = 0.005$, respectively).
We observed a higher rate of CD80+, MHC-I+ and MHC-II+ epithelial cells ($p = 0.004$, $p = 0.02$ and $p = 0.002$, respectively) and of activated lymphocytes (CD4 + CD25+, CD8 + CD28+ and CD8 + CD69+) ($p = 0.002$, $p = 0.002$ and $p = 0.015$, respectively) in mice sacrificed at 4 months than in those sacrificed at 6 months. Administration of anti-CD80 significantly increased the frequency of HGD ($p = 0.02$).
Conclusion: Epithelial cells of colorectal adenoma activate their capability of antigen presentation without eliciting a strong immune response. In the AOM mouse model, the antigen presenting activity and the immune response is more activated in a very early stage of the carcinogenesis. Our hypothesis is that some inhibitors (CTLA-4 or PD-1) can interfere with the immunesurveillance mechanisms in non inflammatory colorectal carcinogenesis.
Disclosure of Interest: None declared

P1032 ASYMPTOMATIC RADIOLOGICALLY DETECTED COLONIC PERFORATIONS IN THE ENGLISH NHS BOWEL CANCER SCREENING PROGRAMME (NHSBCSP)

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Introduction: Colonoscopies in the English NHSBCSP are offered to 60-74 year olds with an abnormal Faecal Occult Blood Test. Colonoscopic perforation remains one of the most serious adverse events associated with colonoscopy. Patients typically present with symptoms as a result of peritoneal irritation, however, colonic perforation may be diagnosed radiologically in patients who are entirely asymptomatic.
Aims & Methods: The aims of this study were to identify cases of asymptomatic radiologically detected colonic perforation in the English NHSBCSP, describe similarities between them and explore why such perforations occur. We identified all reported cases of colonoscopic perforation from the start of the NHSBCSP in 2006 up to and including 13/03/2014 from the web-based database used by the NHSBCSP, the Bowel Cancer Screening System. The NHSBCSP definition of perforation is: air, luminal contents or instrumentation outside the gastrointestinal tract. Bowel Cancer Screening Centres were subsequently asked to complete an online questionnaire relating to the patient's post perforation presentation, assessment management, and outcome.
Results: Of 147 perforations identified, complete data on 117 was received. Four asymptomatic radiologically detected colonic perforations were identified. Case 1 was a biopsied rectal cancer. Staging Magnetic Resonance Imaging (MRI) and staging Computed Tomography (CT) 12 and 14 days respectively following colonoscopy noted a sealed off perforation posterior to the rectum. Two cases were associated with a biopsied sigmoid cancer; one a perforation identified at staging CT 2 days following colonoscopy, the other on a same day completion CT virtual colonoscopy after the cancer was impassable endoscopically, showing gas to the right of the tumour. Case 4 was a biopsied cancer at the hepatic flexure with perforation diagnosed on staging CT 24 hours later. TNM classification was reported in 3 cancers: T3N0M0, T4N1MO and T4N2M0. Histology confirmed either well or moderately differentiated adenocarcinoma in 3 cancers. Two of these patients were recalled to hospital following CT findings, subsequently having surgery. The other 2 did not require immediate admission.
Conclusion: All asymptomatic radiologically detected perforations were associated with colorectal cancer seen on staging radiological investigation where the cancer had been cold biopsied. It is likely that only perforations associated with cancer will present asymptomatically as it is only they that have staging radiological investigation. The cancers were in the rectum, sigmoid colon and hepatic flexure. TNM classification was at least T3. Emergency surgery was not required in three of these patients. The underlying cause of this is sub group of perforations is perhaps more likely to be due to invasion of the cancer and not the biopsy, however, a larger case series is required to confirm these findings.
Disclosure of Interest: None declared

P1033 POSITIVE PREDICTIVE VALUE INCREASES WITH AGE IN A FECAL IMMUNOCHEMICAL TEST BASED COLORECTAL CANCER SCREENING PROGRAM

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Introduction: There is a good correlation between concentration of fecal hemoglobin (Hb) in fecal immunochemical tests (FITs) and age. Previous studies have shown that fecal Hb concentrations in stool and positivity rate (PR) increase with age. It is currently unknown whether that increase is mainly the result of a higher detection rate (DR) of advanced neoplasia (AN) or an increase in false positive rate (FPR). Quantitative FIT enable to choose the preferred fecal Hb concentration for colonoscopy referral. So far, cutoff values have been set to one fixed level for all ages. However, age partitioned reference values for fecal Hb concentration may be warranted if FPR increases relatively more with age than DR. The aim of this study was to assess the relation of FPR and DR with age and its influence on positive predictive value (PPV).
Aims & Methods: All average risk individuals, aged 55-75 years, who completed one sample FIT in a first round of a population-based colorectal cancer (CRC) screening pilot were included. A positivity cut-off level of 10 µg Hb/gram feces (> 50 ng Hb/ml) was used. All screenees with a positive test were offered colonoscopy. We calculated age-specific PR, DR, FPR and PPV. Logistic regression analyses were performed to determine the independent association of PPV with multiple variables (sex, age, social economic status, fecal Hb concentration). Variables achieving a P value of less than 0.05 were included in a multivariate logistic regression analyses, as were variables included by the clinician's rationale (gender).
Results: Of the 10.008 invitees, 5,986 persons (mean age 60.4 (±6.8) years; 49.7% males) participated and 503 (8.4%) persons had a positive test. Attendance rate, PR and DR were significantly higher in the older age categories ($p < 0.001$). Multivariate logistic regression analyses, with age as continues variable, showed PPV increased significantly with age and fecal Hb concentration when corrected for gender, Table 1. There were no significant differences in frequencies between the observed values and the predicted values of the model (Hosmer and Lemeshow Goodness-of-Fit Test; $p = 0.183$).

Table 1: Uni- and multivariate logistic regression analyses with the positive predictive value of having advanced neoplasia as dependent variable.

	Univariate Odds ratio (95% CI)	p-value	Multivariate Odds ratio (95% CI)	p-value
Sex male	1.31 (0.90-1.90)	.154	1.17 (0.79-1.74)	.435
Age (per ten years)	1.55 (1.18-2.06)	.002	1.55 (1.16-2.09)	.004
Socio-economic status		.330		
High	*Reference*			
Middle	1.14 (0.70-1.87)			
Low	1.36 (0.91-2.04)			
Fecal Hb concentration (per 10 µg Hb/g feces)	1.07 (1.05-1.09)	<.001	1.07 (1.05-1.09)	<.001

Conclusion: PPV increases significantly with age and fecal Hb concentration in a FIT-based CRC screening program. This implies a relatively larger increase of DR compared to FPR with age. These results suggest age-partitioned reference values for fecal Hb concentration are not warranted.
Disclosure of Interest: None declared

P1034 SENSITIVITY OF PRETARGETED 68GA PET-CT TO DETECT COLORECTAL CARCINOMA LIVER METASTASIS IN A MOUSE MODEL: COMPARISON WITH 18FDG PET-CT

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Introduction: The aim of our study was to compare the performances of a pretargeted PET (pPET) imaging with anti-CEA (carcinoembryonic antigen) and anti-HSG (histamine-succinyl-glycine) recombinant humanized bispecific monoclonal antibody (TF2) and ^{68}Ga-labeled HSG peptide (IMP288) to conventional ^{18}FDG PET in an orthotopic murine model of colorectal cancer liver metastasis.
Aims & Methods: CEA expression of colorectal cancer cells (LS174T Luc) was assessed *in vitro* by flow cytometry and *in vivo* by CEA staining. Hepatic tumors were grafted by intraportal injection and tumor burden was confirmed using bioluminescence. One group was pretargeted with TF2 and received IMP288-^{68}Ga 24 hours later (n = 8). One group received ^{18}FDG (n = 8). One group had both imaging modalities (n = 7). PET acquisitions started 1 hour after radionuclide injection. Biodistributions of the ^{68}Ga labeled peptide and ^{18}FDG in tumors and normal tissues were assessed one hour after imaging.
Results: LS174T Luc cells expressed CEA. Considering tissues uptakes, Tumor/Organ ratio with ^{68}Ga-PETp were statistically significantly higher compared to ^{18}FDG PET ($p < 0.05$) with both imaging and biodistribution data. ^{68}Ga-PETp sensitivity for tumor detection was 67% versus 31% with ^{18}FDG PET ($p = 0.049$). For smaller tumors less than 200 mg, the sensitivity was 44% with ^{68}Ga-PETp versus 0% with ^{18}FDG PET ($p = 0.031$). A strong correlation was demonstrated between signals measured on PET images and biodistribution analyzes ($r^2 = 0.85$).
Conclusion: ^{68}Ga-PETp was more sensitive than ^{18}FDG-PET for the detection of colorectal liver metastasis in an orthotopic murine model. Improved Tumor/Organ ratio allows imaging and therapeutic considerations.
Disclosure of Interest: None declared

P1035 DIAGNOSTIC ACCURACY AND INTEROBSERVER CONSISTENCY FOR THE ENDOSCOPIC PREDICTION OF SESSILE SERRATED ADENOMAS/POLYPS

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Introduction: It may be challenging to recognize sessile serrated adenomas/polyps (SSA/Ps) and to differentiate them from hyperplastic polyps (HPs) or tubular adenomas (TAs) during colonoscopy evaluation. Although several studies suggested endoscopic features of SSA/Ps, the external validity and interobserver consistency of those features are not well studied.
Aims & Methods: This study aimed to examine diagnostic accuracy and interobserver consistency of endoscopic features for the diagnosis of SSA/Ps using high-resolution white-light endoscopy.
Endoscopic images of 81 polyps (29 SSA/Ps, 19 HPs, and 23 TAs) from 43 patients undergoing screening colonoscopy between March 2005 and April 2014 at a single tertiary care center were retrospectively evaluated by 10 colonoscopists. Eight endoscopic features of SSA/Ps (indistinctive border, irregular shape, rim of debris, cloud-like surface, mucous cap, nodular surface, absence of vessels, and dark spots) were assessed for each polyp in three stages: learning set, consensus meeting, and validation set.
Results: In the validation set, the prevalence of the features was ranged from 21.7% of SSA/Ps for dark spots to 51.0% for indistinctive border. In the multivariable analysis, mucous cap (odds ratio [OR], 10.10; 95% confidence interval [CI], 6.44–16.00, $p < 0.001$), cloud-like surface (OR, 3.05; 95% CI, 1.74–5.32, $p < 0.001$), indistinctive border (OR, 2.38; 95% CI, 1.53–3.69, $p < 0.001$), rim of debris (OR, 2.04; 95% CI, 1.43–3.55, $p < 0.001$), and dark spots (OR, 1.76; 95% CI, 1.11–2.80, $p = 0.016$) were independent predictors of SSA/Ps compared to HPs and TAs. The number of the independent predictors showed excellent discrimination (area under the receiver-operating characteristic curve [AUROC], 0.80). When ≥1 of the predictors were observed, SSA/Ps could be diagnosed with a sensitivity of 85.2% and specificity of 63.9%. Nevertheless, the interobserver agreement on the independent predictive findings demonstrated only moderate to fair κ-values (range, 0.25–0.41) except for dark spots, which showed poor interobserver agreement ($\kappa = 0.12$).
Conclusion: Several features of SSA/Ps were found to provide reliable accuracy for the endoscopic prediction of SSA/Ps. However, the interobserver agreements of the features remain to be improved.
Disclosure of Interest: None declared

P1036 MODEL OF INVITATION TO ENSURE HIGH PARTICIPATION ON THE COLORECTAL CANCER SCREENING PROGRAMME OF THE BASQUE COUNTRY (SPAIN)

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Introduction: : The aim of this study is to evaluate the evolution of Participation Rate (PR) and trends of the Colorectal Cancer Screening Programme carried out in the Basque Country. This Programme started in 2009, based on the detection of occult blood in faeces every two years and colonoscopy under sedation as a confirmed diagnosis. According to the European Guidelines (2010) recommendations, the key point to obtain an efficient program depends on the overall PR. Involving and Coordinating staff of different health care levels and developing innovative methods can increase PR.
Aims & Methods: a) Before the invitation, the Program Coordination Centre staff plans and organizes the elected Primary Care Center involved and agrees with hospitals the capacity to perform screening colonoscopies. b) A specific program software connected with other electronic medical data bases (medical records, hospital discharges, Cancer Registries and mortality), selects (50-69 year-old residents) and excludes (CRC diagnosed, colonoscopy in the last 5 years). c) Certified training is offered to all staff in the health centers. d) A personalized invitation letter, explaining the aims and methods of the programme was sent, including a free phone line, e-mail and web-site for further clarifications. Nevertheless, the person decides to participate or not. e) Afterwards, the kit, instruction leaflet with a personal code is delivered by post. f) Once the person decides to participate, the kit can be left in Health Care Centers without any previous appointment and guaranteed quality controls.
Results: : At the beginning of the program (2009) the overall PR was 58.1%, reaching 68.9% in first round in 2013. Once analyzed by sex PR for women increased from 61.3% to 71.3% and from 54.6% to 66.3% for men. All trends of PR were positive, 1.032 for overall PR ($p < 0.001$); 1.034 for women ($p < 0.001$) and 1.029 for men ($p < 0.001$). In the second round we have observed that the PR also increased, overall PR went from 67.0% to 70.7% (Trend = 1.029, $p < 0.001$), in women from 71.4% to 73.1% (Trend = 1.019, $p < 0.001$) and in men from 62.5% to 68.2% (Trend = 1.043, $p < 0.001$). We have analyzed trends by sex/age ranges (younger/older than 60 years), and we observed that all trends were positive being higher in women and participants older than 60 years.
Conclusion: This work demonstrates that the strategy invitation in a screening programme markedly influences on PR. The choice of the kit, way of shipping/collection and other factors such as the involvement of primary care physicians could be crucial.
Disclosure of Interest: None declared

P1037 CLINICOPATHOLOGICAL FEATURES OF T1 COLORECTAL CARCINOMAS WITH "SKIP INVASION"

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Introduction: With recent advances in endoscopic treatment, many T1 colorectal carcinomas are now resected endoscopically with negative margins. However, there are some cases with "Skip Invasion", which is defined as discontinuous foci of carcinoma cells in the deeper layer of the colon apart from the invasive front, and "Skip Invasion" cannot be diagnosed with current endoscopic procedures.
Aims & Methods: The aim of this study was to investigate the clinicopathological features of T1 colorectal carcinomas with "Skip Invasion".
Of the 23725 colorectal neoplasms excluding advanced carcinomas which have been resected endoscopically or surgically at our institution from April 2001 to November 2014, 653 T1 carcinomas surgically resected were investigated. Then clinicopathological features of T1 carcinomas with and without "Skip Invasion" were compared. The factors for the analysis were patient age, sex, tumor size, location, morphology, degree of submucosal invasion, lymphovascular invasion, tumor budding, and histological type (por or muc component).
Results: There were 4 lesions (0.6%) with "Skip Invasion". All lesions with "Skip Invasion" were observed in sigmoid colon ($p = 0.02$) and showed lymphovascular invasion ($p = 0.13$). There were no significant differences in the other factors. One of 4 lesions showed the presence of lymph node metastasis.
Conclusion: All lesions with "Skip Invasion" were in sigmoid colon and showed lymphovascular invasion. These lesions were rare, but they certainly exist and might cause poor prognosis. Further caution should be needed for lesions with lymphovascular invasion, especially in sigmoid colon.
Disclosure of Interest: None declared

P1038 FECAL OCCULT BLOOD TESTS SHOW LOWER CANCER DETECTION RATE IN THE PROXIMAL COLON: A META-ANALYSIS OF 47 DIAGNOSTIC STUDIES

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Introduction: Diagnostic accuracy of fecal occult blood tests (FOBTs) differ widely in studies of colorectal cancer screening. This meta-analysis aims to evaluate the diagnostic accuracy of FOBTs for the detection of colorectal cancer (CRC) in the proximal colon.
Aims & Methods: Studies assessing performance of FOBTs were searched from the OVID databases up to 28 February 2015. Studies were eligible if subjects received FOBTs to estimate the diagnosis of CRC which was confirmed by colonoscopy. Analyses were conducted separately for Guaiac-based and

Immunochemical-based FOBT (gFOBT and iFOBT). Main outcomes included sensitivity and specificity of FOBTs. Bivariate random-effects model was applied to combine the results from individual studies. Subgroup analyses were performed to evaluate the test performances based on location of neoplasia and the brands of FOBTs.
Results: A total of 47 studies with 79,605 subjects (gFOBTs: 28 cohorts; iFOBTs: 42 cohorts) were identified from 18 geographic regions. In the gFOBT group, the combined sensitivity and specificity for CRC were 62.2% (95% CI = 51.0% to 72.2%) and 93.4% (95% CI = 91.0% to 95.2%) respectively. In iFOBT group, the combined sensitivity and specificity for CRC were 84.4% (95% CI = 79.9% to 88.1%) and 92.3% (95% CI = 89.7% to 94.3%). The diagnostic performance of gFOBT was significantly lower than that of iFOBT (AUC = 91% vs 95%, p = 0.014). Subgroup analysis showed that both FOBTs have higher sensitivity and comparable specificity for CRC detection in the distal colon compared with the proximal colon. (iFOBT sensitivity: 80% vs 72%; gFOBT sensitivity: 72% vs 64%). The diagnostic performances across different brands of FOBTs were comparable.
Conclusion: The diagnostic accuracy of FOBTs for CRC is good. iFOBTs showed better performance than gFOBT, and both FOBTs showed better CRC detection on the distal colon. Annual screening with iFOBT is recommended to reduce the chance of missing detection on proximal colon.
Disclosure of Interest: None declared

P1039 CLINICAL SIGNIFICANCE OF SUBCLASSIFICATION FOR COLORECTAL LATERALLY SPREADING TUMOR (LST) GRANULAR TYPE

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Introduction: Colorectal laterally spreading tumor-granular type (LST-G) is divided into 2 subtypes according to its morphology: homogenous type and nodular mixed type. However, the present LST-G subtype classification has not been defined by concrete objective findings but the concept of morphology without definite criteria.
Aims & Methods: This study was aimed to clarify the clinical significance of concrete objective LST-G subclassification according to the diameter of their granules or nodules. A total of 636 consecutive cases with LST-G that was resected endoscopically or surgically in Hiroshima University Hospital and Hiroshima City Asa Hospital between January 2008 and December 2014 entered this study. LST-Gs were divided into three types as follows; Type1: a lesion with homogenous uniform granules (<5mm), Type 2: a lesion with granules and small nodules (5mm≤, <10 mm), Type 3: a lesion accompanied by large nodules (≥10 mm). We evaluated interobserver agreement for subclassification of LST-G and accuracy in each group. Also, we investigated case characteristics and clinicopathologic features (sex, age, tumor size, location, histology, and invasion depth) for each LST-G subtype in whole 636 lesions. In validation study, a total of 194 fine images in 97 cases with conventional endoscopy and chromoendoscopy with indigo carmine dye spraying were distributed in randomized order to medical students with no prior endoscopy experience (Student Group), less-experienced endoscopists (LEE Group) and high-experienced endoscopists (HEE Group).
Results: Interobserver agreements were >0.6 representing good agreement in all groups. Diagnostic accuracy in HEE Group was higher than students and LEE Group. Chromoendoscopy had higher accuracy rate than conventional endoscopy in LEE Group (74% vs 69%, $p < 0.05$) and HEE Group (84% vs 78%, $p < 0.05$). As for the misdiagnositc lesions, participants in all groups tended to misdiagnose Type 1 as Type 2, and Type 3 as Type 2. Meanwhile, in the lesion of Type 2, lesions were prone to misdiagnose as Type 3 in LEE Group and HEE Group but as Type 1 in Student Group. Type 2 and Type 3 lesions were significantly larger than Type 1 lesions (Type 1: 21 ± 10mm, Type 2: 39 ± 22mm, Type 3: 46 ± 20mm, $p < 0.01$). The incidence of carcinoma in Type 1 was much lower than that in Type 2 and Type 3 (3% [4/154], 62% [141/226], 63% [162/256], respectively; $p < 0.01$). The incidence of submucosal invasive carcinoma in each type (Type 1, Type 2 and Type 3) were 0% (0/154), 7% (16/226) and 15% (38/256), respectively. The incidence of submucosal deep invasive carcinoma [≥1000 mm] in Type 3 was higher than that in Type 2 (11% [29/256] vs 3% [7/226], $p < 0.05$).
Conclusion: This subclassification for LST-G according to the diameter of granules and nodules using chromoendoscopy with indigo carmine dye spraying was universal, and may be clinically useful for choosing therapeutic strategy.
Disclosure of Interest: None declared

P1040 LOW RATE DETECTION OF ADVANCED ADENOMAS WITH A SINGLE-SAMPLE FECAL IMMUNOCHEMICAL TEST IN AVERAGE-RISK INDIVIDUALS: A PROSPECTIVE PILOT STUDY USING COLONOSCOPY AS REFERENCE STANDARD

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Introduction: Fecal immunochemical test (FIT) have been recommended for colorectal cancer (CRC) screening in several clinical practice guidelines and is the initial option in same regions due to limited availability or high costs of colonoscopy. However some studies have reported inconsistent results about FIT performance.
Aims & Methods
Aim: To compare the results of single-sample FIT with colonoscopy findings and calculate the accuracy for advanced neoplastic lesions or CRC detection.
Methods: Asymptomatic average-risk individuals scheduled for screening colonoscopy were invited to provided one stool sample one week before the exam. We used a cualitative FIT manufactured by ABONTM Biopharm (Hangzhou) co., Ltd., without diet or medication restrictions. The lower limit of haemoglobin detected by this test is 50 ng/ml. The positivity rate of the FIT in relation to colonoscopic findings and the accuracy (sensitivity, specificity, area under ROC curve) of the FIT for CRC and advanced neoplastic lesions detection were determined.
Results: Of a total of 146 individuals invited, 119 (81.5%) returned the FIT kit with adequate stool sample and completed their colonoscopy. Mean age was 58.4 (33-85) years and 58.8% were males. An advanced neoplasm was found in 14 (11.7%) individuals: a CRC in 2 (1.7%) and an advanced adenoma (>10 mm, villous histology or high grade dysplasia) in 12 (10.1%) subjects. In 31 individuals (26%) the FIT was positive. The positivity rate of the test in relation to colonoscopic findings was: 24.5% in patients with normal colonoscopy, 17.6% in hyperplastic polyps, 20% in sessile serrated adenomas, 25.8% in adenomas, 36.4% in advanced adenomas, and 100% in CRC. The sensitivity and specificity of the FIT (95% confidence intervals) for advanced adenomas or CRC was 50% (25% to 75%) and 77% (74% to 80%) respectively. The area under ROC curve was 0.99. FIT sensitivity for CRC was 100% (20% to 100%), whereas specificity was 75% (74% to 76%). For advanced adenomas, sensitivity was 42% (17% to 70%) and specificity 76% (73% to 79%).
Conclusion: In this preliminary report of a single-sample FIT before screening colonoscopy, the positivity rate was significantly high (26%) but the test only detected little more than a third of advanced adenomas. However all CRC were detected (sensitivity 100%).
Disclosure of Interest: None declared

P1041 CLINICAL EVALUATION OF UNEXPECTED COLONIC FOCAL UPTAKE DETECTED BY FDG-PET/CT

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Introduction: FDG-PET/CT is recognized as a useful tool to manage colorectal cancer and has been shown to have an additional value in the detection of colorectal cancer recurrence. Some studies reported that FDG accumulated in adenomatous polyps, and the possibility that FDG-PET/CT can detect early premalignant colorectal lesions was suggested. However, few studies have evaluated FDG-PET/CT for incidental premalignant colonic lesion detection.
Aims & Methods: FDG PET/CT studies were performed for two-year periods in 5088 consecutive patients with various malignant diseases. We retrospectively analyzed the records of 240 consecutive patients who had undergone colonoscopy and FDG-PET/CT scan for malignant disease from December 2012 to November 2014 at our hospital; colonoscopy and FDG-PET/CT were done within six months of each other. Patients with a previous history of colorectal cancer were excluded from analysis.
Results: Seventy-four patients had 86 foci of incidental colonic activity on PET and were designated Group A (mean age 67.0 years, males 66%). The other 166 patients had no incidental colonic foci and were designated Group B (mean age 63.6 years, males 65%). The locations of colorectal foci were in the right side in 25 patients, in the left side in 41 patients, and in the rectum in 20 patients. In group A, 26 patients (35%) had malignant tumors (22 colorectal cancers, three malignant lymphomas, and one metastatic tumor) detected on colonoscopy. In group B, three patients (2%) had malignant tumors (two colorectal cancers and one metastatic tumor). Overall, the sensitivity, specificity, PPV (positive predictive value), NPV (negative predictive value), and accuracy of PET-CT for detecting malignant colonic tumors were 90%, 77%, 35%, 98%, and 79%, respectively. For detecting malignant colonic tumors and adenomas 10 mm or more in diameter, the sensitivity, specificity, PPV, NPV, and accuracy of PET-CT were 84%, 86%, 66%, 95%, and 86%, respectively.

Conclusion: FDG-PET/CT is a useful tool for detecting both malignant colorectal tumors and adenomas 10mm or more in diameter. Incidental colonic activity detected by PET-CT warrants further evaluation with colonoscopy. However, negative PET-CT does not rule out malignant colorectal tumors.
Disclosure of Interest: None declared

P1042 THE POSSIBILITIES OF THE OPTICAL METHODS FOR THE STUDY OF BLOOD IN COLORECTAL CANCER STAGING DIAGNOSING

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Introduction: Colorectal cancer (CC) is the second most common form of cancer in the world. The limitations of the currently available methods and biomarkers for CC management highlight the necessity of finding novel markers.
Aims & Methods: The aim of this work was to assess the potential of the optical methods for studying erythrocytes (Er) and blood serum (BS) of patients with CC in staging diagnosing.
A total of 36 persons (53±9 years old) with CC (histologically – adenocarcinoma) in the T1-2 stage (the 1st group) and in the stage T3-4 (the 2nd group) were examined. The control group consisted of 16 healthy people. Electric and viscoelastic Er parameters were investigated by dielectrophoresis, their membrane structure - by TLC and gas chromatography. The optical properties of BS were studied by the methods of ellipsometry. The reaction of the monoclonal antibody CD 24 with BS antigens of CC patients was studied by spectroscopic ellipsometry close to the conditions of surface plasmon resonance (SPR) (ProteOn XPR36 (BioRad).
Results: We observed differences in Er parameters, associated with the CC stage. Given in the 2nd group summarized rigidity, viscosity, electrical conductivity, the relative polarizability, indexes of aggregation and destruction were higher than those in the 1st and in the controls ($p < 0.001$-0.05). At the same time the patients of the 2nd group had marked disturbances of Er deformability, leading to the development of microcirculatory disorders and tissue hypoxia. We observed high levels of cholesterol fraction, oleic, stearic acids, high index of cholesterol/phospholipids (PHL) and low levels of total lipids, easily oxidable PHL, arachidonic acid, omega-3 index in Er membranes in the 2nd group in comparison with those in the 1st group of patients ($p < 0.0001$-0.03). Scanning ellipsometry showed marked heterogeneity in thickness and composition, the abundance of discontinuities in thin films of BS of patients in the 2nd group compared to the 1st one ($p < 0.001$). Increasing the refractive index in combination with the reduction in film thickness as CC stage was weighting has been observed ($p < 0.01$-0.05). The concentration of the antigens to the CD24 in the BS of patients (obtained by SPR) in the terminal stages of CC was higher than that in the T1-2 ($p < 0.001$). We revealed correlations between Er parameters, BS ellipsometry characteristics and biochemical parameters, which reflected the interaction between these components depending on the CC stage.
Conclusion: Identified microcirculatory disturbances probably aggravate the course of CC and, therefore, require additional therapeutic effects. Differences in Er and BS parameters associated with the stage of CC, give hope for the development of new diagnostic methods at the early stages of the disease.
Disclosure of Interest: None declared

P1043 CHARACTERIZATION OF THE ENDOSCOPIC AND PATHOLOGIC MEASUREMENTS OF COLORECTAL POLYP SIZES AND ITS ASSOCIATION WITH POST-POLYPECTOMY COLONOSCOPY SURVEILLANCE GUIDELINES

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Introduction: Colorectal cancer (CRC) is the main leading cause of cancer related deaths in Portugal. After removing colorrectal polyps (CRPs), ESGE[1], ASGE[2] and UK guidelines[3] recommend endoscopic surveillance based on size, number and histological findings of CRPs. While UK guidelines use the endoscopical measured size (EMS), the preferred method (endoscopical versus histological) for CRP size assessment is not specified in the ESGE and ASGE guidelines. The preferred CRP size assessment method is controversial.
Aims & Methods: To characterize the discordance and correlation between the pathological measured size (PMS) and EMS of CRPs, according to its anatomic location and histological findings.
All colonoscopies in which CRPs were observed between 1/Jan/2013 and 31/Dec/2013 were identified. CRPs removed by polypectomy snare in a single fragment and with available endoscopic and histological reports were selected. The endoscopic and pathologic measurements of CRPs sizes were performed.
Results: The PMS (mean 8.03 mm ±1.41 SD) was significantly smaller than the EMS (mean 10.46 mm ±7.36 SD) in the 552 CRPs included in the study (360 patients, 68.6% male, years median 69), independently of anatomic location (right colon, transverse colon or left colon + rectum) and EMS sub-group (≥1cm or <1cm). There was a good correlation between the EMS and PMS in the adenomas (=0.807, 95% confidence intervals [CI]) and a moderate correlation in the serreated polyps (SP) (=0.647, 95% CI). However, 32.0% of the adenomas and 63.2% of the SPs with EMS ≥ 1 cm presented PMS < 1 cm.
Conclusion: In a considerable portion of adenomas and SP where EMS is >1 cm, the PMS is <1 cm. This divergence may lead to alternative colonoscopy surveillance intervals after polypectomy, which may have both clinical and economic implications.

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Disclosure of Interest: None declared

P1044 SCREENING COLONOSCOPY FOR SUBJECTS OLDER THAN 85 YEARS OLD

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Introduction: According to US multi societies guideline for colonoscopy surveillance after screening and polypectomy, subjects elder than 85 are recommended to stop undergoing colonoscopy. However, asymptomatic elder subjects often come to hospital only due to positive fecal occult blood test in Japan with population aging.
Aims & Methods: This study was aimed to evaluate safety and efficacy of colonoscopy for subjects elder than 85 years old. This is a retrospective cohort study. From April 2006 to March 2010, 265 subjects elder than 85 years old underwent colonoscopy at our hospital. Of them, 16 patients who underwent surveillance after surgery for colorectal cancer and 54 patients who had been already pointed out some abnormalities were excluded and total 195 subjects were included for analysis. The subjects were divided into screening groups who were free from symptoms (hemoglobin <10g/dL, abdominal pain, or hematochezia) and symptomatic group. The association between detection rate of advanced colorectal cancer and various background factors (age, sex, presence or absence of symptom, hemoglobin, or mean corpuscular volume (MCV) using Logistic Regression model. Factors which revealed statistical tendency ($p < 0.10$) were included multivariate multivariate analysis. Cumulative overall survival rate of patients with advanced colorectal cancer was calculated using Kaplan-Meier method.
Results: There were 47 asymptomatic subjects and 148 symptomatic subjects. Advanced colorectal cancer was detected in 6.5% of asymptomatic and in 17% of symptomatic subjects respectively (p=0.0946). Low MCV revealed significance, and to be female (p=0.706) and presence of symptom (p=0.0581) revealed marginal significance for detection of advanced cancer. In multivariate analysis, only low MCV was independent risk factor (Odds ratio (every 5 decrease) 1.63 [1.29-2.11]). The cumulative overall survival rate at 3 and 5 years of patients with advanced colorectal cancer was 76% and 62%, respectively.
Conclusion: Colonoscopy for symptomatic patients would not be a contraindication because prognosis of advanced colorectal cancer was not so poor in our study. MCV might be a useful predictor for determination of the indication of colonoscopy for extremely elderly subjects.
Disclosure of Interest: None declared

P1045 LONG TERM ONCOLOGIC OUTCOMES OF THE COLORECTAL TIS CANCER

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Introduction: The incidence of early colorectal cancers is on rise with increase of screening colonoscopy. Thus, risk factors of lymph node metastasis or recurrence in early colorectal cancer is also important medical issue for endoscopists and colorectal surgeons.
Aims & Methods: The aim of this study was to evaluate that the depth of invasion in Tis cancer was associated with recurrence or lymph node metastasis. Additionally, this study was to assess the long-term outcome of patients with colorectal Tis cancer. A total of 496 colorectal Tis cancers from 481 patients between March 2003 and December 2013 were analyzed retrospectively. We evaluate the pathologic and clinical risk factor of colorectal Tis patients.
Results: The mean age of study population was 64.7 years and the median follow up time was 30.3 months. Of a total of 496 Tis cancers. There were no radiological lymph node metastases in 177 patients who conducted the computed tomography. 1.2% of Tis cancer showed angiolymphatic invasion. Three patients (0.62%) had proven distant or local recurrence. Local recurrences were occurred in 2 patients. And one patient who had peritoneal seeding and ovarian metastasis showed positive resection margin and tumor invading lamina propria at primary resection.

Conclusion: 1.2% of colorectal Tis cancer had positive results of angiolymphatic invasion. In recurrence cases what it were too small, all of recurrence patients had positive margin after resection. Thus, clinicians pay attention to angiolymphatic invasion and positive resection margin in pathologic results of colorectal Tis cancer after treatment.

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P1046 EFFECTIVENESS AND SAFETY OF COLORECTAL ESD IN ELDERLY PATIENT

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Introduction: Colorectal endoscopic submucosal dissection (ESD) has been established as a useful treatment for early colorectal tumors. The prognosis of early colorectal cancer is expected over several years without treatment. However, elderly people who often have various comorbidities might die of any other diseases, so colorectal ESD for elderly people is still controversial.
Aims & Methods: To analyze the potential benefits and risks of colorectal ESD in elderly compared to younger patients, we analyzed patients retrospectively who underwent ESD for early colorectal cancer in Omori Red Cross Hospital from 2012 May to 2015 March. We divided the patients into two groups: patients older than 80 years (group A) and patients 79 years of age or younger (group B). The two groups were compared with respect to their clinical backgrounds, medication (antiplatelet, anticoagulation), tumor characteristics, operation time, resection speed (mm^2/min), complication, rate of en bloc or curative resection, and survival rate. Statistical analysis included univariate analysis by chi-squared tests and Student's t-tests for comparing two groups (statistical significance was defined as $p < 0.05$).
Results: 156 lesions (male/female:81/75) underwent ESD procedures; 27 in group A and 129 in group B. Group A had significantly more comorbid diseases (hypertension, diabetes, renal or liver dysfunction, cardiac disorder) than group B (55.6% vs. 24.8%, $p < 0.01$). Patients in group A tended to take more antithrombotic medication than group B (22.2% vs. 11.6%, $p = 0.14$). Tumor size, specimen size, operation time, resection speed (mm^2/min), rate of complete en bloc resection, rate of curative resection, complication and survival rate were similar: 29.4 ± 18.2mm, 37.8 ± 18.3mm, 43.9 ± 35.6min, 25.8 ± 13.8(mm^2/min), 27/27 (100%), 27/27 (100%), 0/27 (0%), 26/27 (96.3%) in group A, and 29.1 ± 15.4mm, 37.6 ± 16.9mm, 44.3 ± 45.1min, 28.0 ± 15.3 (mm^2/min), 128/129 (99.2%), 124/129 (96.1%), 2/129 (1.6%), 128/129 (99.2%) in group B, respectively. Perforation occurred in 2 cases in group B. There were no differences in hospitalization periods and post-operative clinical courses between two groups. All of the 5 non-curative cases in group B are alive at the end of the follow up period (average 17.0 months. range: 6-28). Only one of 27 patients in group A died suddenly of heart failure about 1 month after the colorectal ESD, and the others are alive at the end of the follow up period (average 13.6 months. range: 1-32).
Conclusion: Colorectal ESD is almost equally effective and safe both in elderly and in younger patients. However, elderly patients have more comorbid diseases and tend to have more antithrombotic agents. Therefore, preoperative assessment of comorbid conditions and adequate perioperative care are necessary for elderly patients. Furthermore, to evaluate the exact prognosis of elderly patients performed colorectal ESD, we should continue to follow up them in longer period.
Disclosure of Interest: None declared

P1047 THE VALIDITY OF THREE STEPS LEARNING SYSTEM OF COLORECTAL ESD

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Introduction: Endoscopic submucosal dissection (ESD) for early colorectal cancer has become a widespread treatment over the world, but severe complications are reported still now and the appropriate training system of colorectal ESD is controversial.
Aims & Methods: In our hospital, the qualifications of an ESD trainee (A) are 1000 upper/300 lower endoscopy, 30 gastric ESD, and 20 colorectal ESD assistance. Colorectal ESD is performed with support by an expert (B) following these 3 steps. a) 0-5 cases: the position is all rectum, and have no fibrosis (F0), b) 6-20cases: tumor size is ≤50mm with no or mild fibrosis (F0/F1) and the expert gives every possible advices during procedures, c) 21cases-: The expert gives important advices or hands-on support only when the situation has technical difficulty or the trainee does dangerous procedure. We call this method "Three steps learning system (TSLS)". 154 consecutive ESD procedures performed in Omori Red Cross Hospital from 2012 April to 2015 March were retrospectively analyzed. We evaluated clinical backgrounds, outcomes of ESD procedures, and complications.
Results: A/B performed 23/131 cases respectively. The mean age, sex, comorbid diseases (hypertension, diabetes, renal dysfunction, cardiac disease), rate of having antithrombotic agents were similar between two groups. The location was C3/A1/T5/D3/S3/R8 in group A and C20/A24/T25/D17/S16/R29 in group B ($p = 0.578$). In terms of tumor shape, there was no protruded tumor in group A. There were also no significant differences in specimen size, tumor size, en bloc resection rate, and complication: 40.9 ± 23.3mm, 30.3 ± 20.4mm, 100%, and 1 case (perforation) in group A and 37.1 ± 16.0mm, 29.0 ± 15.2mm, 99.2% (130/131), and 1 case (perforation) in group B, respectively. Meanwhile, operation time and speed of resection (that is specimen size (mm^2) / operation time (min)) in group B were much faster than group A: 73.0 ± 52.6min, $16.1 \pm 8.7$$mm^2$/min in group A and 38.3 ± 39.1min, $29.9 \pm 15.0$$mm^2$/min ($p < 0.01$). The rate of fibrosis was 13.0% (F0/F1/F2: 20/3/0) in group A, 26.0% (F0/F1/F2: 97/29/5) in group B ($p = 0.18$). Self-completion rate was 18/23 (78.3%) in group A. In group A, five cases were not self-completion and the factors were followings: with fibrosis, lesion at a fold, invaded submucosa, or large lesion (≥10cm). R0 resection rate were similar, 95.7% (22/23) in group A, and 96.9% (127/131) in group B. Of the five non-curative resection cases, 4 cases were performed additional operation, and 1 case chose a conservative course. The clinical courses after procedures (fever, WBC, CRP) were also similar.
Conclusion: The advices of experts are very important for keeping safety ESD and an independence of novice is also essential. Colorectal ESD under our training system (TSLS) was appropriate and safe. However, in this study, there were few difficult lesions in group B. For verifying the validity of our system or improving self-completion rate, more cases will be required.
Disclosure of Interest: None declared

P1048 ADJUVANT CHEMOTHERAPY WITH TEGAFUR-URACIL PROVIDED GOOD OUTCOME FOR LOW-RISK STAGE II COLON CANCER

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Introduction: The benefit of adjuvant chemotherapy with Tegafur-uracil for the low-risk patients of stage II colon cancer is still uncertain. Our primary aim is to determine the outcome of disease free survival (DFS) and 5-year overval l survival (OS) provided by adjuvant chemotherapy using Tegafur-uracil for stage II colon cancer.
Aims & Methods: From January 2004 to December 2011, 404 low-risk stage II colon cancerpatients received curative operation in a single medical center. The clinical data were extracted from the retrospectively collected colon cancer database. The patients were divided to adjuvant chemotherapy with Tegafur-uracil, adjuvant chemotherapy with 5-fluorouracil and radical surgery alone. The DFS curves and OS curves were calculated with Kaplan-Miere's analysis.
Results: Among the 404 low-risk stage II colon cancer patients, 180 (44.6%) had adjuvant chemotherapy with Tegafur-uracil, 79 (19.5%) received adjuvant chemotherapy with 5-fluorouracil, and 145 (35.9%) underwent radical surgery alone. Within the median of 49 months follow-up, recurrence developed in 36 patients (8.18%). However, patients who received adjuvant chemotherapy with Tegafur-uracil had improved OS compared to others who underwent surgery alone. Multivariate analysis showed that only adjuvant chemotherapy with Tegafur-uracil > 1 year ($P = 0.001$) was independent factors for DFS. Moreover, only age < 70 years ($p = 0.043$) and chemotherapy with Tegafur-uracil ($p = 0.001$) related good OS.
Conclusion: We suggested adjuvant chemotherapy with Tegafur-uracil, especially consecutive administration more than one year, providing good DFS and OS for the low-risk patients of stage II colon cancer after radical surgery.

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P1049 CLINICAL OUTCOMES OF RECTAL NEUROENDOCRINE TUMORS TREATED BY ENDOSCOPIC RESECTION

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Introduction: According to 2010 WHO classification, neuroendocrine tumors (NET) are classified into three categories (G1, G2 and G3). Of these tumors, G1 NET smaller than 10 mm, mainly located at the rectum, metastasize only rarely, and thus can be treated by endoscopic resection. However, complete resection is occasionally difficult due to their localization in the submucosal layer. In addition, even NET smaller than 10mm might have lymphovascular invasion. We conducted this retrospective study to evaluate the risk of recurrence after endoscopic treatment and to search for a suitable treatment of rectal NET.
Aims & Methods: Between January 2005 and March 2014, 137 patients with 139 rectal NET lesions underwent endoscopic treatment in our hospital. Firstly, we investigated complete and curative resection rate of EMR (EMR/EMR-C/EMR-L) and ESD groups. We defined curative resection as complete resection, smaller than 10mm, and lack of microscopic lymphovascular invasion. Resection that fail to meet either of the above three criteria was defined as non-curative. When additional surgical resection was performed, the rate of positive histological lymph node metastasis was calculated. Subsequently, we investigated long-term outcomes of endoscopic resection for rectal NET.
Results: Most of the tumors were located at Rb (80%), and the median diameter was 5.7 mm. Numbers of cases treated with EMR/EMR-C/EMR-L/ESD were 10/3/114/12. Of the 139 tumors, 129 achieved complete resection (93%). Regarding the 10 incomplete resection cases, the treatments were EMR, EMR-C, and ESD in 5, 1, and 4 cases, respectively. No tumors presented muscular invasion. 79 lesions (57%) achieved curative resection, and no recurrence was identified in this group during the follow-up periods (median 27 months). 53 of the 60 lesions with non-curative resection were followed without additional resection, but no case had recurrence during the follow-up period (median 42 months). Seven of the non-curative resection cases underwent additional resection, among whom one case had lymph node metastasis; in that case, the tumor was larger than 10mm, positive for vascular invasion, and the treatment was incomplete resection. As a whole, recurrence was identified in none of the total 139 cases during the follow-up period (median 33 months). Focusing on adverse events, 10 delayed bleedings occurred (5 EMR, 4 EMR-C and 1 ESD cases), and one perforation occurred in a patient undergoing ESD.
Conclusion: EMR-L is generally thought to be a feasible measure as an endoscopic treatment of rectal NET, even though delayed bleeding rate is relatively high. Current curative criteria including complete resection, smaller than 10mm, and no lymphovascular invasion is considered to be appropriate in that cases meeting the criteria can be regarded as cured. However, given that there was no recurrence without additional resection in cases regarded as "non-curative" resection, mainly due to lymphovascular invasion and/or larger size, observation without additional resection might be allowed, although the observation period was not long enough in the present analysis. To establish curative criteria and indication for endoscopic treatment, further studies including those with longer follow-up periods are needed.
Disclosure of Interest: None declared

P1050 MAGNIFYING CHROMOENDOSCOPY IS DECISIVE TO DEFINE MANAGEMENT OF COLORECTAL NEOPLASTIC LESIONS

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Introduction: Early colorectal cancer with submucosal deep invasion should not be treated by endoscopic resection due the high risk of lymph-nodes metastases. Magnifying chromoendoscopy and evaluation of pit pattern can predict the malignant potential of colorectal lesions. Accurate diagnosis of lesions allows indication of the best treatment, endoscopic or surgical.
Aims & Methods: Evaluate efficacy of magnifying chromoendoscopy in the definition of management of colorectal neoplastic lesions. Between April 2009 and August 2014, patients with colorectal neoplastic lesions with high risk of submucosal invasion (sessile $\geq$ 20 mm, depressed type and LST-type lesions) underwent magnifying chromoendoscopy. The therapeutic approach (endoscopic or surgical) was defined according to the endoscopic evaluation. Lesions with Vn pit pattern were referred to surgical resection. Lesions without Vn pit pattern were referred to endoscopic treatment and the decision of therapeutic approach was according to pit pattern, location and size. Final staging was possible with the histology of the surgical or endoscopic specimen. Lesions that were not resected or those where it was not possible to visualize the pit pattern due eroded surface were excluded.
Results: A total of 104 lesions were found in 103 patients (47% male, mean age of 64.4 years-old). Six lesions were excluded. The average size of lesions was 45.1 ± 31.9 mm. The macroscopic classification was 15.3% sessile, 4.1% depressed and 80.6% LSTs. The endoscopic treatments were polypectomy in 2.0%, EMR in 15.3%, EPMR in 13.3%, ESD in 45.9% and TEM in 9.2%. Surgical resection was referred in 14.3% of the lesions. The correlation of pit pattern with pathology was:- II: 100% adenomas with low-grade dysplasia (2/2)- IIIL: 69.2% of low-grade adenoma (9/13)- IIIS: 100% intramucosal adenocarcinoma (1/1)- IV: 72.0% of adenoma with high-grade dysplasia or intramucosal adenocarcinoma (18/25)- Vi: 86.9% of intramucosal adenocarcinoma or superficial submucosal invasion $<$ 1000 μm (40/46) / 6.5% adenocarcinoma with massive submucosal invasion $>$ 1000 μm (3/46)- Vn: 54.5% of adenocarcinoma with massive submucosal invasion (6/11); 45.5% of adenocarcinoma with invasion to the muscularis propria. The therapeutic indication based on magnifying chromoendoscopy and pit pattern classification was considered correct in 96.9% of cases (95/98). Three cases Vi pit pattern lesions were endoscopically resected and the histology demonstrated massive submucosal invasion. These patients were sent to surgical resection. Magnifying chromoendoscopy and pit pattern classification had a 78.6% sensitivity, a 100% specificity, a 100% predictive positive value, a 96.6% negative predictive value and a 96.9% accuracy to detect submucosal massive invasion, or deeper.
Conclusion: Magnifying chromoendoscopy is accurate to detect submucosal massive invasion, or deeper, of colorectal neoplastic lesions which allows correct selection of patients to surgical or endoscopic resection. The Vn pit pattern contraindicates endoscopic resection.

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P1051 ENDOSCOPIC MANAGEMENT AND CLINICAL OUTCOMES OF MALIGNANT COLORECTAL POLYPS

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Introduction: The endoscopic management of colorectal polyps containing adenocarcinoma is increasing in nowadays due to colorectal cancer screening programs. The aim of this study was to evaluate the safety and efficacy of endoscopic resection of malignant colorectal polyps.
Aims & Methods: Patients who underwent endoscopic resection for colorectal polyps which containing adenocarcinoma from August 2001 to July 2014 in Ajou university hospital of Korea. The data were retrospectively reviewed. Clinical outcomes such as complete resection rate, recurrence rate, complications were analyzed.

Results: Table1: Relationships between recurrence and complete resection status, risk of polyps

	Recurrence after polypectomy No	Yes	p value
Complete resection (CR)			
CR (n = 266)	258 (97.0%)	8 (3.0%)	
ICR (n = 143)	130 (90.9%)	13 (9.1%)	0.008
Risk of malignant polyp			
Low risk (n = 252)	245 (97.2%)	7 (2.8%)	
High risk (n = 157)	143 (91.1%)	14 (8.9%)	0.020
Total	388	21	409

Total 482 polyps in 462 patients were analyzed in this study. 444 lesions were resected by snaring polypectomy including endoscopic mucosal resection (EMR) and 38 lesions by endoscopic submucosal dissection (ESD). The high risk malignant polyps were defined as having: tumor invasion in the margin or an uncertain margin; poor differentiation (WHO classification grade III); or invasion of lymphatic or venous vessels. Low risk malignant polyps did not have any of these three histological signs. We analyzed the recurrence rate of the 409 lesions followed up for at least 3 months. The recurrence rate was 5.1% (21/408), and it was affected by complete resection status ($p = 0.008$) and risk of polyps ($p = 0.006$). Procedure-related complications developed in 20 lesions; perforations in 8 lesions (1.7%) and significant bleedings required additional endoscopic procedure in 12 lesions (2.5%).

Conclusion: Endoscopic polypectomy could be adequate and effective treatment for patients with malignant colorectal polyps, especially low-risk polyps.

Disclosure of Interest: None declared

P1052 TERPINEN-4-OL: A NOVEL AND PROMISING THERAPEUTIC AGENT FOR HUMAN COLORECTAL CANCER TERPINEN-4-OL

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Introduction: Background: Monoterpenes are major secondary metabolites present in plants and known to be associated with the plant defense mechanisms. Terpinen-4-ol is a naturally occurring monoterpene, found in the essential oils of many aromatic plants and is the main bioactive component of tea tree oil. It has been shown to have antiviral, antibacterial, antifungal, and insecticidal effects as well as anti-oxidant and anti-inflammatory activities. It was demonstrated to induce primary necrotic cell death and cell cycle arrest in melanoma and non-small cell lung cancer cells.

Aims & Methods

Aim: To study the antitumor effects of terpinen-4-ol and its mechanism of action in various types of GI malignancies, alone and in combination with several chemotherapeutic and biological agents.

Methods: Terpinen-4-ol was administrated alone or combined with standard anti-CRC agents including, oxaliplatin, fluorouracil (5-FU), cetuximab and bevacizumab. It was also combined with humanized anti-CD24 monoclonal antibodies previously developed in our lab (*Shapira Gastro 2011*). Killing effects were measured qualitatively by light microscopy and quantitatively using the MTT assay. The *in vivo* toxicology, LD_{50} value, of various doses of Terpinen-4-ol was tested following several routes of administration (oral, intramuscular, topical, and by subcutaneous and intra-peritoneal injection). Subcutaneous tumors were produced by injection of $5x10^6$ of DLD-1 CRC cell lines into nude mice. When the tumors reached a dimension of 5 mm, the animal's treatment was initiated.

Results: The LD_{50} value of Terpinen-4-ol after intra-peritoneal injection in mice is 120 mg/kg body. Terpinen-4-ol induces a significant growth inhibition of CRC cell lines, including HCT116, DLD1 and COLO320, in a dose-dependent manner. Terpinen-4-ol and various anti-cancer agents (0.2 μM oxaliplatin, 0.5 μM fluorouracil (5-FU), 1 μM cetuximab and 50 μM bevacizumab) demonstrated a synergistic inhibitory effect of cancer cell proliferation. Subtoxic concentrations of terpinen-4-ol potentiate anti-CD24 mAb-induced growth inhibition. The anti-tumor activity of terpinen-4-ol alone or in combination with cetuximab was evaluated. Considerable reduction in tumor volume was seen following terpinen-4-ol (0.2%) treatment alone and in combination with cetuximab (10 mg/kg) (40% and 63%, respectively) in comparison to the control group that received PBS (+DMSO).

Conclusion: Terpinen-4-ol significantly enhances the effect of several anticancer agents, including chemotherapeutic and biological drugs, in particular therapeutic antibodies. The possible molecular mechanism for the activity of Terpinen-4-ol involves induction of cell death rendering this compound as a potential anticancer drug alone or in combination, for the treatment of a wide range of malignancies (was tested on pancreatic, prostate and stomach), including CRC.

Disclosure of Interest: None declared

P1053 SELECTIVE CYCLOOXYGENASE-2 INHIBITOR ATTENUATES PRO-METASTATIC AND ANTI-APOPTOTIC EFFECTS OF ENDOTOXIN-LIPOPOLYSACCHARIDE

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Introduction: Growing evidence indicates that bacterial infections and following inflammation is contributing to cancer growth. Recent studies showed promotional influence of endotoxin-lipopolysaccharide (LPS) on cancerogenesis and metastatic growth, which in part is associated with involvement of cyclooxygenase-2 (COX-2). Elevated tumour COX-2 is associated with increased angiogenesis, tumour growth and promotion of tumour metastasing and resistance to apoptosis. The mode of action of COX-2 and its inhibitors remains unclear. We hypothesized that inhibiting of COX-2 may decrease inflammation contributing to metastatic growth.

Aims & Methods: Murine model including 2 groups (25 each) of adolescent mice was used. Metastatic process was modeled by i/v injection of 200 μl spontaneously metastasizing mammary adenocarcinoma cell culture suspension. Both control and experimental group animals received 200 μl suspension of 10 μg LPS per mouse. Experimental group received selective COX-2 inhibitor celecoxib orally from day 1. Metastatic growth evaluated hystochemically within pulmonary metastases. TNF-α, VEGF quantified with ELISA; COX-2 with Western Immunoblotting.

Results: Control group mice developed a mean number of 35.27 ± 6.19 macroscopic metastases by day 15. Both the weight and quantitative parameters of metastatic growth were significantly lower in study group compared to control ($p < 0.005$-0.0001). Experimental group metastatic growth was characterized by 48.8% lower mitotic index (MI) and 37.6% higher apoptotic index (AI). MI/AI ratio in the experimental group was 2.1 times lower ($p < 0.001$) than the ratio observed in control group mice. Systemic COX-2, TNF-α and VEGF were significantly lower in celecoxib group ($p < 0.005$-0.001) compared to control.

Conclusion: It is becoming evident that selective COX-2 inhibitors have a growing potential as a beneficial target for chemopreventive and tumour regression for many cancers. Although expression of COX-2 has been associated with development and progression of numerous malignancies, its precise role in promotion of cancer cell dissemination is still poorly understood. TNF-α – a major proinflammatory cytokine is released in response to LPS associated increase of VEGF production via COX-2 pathway. Current study shows that pro-cancerogenic effect of endotoxin in experimental murine model could be inhibited by neutralizing COX-2 associated pathway. Treatment with celecoxib was effective in reducing metastasis volume, suggesting that COX-2 contributes to metastatic growth. However, there is no direct evidence that all metastases are/could be sensitive to COX-2 inhibition.

Disclosure of Interest: None declared

P1054 SHORT-TERM RESULTS OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Colorectal endoscopic submucosal dissection (CR-ESD) is accepted as a minimally invasive treatment for large (≥20 mm) neoplastic lesions. It is less invasive than surgery and provides higher *en bloc* resection rate than endoscopic mucosal resection (EMR). The purpose of this study is to evaluate short-term results of CR-ESD in a single western institution.

Aims & Methods: All patients treated by CR-ESD between November 2011 and October 2014 were included. CR-ESD was indicated according to the Japanese Colon ESD Standardization Implementation Working Group criteria and was performed by using Dual-knife and/or IT-knife nano. The complete resection of the lesion, *en bloc* resection, R0 resection, the curative resection, the 30- day mortality and complications were considered as short-term results.

Results: Among 43 patients, 32 (74.4%) were males and 11 (25.6%) were females. Mean age was 69. 6 (range 53-89) years. The mean lesion size was 24 (range 5-70) mm. From a total of 43 lesions, 32 (74.4%) were localized in the rectum, 8 (18.6%) in the distal colon and 3 (6.9%) in the proximal colon. The types of the lesions were as follows: 0-Is 7 (16.2%), LST-GH 2 (4.6%), LST-GM 7 (16.2%), LST-NG 3 (6.9%), LST-NGPD 11 (25.6%), 0-IIc 2 (4.6%), 0-IIa 2 (4.6%) and post-EMR residual lesion 9 (20.9%).

The complete resection of the lesion was achieved in 41 (95.3%) of cases. The 30-day mortality was none. *En bloc*, R0 and curative resection was achieved in 30 (69.8 %), 24 (55.8 %) and 24 (55.8 %) cases respectively. From a total of 5 (11.6 %) perforations 4 were closed by clips and one remaining required emergency surgery. In 2 (4, 6%) cases, perforation resulted in incomplete resection of the lesion. Delayed bleeding occurred in 2 (4.6 %) cases, both were managed endoscopically.

The final histology in cases with complete resection was as follows: LGIEN 5 (11.6%), HGIEN 17 (39.5%), intramucosal carcinoma 8 (18. 6%), T1 sm1 carcinoma 6 (13.9%), T1 sm2 and sm3 carcinoma 2 (4.6%), T2 carcinoma 1 (2.3%), neuroendocrine tumor 1 (2.3%) and xanthelasma 1 (2.3%).

Conclusion: Colorectal endoscopic submucosal dissection in our institution appears to be feasible and safe. Nevertheless, curative resection was achieved in 55.8% of cases only. This was caused mainly by high number of post-EMR residual lesions associated with severe fibrosis. Perforation occurred in 11.6% and resulted in emergency surgery and incomplete resection in 1 (2.3%) and 2 (4.6%) of cases.

Disclosure of Interest: None declared

P1055 DIFFERENTIAL CHARACTERISTICS OF COLORECTAL CANCER FOLLOWING THE SERRATED PATHWAY

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Introduction: Recently, it has been described a new colorectal cancer (CRC) carcinogenetic pathway due to methylation of CpG islands (methylator phenotype or CIMP). There's some controversy about its prognostic and response to adjuvant Chemotherapy (CT).
Aims & Methods: The aim of this study is to determine differential characteristics of CIMP CRC and to evaluate its prognostic and response to CT. There were been included 701 CRC patients consecutively from the national and multicentre Epicolon II project. Hypermethylation of CpG islands was studied by MS-MLPA method using RUN-X3, CACNA1G, IGF2, MLH1, NEUROG1, CRABP1, SOCS1 and CDKN2A markers in 614 patients, taking into account for CIMP+ the methylation of 5 or more of these markers.
Results: The median of age was 72 years old [34-93], being men 58.9%. The median of follow-up was 57.7 months. It was produced a recurrence in 146 patients (20.8%) and 278 (39.7%) were deceased at the end of the follow-up period (82.7 months). The study of methylator phenotype was possible to value in 543 patients (77.5%), distributed in 146 CIMP+ (26.9%) and 397 CIMP- (73.1%) patients. Some features between CIMP+ and CIMP- CRCs were compared. The age of the firsts at diagnosis was higher (CIMP+ 72.8 [39-93]; CIMP- 70.8 [34-93]; $p < 0.043$) and some trend to be located at right colon was observed (CIMP+ 55.6%; CIMP-26.6%; $p < 0.001$). It was also found a higher KRAS mutations proportion in CIMP+ (43.7% CIMP+; 31.7% CIMP-; $p < 0.013$), as well as in BRAF genes (14.9% CIMP+; 0.8% CIMP-; $p < 0.001$) and DNA mismatch repair genes alterations (24.3% CIMP+; 5.6% CIMP-; $p < 0.001$), without any difference in sex field. In addition, there weren't observed any difference neither survival nor recurrence between overall CIMP+ and CIMP-. However, when we stratified by genetic profile, we observed a higher survival in CIMP+ CRC with KRAS mutation (log Rank $p < 0.023$) conversely to those with KRAS mutation but CIMP- (log Rank $p < 0.759$). It was also observed a higher intrinsic survival in microsatellite instability (MSI) and CIMP- CRCs (log Rank $p < 0.032$) than those MSI and CIMP+ CRCs (log Rank $p < 0.384$). By receiving CT with curative purpose (II with poor prognosis and III stages), some differences were found between CIMP+ and CIMP- CRCs. Patients with CIMP- CRC obtained benefits in disease-free survival terms (log Rank $p < 0.001$), something that didn't occur in patients with CIMP+ CRC (log Rank $p < 0.180$). Moreover, after stratifying by genetic profile, those microsatellite stable (MSS) and CIMP- CRCs were benefiting from receive CT in disease-free survival terms (log Rank $p < 0.001$), situation that didn't happened in MSS and CIMP+ CRCs (log Rank $p < 0.164$).
Conclusion: There are observed certain differential features in methylator phenotype CRC. Overall, those patients present a worse response to adjuvant CT with curative purpose.
Disclosure of Interest: None declared

P1056 THE TOP 100 INFLUENTIAL MANUSCRIPTS IN COLORECTAL CANCER: A BIBLIOMETRIC ANALYSIS

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Introduction: Colorectal cancer (CRC) is a significant cause of mortality and morbidity worldwide. There is a large and growing body of evidence on the topic. Recently bibliometric citation analysis has been used to determine the most influential scientific papers in several surgical fields. To date, no study has been undertaken to determine the most influential papers in the field of CRC.
Aims & Methods: To analyse the 100 most cited manuscripts in the field of CRC to highlight the key topics and studies which have led to the current understanding and treatment of the disease.
A search of the Thomson Reuters Web of Science citation indexing database was completed using the search terms 'colorectal cancer,' 'colon cancer,' 'rectal cancer,' 'colorectal carcinoma,' 'colon carcinoma,' 'rectal carcinoma' or 'colonoscopy.' Only English language and full manuscripts were included. The 100 most cited papers were further analysed by topic, journal, author, year and institution
Results: 146,833 eligible papers were returned. Of the top 100, the most cited paper (by Hurwitz) focused on chemotherapy (5340 citations). The *New England Journal of Medicine* published the highest number of papers in the top 100 (n = 24, 37,858 citations). The country and year with the greatest number of publications were the USA (n = 60) and 2004 (n = 13) respectively. The most covered topic was genetics in CRC (n = 51), followed by chemotherapy (n = 21) and surgical management (n = 6).
Conclusion: These most cited manuscripts have contributed to the current understanding and treatment of CRC. We provide an analysis and reference of what could be considered the most influential papers in CRC
Disclosure of Interest: None declared

P1057 OUTCOME OF SELF-EXPANDABLE METALLIC STENT(SEMS) PLACEMENTS FOR COLORECTAL OBSTRUCTION AND EXPERIENCE WITH COLONOSCOPY THROUGH A COLORECTAL STENT

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Introduction: In January 2012, endoscopic stenting with a self-expandable metallic stent(SEMS) for malignant colonic obstruction was covered by the national health insurance in Japan. And this procedure is widely accepted in Japan.
In our institution, this procedure was performed aggressively for the cases of symptomatic malignant colorectal obstruction.
Aims & Methods: The aim of this study is to research the safety and feasibility of SEMS placement as a bridge to surgery (BTS) for malignant colorectal obstruction, and showed the utility of total colonoscopy (TCS) pass through a SEMS.
From July 2012 to July 2014, a prospective study was performed on 29 patients with malignant colorectal obstruction who treated with SEMS. Only colon cancer patients who underwent BTS SEMS placement were selected. After SEMS placement,11 patients was performed a TCS pass through a SEMS.
Results: In total, 20 patients were included. The median age 68 years (43-89 years), sex ratio 10:10, stenting sites transverse colon 3 cases, descending colon 3 cases, sigmoid colon 7 cases, rectum seven cases. The median time from diagnosis to stenting was one day, the average treatment time 29 minutes, procedural success rates was 100%, and a clinical success rates was 95%. Procedure related contingent disease has not been observed, perforation was observed in one case after placement of SEMS. The median time of the start meal after SEMS placement was two days. The median time from SEMS insertion to surgery was 21.5 days. Open surgery was performed in 16 cases and laparoscopic colectomy was performed in 4 cases. The overall stoma creation was 2 cases (perforated case and intestinal necrosis case).
In 11 cases, TCS after stenting was carried out under CO2 air, and under fluoroscopic guidance. The median time from stenting to TCS was 12 days. Average time to cecum reached was 20 minutes. Complications associated with TCS were not observed. The eight of the eleven cases were observed other lesions such as adenoma and cancer. In four cases, cancer was observed in deep colon than stent. EMR was performed in one case of adenoma, complications were not observed. EMR is performed in one cases of adenoma, complications were not observed.
Conclusion: Stenting for the BTS is safe and effective. Furthermore, TCS pass through a SEMS after SEMS placement was very useful for diagnosis. It becomes possible to evaluate the deep large intestine than stent. The incidence of concurrent colorectal cancer was reported around 8%. TCS pass through the SEMS can be possible to correct preoperative diagnosis, it is considered to be useful in the selection of the surgical procedure.
Disclosure of Interest: None declared

P1058 PROOF-OF-PRINCIPLE FOR A NOVEL GAS-SENSING CAPSULE AS AN IN VIVO MARKER FOR INTESTINAL GAS PRODUCTION

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Introduction: The production of intestinal gases are closely linked with the genesis of gastrointestinal symptoms. However, direct measurements of these gases in vivo are limited and have involved invasive or indirect (e.g., via breath) sampling techniques (1). A novel gas-sensing capsule was recently developed to detect concentrations of specific gases in real time within the gastrointestinal tract (1).
Aims & Methods: The aim of this preliminary study was to validate the use of gas sensor capsule in an animal model following diets varying in readily fermentable carbohydrate content. Six pigs were randomised to 30 MJ diets containing either low (7 g resistant starch (RS) & 0 g oligosaccharides) or high (29 g RS & 31g oligosaccharides) fermentable carbohydrates for 4 days after 1-week of acclimatisation to human-type diets. On the second day of each diet, carbon dioxide (CO_2)-sensing capsules were administered via gavage and data transmitted every 5 minutes to an external receiver. The readout represents relative CO_2 concentration (ppm) sampled at a specific timepoint. Passage rate of the capsules were also determined.
Results: In pigs receiving a high-fibre diet, all 3 gas capsules were passed within 10 days of administration whilst only 1 of 3 capsules were passed within this time period in those on a low-fibre diet. 2 capsules failed (one did not empty from the

stomach, one transmission failure). 4 devices successfully transmitted data on CO_2 production for 8-24 hoursand results are shown in the Table. In the first 8 hours when the capsule is in the stomach and small intestine, mean CO_2 concentrations were 53 x 10^3 ppm with no clear differences between diets. The 2 capsules with long duration of transmission showed a divergence of CO_2 concentrations from 10 to 16 hours. This divergence of CO2 concentrations probably represents exhaustion of fermentable substrates of carbohydrates in the proximal colon, consistent with the anticipated site of such fermentation. The convergence of CO_2 production after 16 hours is consistent with fermentation of endogenous or of less readily fermented carbohydrates common to both diets.**Table:** Capsule sensor results. FC = fermentable carbohydrate, X = no data transmission

Capsule sensor ID	Mean CO_2 concentrations (x 10^3 ppm) at 2-hour intervals									
	0 h	8 h	10 h	12 h	14 h	16 h	18 h	20 h	22 h	24 h
Sensor 1 (Low FC)	0	55	X	X	X	X	X	X	X	X
Sensor 2 (High FC)	0	68	X	X	X	X	X	X	X	X
Sensor 3 (Low FC)	0	46	46	46	33	33	56	64	64	62
Sensor 4 (High FC)	0	41	51	54	51	54	54	54	59	X

Conclusion: We have provided a proof-of-principle for the utility of a gas-sensing capsule for measuring gas concentrations within the gastrointestinal tract with demonstration of the anticipated differences associated with variations of fermentation patterns. Further work on refining the reliability of the capsule's transmission mechanism and in identifying sites of gas measurement are needed to become a valuable, non-invasive marker of intestinal gas production.

Reference

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Disclosure of Interest: None declared

P1059 MULTIDRUG RESISTANCE-ASSOCIATED PROTEIN 4 REGULATES LINACLOTIDE-INDUCED CYCLIC GMP AND ELECTROLYTE SECRETION

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Introduction: Multidrug resistance-associated protein 4 (MRP4) is an ATP-binding cassette transporter that mediates the efflux of prostaglandins and cyclic nucleotides (cAMP and cGMP). MRP4 acts as an important regulator of these secondary messengers and thereby affects signalling events mediated by cAMP and cGMP. MRP4 is expressed on intestinal epithelial cells and has recently been found to be downregulated in patients with irritable bowel syndrome with constipation (IBS-C). Moreover, intestinal MRP4 has been implicated in the compartmentalised regulation of cAMP-mediated signalling.[1] Linaclotide, a potent and selective guanylate cyclase-C (GC-C) agonist, is approved for the treatment of IBS-C in the United States and Europe and in the United States at a lower dose for the treatment of chronic idiopathic constipation. GC-C activation by linaclotide results in increased cGMP synthesis; however, the role of intestinal MRP4 in regulating the levels of intracellular cGMP has not been studied.
Aims & Methods: The objective of this study was to evaluate the role of MRP4 in the regulation of cGMP levels in linaclotide-stimulated rat colonic epithelium and to simultaneously assess the effect of MRP4 inhibition on GC–C–mediated transepithelial ion (Isc) current. Ussing chamber assays were used to study the role of MRP4 on linaclotide-induced secretion of electrolytes and cGMP. The kinetics of the deactivation of linaclotide-induced Isc was studied using a GC-C/Fc fusion protein. MRP4 expression was assessed by Q-PCR and immunohistochemistry.
Results: Staining of rat colonic epithelium with anti-MRP4 antibodies showed expression of MPR4 in the apical membrane. Stimulation with linaclotide resulted in the accumulation of intracellular cGMP and induced Isc in isolated intestinal epithelium. Pretreatment of mucosa with the specific MRP4 inhibitor MK571 potentiated linaclotide-induced electrolyte secretion and augmented intracellular cGMP accumulation. Additionally, pretreatment of colonic mucosa with the phosphodiesterase type 5 inhibitor sildenafil increased basal Isc but had no amplifying effect on linaclotide-induced ion current. Inhibition of MRP4 only affected the activation, not the deactivation, phase of linaclotide-induced Isc, an effect elicited by the GC-C/Fc chimera. Stimulation with linaclotide induced cGMP secretion from both apical and basolateral membranes of the colonic epithelium. However, MK571 inhibited cGMP efflux from the apical but not from the basolateral membranes.
Conclusion: MRP4 is highly expressed on the apical membrane of rat colonocytes, and apical MRP4 mediates cGMP efflux from linaclotide-stimulated colonic epithelium. MK571 inhibition of cGMP efflux increases Isc induced by linaclotide. The selective inhibition of apical cGMP secretion by MK571 suggests the involvement of transporters other than MRP4 for basolateral cGMP secretion. A potential role of MRP4 in IBS-C is under investigation.

Reference

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Disclosure of Interest: B. Tchernychev Financial support for research: Ironwood Pharmaceuticals/Actavis, Conflict with: Employee of Ironwood Pharmaceuticals, P. Ge Conflict with: Employee of Ironwood Pharmaceuticals, D. Wachtel Conflict with: Employee of Ironwood Pharmaceuticals, R. Solinga Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals, M. Kessler Conflict with: Employee of Ironwood Pharmaceuticals, S. Ranganath Shareholder: Enumeral Biomedical Corporation, Conflict with: Employee of Enumeral Biomedical Corporation, Former employee of Ironwood Pharmaceuticals, G. Hannig Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals, I. Silos-Santiago Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals

P1060 LINACLOTIDE INDUCES SECRETION OF CYCLIC GMP INTO THE COLONIC SUBMUCOSAL LAYER: AN IN VIVO MICRODIALYSIS STUDY IN RATS

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Introduction: Linaclotide, a guanylate cyclase-C (GC-C) agonist, is currently approved for irritable bowel syndrome with constipation (IBS-C) in the United States and Europe and in the United States at a lower dose for the treatment of chronic idiopathic constipation. The effects of linaclotide on intestinal transit and secretion are mediated through cyclic guanosine monophosphate (cGMP) production. In addition, cGMP mediates the effect of linaclotide on visceral pain, and it has been hypothesised that this effect is through the direct inhibition of nociceptors found in the colonic submucosa. However, the levels of cGMP in the colonic submucosa after GC-C activation have not yet been measured.
Aims & Methods: The objective of this study was to assess the release of cGMP in the rat colonic submucosa after linaclotide administration using *in vivo* microdialysis. Microdialysis probes were implanted in the submucosa of the ascending colon of anaesthetised rats. Linaclotide (3 doses: 0.5, 1.7 and 5 μg) or 200 μL vehicle alone were injected directly into the lumen of the colonic loop (n = 4–10/group). cGMP concentrations in the dialysate were measured using liquid chromatography-tandem mass spectrometry (LC-MS/MS). At the end of the study, loops were excised, and length and weight were measured. The change in cGMP concentrations before and after treatment was compared with vehicle group using a two-tailed paired student's t-test. The fluid secretion change after treatment was compared with vehicle group using one-way ANOVA followed by a Dunnett's *post hoc* test.
Results: Linaclotide administered into rat colonic loops resulted in a significant increase in fluid secretion compared with vehicle alone for all doses tested (175–198%; $P \leq 0.001$). In dialysate samples, doses of 0.5, 1.7 and 5 μg linaclotide increased cGMP release into the submucosal layer in a dose-dependent manner by 58%, 73% and 212%, respectively, compared with vehicle control. For all doses of linaclotide, significant increases in cGMP concentration were observed compared with vehicle. Additionally, the changes in cGMP release were time dependent, with the highest dose reaching maximal effect within 12 minutes of linaclotide administration.
Conclusion: Linaclotide induces fluid secretion in the colonic lumen and increases cGMP levels in the colonic submucosa. The release of cGMP into the rat colonic submucosa further supports the mechanism of action of linaclotide on intestinal visceral pain.
Disclosure of Interest: J. Tobin Financial support for research: Ironwood/Actavis, Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals, S. Thomas: None declared, R. Solinga Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals, J. Masferrer Conflict with: Employee of Ironwood Pharmaceuticals, C. Lunte: None declared, G. Hannig Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals, I. Silos-Santiago Shareholder: Ironwood Pharmaceuticals, Conflict with: Employee of Ironwood Pharmaceuticals

P1061 ROLE OF NA+/CA2+ EXCHANGER 1 AND 2 ON THE CONTRACTILITY IN LONGITUDINAL MUSCLES OF MOUSE ILEUM

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Introduction: Increase in intracellular Ca^{2+} concentration are crucial to the regulation of smooth muscle contraction. Ca^{2+} clearance requires Ca^{2+} transport out of the cytosol by pathways involving plasma membrane Ca^{2+}-ATPase, the Na^+/Ca^{2+} exchanger (NCX), the sarco/endoplasmic reticulum Ca^{2+}-ATPase, and mitochondria. NCX electrogenically exchanges Na^+ and Ca^{2+} across the plasma membrane depending on the membrane potential and transmembrane gradients. The physiological roles by which NCX influences gastrointestinal motility are incompletely understood, although its role in heart, brain and kidney is understood.
Aims & Methods: In this study, we focused on the effect of Ca^{2+} movement through NCX on the motility in ileum because Ca^{2+} homeostasis is central to the regulation of smooth muscle function. To determine the role of NCX1 and NCX2 in the ileum, we investigated the frequency–responses to electric field stimulation (EFS) at 1 and 3 Hz in the longitudinal muscle obtained from the ileum in wild-type mice (WT), NCX1-heterozygote knockout mice (NCX1 HET), and NCX2-heterozygote knockout mice (NCX2 HET).

Abstract number: P1065

Manometric data		Volunteers	Incontinence	Constipation
Rest	HPZ pressure (mmHg) *	50 (42-55)	42 (34-47) †	47 (40-62) ‡
HPZ height (cm) *	3.5 (3.0-4.0)	3.0 (2.5-3.8) †	3.3 (2.4-4.1)	
Squeeze	HPZ pressure (mmHg) *	81 (68-106)	56 (45-69) †	64 (54-96) † ‡
HPZ height (cm) *	4.5 (4.2-4.9)	4.1 (3.4-4.6) †	4.4 (4.0-4.9) ‡	
Push	Ratio [push/rest] mean pressure *	0.98 (0.81-1.21)	0.98 (0.89-1.14)	1.02 (0.82-1.26)
% of patients withratio > 0.8	19 (79%)	20 (71%)	21 (75%)	

*median (IQR)† $p < 0.05$ (compared to volunteers)‡ $p < 0.05$ (compared to incontinence)

Results: In the ileum, EFS induced a phasic contraction that persisted during the stimulus, and a tonic contraction that recorded after the end of the stimulus. Under the condition of EFS at 1 Hz, we found that the amplitudes of phasic contraction were significantly smaller in NCX2 HET, but not NCX1 HET, than in WT. Like phasic contraction, the amplitudes of tonic contraction were significantly smaller in NCX2 HET, but not NCX1 HET, than in WT. Under the condition of EFS at 3 Hz, the amplitudes of tonic contraction were significantly smaller in NCX2 HET, but not NCX1 HET, than in WT. However, the amplitudes of phasic contraction were same among WT, NCX1 HET, and NCX2 HET, unlike 1 Hz. Next, we determined whether NCX deficiency affects contraction in response to acetylcholine (ACh) and substaqnce P (SP) in smooth muscle cells. NCX2 HET, but not NCX1 HET, demonstrated that magnitude of ACh-induced and SP-induced contractions was smaller than that of WT.
Conclusion: In this study, we demonstrated that NCX2 regulated the motility in ileum through by controlling the sensitivity of ileal smooth muscles to ACh and SP.
Disclosure of Interest: None declared

P1062 ROLES OF NA+/ CA2+ EXCHANGER 1 AND 2 IN MOUSE DIARRHEA MODEL

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Introduction: The Na+/Ca^2+ exchanger (NCX) is a plasma membrane transporter involved in regulating intracellular Ca^2+ concentrations. NCX is critical for Ca^2+ regulation in cardiac muscle, vascular smooth muscle, and nerve fibers. However, little is known about the physiological role of NCX in the gastrointestinal tract. Using in vitro magnus method, we have previously demonstrated that NCX2, but not NCX1, regulates colonic motility by altering acetylcholine release onto myenteric neurons of the distal colon. Alterations in colonic motility relates to the cause of diarrhea as one proposed mechanism.
Aims & Methods: The aim of this study was to characterize the role of NCX1 and NCX2 on gastrointestinal motility in vivo in normal conditions and diarrhea models. Both NCX1 heterozygous mice (HET) and NCX2 HET on the C57BL/6 background were comparable in all analyses to age-matched wild-type mice (WT). Diarrhea was induced by oral administration of $MgSO_4$ (2 g/kg), i.p. administration of serotonin (3 mg/kg) or prostaglandin E_2 (0.1 mg/kg). The stool output was assessed in each mouse. The number and weight of stool was counted over 9 hour for $MgSO_4$, or 60 min for serotonin and prostaglandin E_2. Stools were graded into three consistency levels as follows: normal, soft, watery.
Results: In $MgSO_4$-induced diarrhea, almost all mouse exhibited watery diarrhea. We found that the number and weight of watery stool in NCX1 HET were clearly greater than those in WT over a period of 5-6 hour. Similarly, the number and weight of watery stool in NCX2 HET were markedly greater than those in over a period 3-4 hour. In serotonin-induced diarrhea, the number and weight of watery stool in NCX2 HET were greater than those in WT over periods 0-15 min and 15-30 min. NCX1 HET displayed no changes of the number and weight of watery stool, unlike $MgSO_4$-induced diarrhea. In prostaglandin E_2-induced diarrhea, it showed no significant alteration in number and weight of watery stool among WT, NCX1 HET, and NCX2 HET.
Conclusion: We demonstrated for the first time using mouse diarrhea model that NCX1 and NCX2 have important roles in the development of diarrhea.

Reference

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Disclosure of Interest: None declared

P1063 ROLE OF TRANSIENT RECEPTOR POTENTIAL C6 CHANNEL ON THE CONTRACTILITY IN CIRCULAR MUSCLES OF MICE ILEUM

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Introduction: Transient receptor potential cation (TRPC) channels are a group of ion channels, which are relatively non-selectively permeable to cations. TRPC channels are activated in downstream of Gq/11-coupled receptors, or receptor tyrosine kinases. There is no direct evidence for role of functional TRPC6 on gastrointestinal tract. Acetylcholine and substance P have been reported to be the representative neurotransmitters that cause contractions in the gastrointestinal tracts of nearly all animal species including human being. There neurotransmitters activate muscarinic and tachykinin receptor, respectively, that belong to G protein-coupled receptor.
Aims & Methods: The aim of the present study was to investigate the role of TRPC6 in gastrointestinal motility. Both smooth muscle-specific TRPC6 transgenic mice (Tg), and smooth muscle-specific dominant-negative TRPC6 transgenic mice (DN) on the C57BL/6 background were comparable in all analyses to age-matched wild-type mice (WT). We used an organ tissue bath system to investigate the motility of circular smooth muscle segments isolated from the ileum.
Results: In the ileum, electric field stimulation (EFS; 60 sec)-induced contraction was showed during the stimulus. The amplitudes of EFS-induced contraction were significantly greater in Tg than in WT, and significantly smaller in DN than in WT. In the experiment in which atropine was added, the first phase of EFS (~15 sec)-induced contraction was completely inhibited in all of three types. Interestingly, second phase of EFS (15~60 sec)-induced contraction were still greater in Tg than in WT, and still smaller in DN than in WT. We next tested the NK1 or NK2 receptor antagonist in addition to atropine. Importantly, NK2 antagonist, but not NK1 antagonist, markedly suppressed the increased contraction in Tg. In DN, both NK1 and NK2 antagonist inhibited the contraction.
Conclusion: In this study, we demonstrated that TRPC6 has physiological roles in the contractility of the ileum and that TRPC6 channels activated by muscarinic and NK receptors to regulate the motility. In case of overexpression of TRPC6 channels, furthermore, our results suggest that relation of TRPC6 with NK2 receptor may alter and affect the motility.
Disclosure of Interest: None declared

P1064 DIFFERENCES ON TIME TO PEAK OF CARBACHOL-INDUCED CONTRACTION IN BETWEEN CIRCULAR AND LONGITUDINAL SMOOTH MUSCLES OF MOUSE ILEUM

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Introduction: Cooperation between contractions on the oral side of contents and relaxation on the anal side in digestive tract is physiologically important for peristaltic movement. The muscular layer in gastrointestinal tract consists of an inner circular muscular layer and an outer longitudinal muscular layer. These muscular layers are responsible for the movement such as peristalsis. Acetylcholine (ACh) has been reported to be the representative neurotransmitter that causes contractions in the gastrointestinal tracts of nearly all animal species. Although there are many reports about contractions of longitudinal smooth muscles induced by activation of muscarinic receptor (MR), little is known about the details of those of the circular smooth muscles. Thus, a detailed investigation of the ACh-induced contraction of circular smooth muscle is needed to provide insight into the regulatory mechanisms of gastrointestinal motility.
Aims & Methods: The aim of the present study was to investigate detailed contractile response in the circular smooth muscles of the mouse ileum. To compare detailed contraction response in the circular and longitudinal smooth muscles, we used circular and longitudinal small muscle strips (0.2 mm × 1 mm) of the mouse

ileum. The time from carbamylcholine (CCh) treatment to peak of contraction, and the amplitudes of contractions were compared between circular and longitudinal muscle small strips.
Results: The time to peak phasic contractile responses to CCh was significantly 5 minutes longer in the small muscle strips of circular muscle (5.7 min) than in those of longitudinal muscle (0.4 min). The amplitudes of contractions in the small muscle strips of circular muscle were similar in that of longitudinal muscle. Tetrodotoxin and N^{ω}-nitro-L-arginine had no effect on CCh-induced contractions of circular muscle. Regarding contraction, the pD_2 values for CCh were 0.86 ± 0.05 mM for circular muscle and 0.82 ± 0.07 mM for longitudinal muscle. The selective M2R antagonist methoctramine (100 nM) had no effect on CCh-induced contraction in circular and longitudinal muscle small strips. In contrast, the selective M3R antagonist 4-diphenylacetoxy-N-methylpiperidine methiodide (10 nM) completely suppressed CCh-induced contractions in both circular and longitudinal muscle small strips. Furthermore, Ca^{2+} channel blocker nicardipine (10 nM) markedly suppressed CCh-induced contractions on the circular and longitudinal muscles.
Conclusion: In this study, we demonstrate that the time to peak, which means the time from M3R activation to contraction, was slower in circular smooth muscles than in longitudinal smooth muscles.
Disclosure of Interest: None declared

P1065 ANORECTAL HIGH DEFINITION MANOMETRY: A COMPARISON BETWEEN HEALTHY VOLUNTEERS, FECAL INCONTINENCE AND FUNCTIONAL CONSTIPATION

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Introduction: Anorectal high-definition manometry (high resolution with 3D, ARHDM) allows a precise definition of pressure profile. However normal values are scarce with this device. Our aim was to determine normal values and manometric profiles in fecal incontinence (FI) and functional constipation (FC) patients in a prospective multicenter trial (NCT01710579).
Aims & Methods: One hundred and twenty seven subjects were included in 3 centers. We are presenting results for 33 healthy volunteers (HV, 25 women, mean age 48 years), 33 FI patients (33 women, mean age 58) defined by Vaizey score > 6 and constipation Kess score < 9 and 37 FC patients (35 women, mean age 53) defined by Kess score > 9 and Vaizey score < 6 . All subjects underwent endoanal ultrasound examination to detect anal sphincter defects. ARHDM was performed using a rigid probe (Given Imaging, Duluth, GA). The protocol consisted of a 2-minute resting period, 2 squeezing periods (> 30 seconds) and 2 push maneuvers. The high-pressure zone (HPZ) corresponding to the anal canal was delineated at the 20-mmHg isobaric contour. The height and mean pressure of the HPZ were measured over a 20-s period at the end of the resting period and after the beginning of each squeezing period, and over a 5-s period s after the beginning of each push period. Because rectal pressure cannot be adequately assessed with this probe, we chose the ratio [push/rest] of the mean pressures of the anal HPZ to quantify the push maneuvers (anal relaxation was considered as present if this ratio was < 0.8). Data are expressed in median (IQR) and compared between groups using non-parametric tests.
Results: FI patients were significantly older ($p < 0.05$ vs the other groups). Anal resting manometric parameters were significantly different between HV and FI (Table). Anal squeezing manometric parameters were significantly different between the 3 groups. In healthy females, anal pressures were similar in those with (4 subjects) and without anal sphincter defect. In FI women, resting, but not squeezing, anal pressures were significantly lower when an anal sphincter defect was present (16 patients, 49%). Increased anal pressure or absence of anal relaxation during push maneuvers was observed in the majority of HV and patients.
Conclusion: This study established normal values for ARHDM, and showed differences between controls, patients with FI and patients with FC for resting and squeezing anal pressures, as well as for HPZ height. More than 70% of HV and patients had no significant anal pressure decrease during push: rectoanal dyssynergia must be assessed differently using this new technology.
Disclosure of Interest: A. GARROS: None declared, A. ROPERT: None declared, M. BOUVIER: None declared, H. DAMON Consultancy: Medtronic/Covidien, C. BROCHARD: None declared, V. VITTON: None declared, L. SIPROUDHIS: None declared, S. ROMAN Financial support for research: Given Imaging/Covidien/Medtronic, Consultancy: Given Imaging/Covidien/Medtronic, F. MION Financial support for research: Given Imaging/Covidien/Medtronic, Consultancy: Given Imaging/Covidien/Medtronic.

P1066 PERCUTANEOUS ENDOSCOPIC CAECOSTOMY: FEASABILITY, EFFICACY AND COMPLICATION RATES IN REFRACTORY COLORECTAL DISORDERS

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Introduction: Percutaneous endoscopic caecostomy (PEC) has been proposed as an alternative to the Malone intervention with promising results to perform antegrade colonic enemas (ACE). However, the small number of patients and short-term follow up require further assessment of PEC. Therefore, the goal of this prospective study was to assess the feasibility and efficacy of PEC in a multicenter study and a larger group of patients.
Aims & Methods: The study was conducted in 2 centers between September 2006 and April 2014. The PEC procedure was standardized between the centers and was performed under general anesthesia during a colonoscopy. It consisted in 1) puncturing the caecum after endoscopic transillumination to introduce the Chait^{TM} catheter (Cook, USA) and 2) creating a caecopexy with 3-4 anchors. The indications of PEC were constipation, fecal incontinence and incontinence after rectal resection, refractory to medical treatment. For each indication the primary endpoint was improvement of quality of life score (GIQLI). GIQLI score, constipation score (Kess), incontinence score (Cleveland) were calculated before the PEC and at 3, 6, 12 and 24 months. The overall success of PEC procedure was defined by improvement quality of life, the absence of removal of the device, of colectomy or colostomy.
Results: A total of 69 patients were included, 67 with follow-up > 3 months (2 were lost to follow-up). Constipation, fecal incontinence and rectal resection groups comprised 43, 19 and 10 patients. Mean follow-up was 2 years in the first two groups and 6 months in the third group. GIQLI scores were significantly improved in constipation group ($p = 0.034$), incontinence group ($p = 0.026$) and rectal resection group ($p = 0.013$). In the constipation group, Kess scores were 25.9 before ACE and 20.6 at 2 years ($p < 0.05 = 0.012$). In the incontinence group, mean Cleveland scores were 14.9 before ACE and 10.4 at 2 years ($p = 0.045$). In the rectal resection group, the scores went from 14.3 to 2.7 at 6 months ($p = 0.014$). Overall, success percentages in the constipation group, incontinence group and rectal resection group were 58.1% (25/43), 73.7% (14/19) and 90.0% (9/10), respectively. Complications rates were as follows: prolonged pain on the catheter site (50.7%), local bud (41.8%), catheter suspected infection in 13 cases (19.4%). 19 devices (28.4%) were withdrawn because of functional failure or complication.
Conclusion: Percutaneous endoscopic caecostomy for antegrade colonic enemas allows obtaining a significant improvement in the quality of life in patients with colorectal disorders refractory to medical treatment. Persistent pain at the catheter site, which was the most frequent complication in our study, suggests that adaptative measures of the PEC technique are needed in order to provide optimal patient's care.
Disclosure of Interest: J. Ricard: None declared, M. Le Rhun: None declared, E. Chabrun: None declared, E. Duchalais: None declared, S. Bruley des Varannes: None declared, F. Zerbib: None declared, E. Coron Financial support for research: Cook Medical, Lecture fee(s): Cook Medical

P1067 EFFICACY AND SAFETY OF PRUCALOPRIDE IN ADULTS WITH CHRONIC CONSTIPATION: AN INTEGRATED ANALYSIS OF SIX RANDOMIZED CONTROLLED CLINICAL TRIALS

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Introduction: Prucalopride, a selective, high-affinity serotonin receptor 4 agonist, stimulates gastrointestinal motility and alleviates common symptoms of constipation in adults.
Aims & Methods: The aim of this study was to perform an integrated analysis of the efficacy and safety of prucalopride 2 mg daily in men and women**.** Data were combined from six phase 3 and 4, international, multicentre, double-blind, randomized, placebo-controlled, parallel-group trials with similar study designs and endpoints. The primary efficacy endpoint was the proportion of patients

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	Entire cohort (n = 51)	Control group (n = 26)	Study group (n = 25)	p-value
Constipation[1]	18 (35%)	0 (0%)	18 (72%)	$p < 0.001$
Laxative Use[2]	9 (18%)	0 (0%)	9 (36%)	0.001
Vomiting[3]	13 (26%)	0 (0%)	13 (52%)	$p < 0.001$
Possiting[4][t1]	4 (8%)	0 (0%)	4 (16%)	0.051
Abdominal Distention[5]	17 (33%)	1 (4%)	16 (64%)	$p < 0.001$
Abdominal Pain[6]	14 (28%)	0 (0%)	14 (56%)	$p < 0.001$
Increased Effort of defecation[7]	16 (31%)	1 (4%)	15 (60%)	$p < 0.001$
Use of Anal Stimulants[8]	18 (35%)	1 (4%)	17 (68%)	$p < 0.001$
Irritability[9]	23 (45%)	4 (15%)	19 (76%)	$p < 0.001$

[1] Defined as moderate or severe constipation[2] Defined as using drugs for a period of 1 month or more[3] Defined as vomiting once a week or more often[4] Defined as many possiting, severe, beyond age of 6 months, which required treatment[5] Defined as moderate or severe abdominal distension[6] Defined as moderate or severe abdominal pain[7] Defined as moderate or severe effort of defecation[8] Defined as using anal stimulants at least once a week[9] Defined as moderate or severe unrest

with a mean frequency of ≥ 3 spontaneous complete bowel movements (SCBMs) per week over 12 weeks of treatment. Several secondary efficacy endpoints were assessed (at baseline and at the final on-treatment assessment) using patient diaries and the validated Patient Assessment of Constipation – Symptoms (PAC-SYM) and Patient Assessment of Constipation – Quality of Life (PAC-QOL) questionnaires. Safety was assessed throughout the studies.

Results: Overall, 2484 patients were included in the integrated efficacy analysis (1237 received prucalopride and 1247 received placebo) and 2552 patients (prucalopride: 1273, placebo: 1279) were included in the integrated safety analysis. Most patients were women (78.3%) and Caucasian (79.0%), and the mean (standard deviation) age overall was 47.5 (15.3) years. The mean duration of constipation was 17.3 (15.0) years and 38.9% of patients had experienced chronic constipation for ≥ 20 years. Consistent with the results of the individual trials, significantly more patients achieved a mean of ≥ 3 SCBMs per week over 12 weeks of treatment in the prucalopride group (27.8%) than in the placebo group (13.2%, $p < 0.001$); the odds ratio was 2.68 (95% confidence interval: 2.16–3.33). Results were consistent in men and women, with response rates for prucalopride and placebo of 31.6% versus 16.7%, respectively, for men and 26.6% versus 12.2%, respectively, for women (both $p < 0.001$). At the final on-treatment assessment, the proportions of patients with an improvement of ≥ 1 point in the PAC-SYM and PAC-QOL total scores from baseline were 33.3% versus 23.9% and 37.1% versus 22.3%, respectively, in the prucalopride group versus the placebo group. Prucalopride showed a consistently good safety and tolerability profile. The most common adverse events were gastrointestinal disorders (nausea, diarrhoea and abdominal pain) and headache, mainly occurring at the start of treatment. No cardiovascular safety signals were identified. The safety and tolerability profile of prucalopride was similar in men and women.

Conclusion: This integrated analysis demonstrates the favourable efficacy and safety profile of prucalopride for the treatment of chronic constipation over 12 weeks in both men and women.

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P1068 NORMAL VALUES FOR 3D HIGH-RESOLUTION ANORECTAL MANOMETRY IN CHILDREN

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Introduction: 3D high-resolution resolution anorectal manometry is the most precise tool to assess function and 3D topographic picture of pressures along the anal canal. Until now, it has been used only in adult population. The normal values in pediatric population have not been evaluated so far.

Aims & Methods: The aim of this prospective study was 3D manometric evaluation of anorectal function in children without symptoms from lower gastrointestinal tract.

Manometry procedures were performed using a rigid probe (Covidien AG, Ireland) without premedication. Pressures within the anal canal and 3D picture of sphincters were obtained. The volume of balloon to elicit rectoanal inhibitory reflex (RAIR) was established. If possible, defecation dynamics and thresholds of sensation were evaluated. Data were expressed as mean (±SD).

Results: 61 children (34 males; age: 2-17 years, mean: 8.28 years) were studied. Mean resting and squeeze sphincter pressures were 83.43 (±23.23) mmHg and 191 (±64.21) mmHg, respectively. The mean length of the anal canal was 2.62 (±0.68) cm and it was correlated with age ($r = 0.49$, $p < 0.0001$). Mean rectal balloon volume to elicit RAIR was 15.66 (±10.9) cc. The first sensation, urge and discomfort were observed at 24.42 (±23.98) ml, 45.91 (±34.55) ml and 91.58 (±50.17) ml of the balloon volume, respectively. Mean resting pressure of puborectalis muscle was 71.54 mmHg (±14.58), mean squeeze pressure was 134.10 mmHg (±35.2). There was no lesions of sphincters according to 3D topographic picture of the anal canal. There was no statistically significant differences in pressure profiles between males and females. Positive correlation between age and volume of balloon needed to elicit discomfort was found.

Conclusion: Normative data of 3D high-resolution anorectal manometry in children without symptoms from lower gastrointestinal tract were established. There were no significant gender differences concerning pressure results.

Disclosure of Interest: M. Banasiuk Conflict with: Equipment support from manufacturer (Covidien AG), A. Banaszkiewicz: None declared, P. Albrecht: None declared

P1069 THE CHRO.CO.DI.T.E. STUDY: MANAGEMENT OF CHRONIC CONSTIPATION IN GASTROENTEROLOGICAL EVERYDAY PRACTICE

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Introduction: Chronic constipation (CC) comprises FC and IBS-C according to Rome-III-criteria, but some patients consider themselves constipated even not meeting these criteria (no Rome Constipation: NRC).

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Table: PAC-SYM scores.

PAC-SYM score,mean observed (mean change from BL) n	**Placebo** Women Score	n	Men Score	n	**Prucalopride ≤ 2 mg** Women Score	*p* value*	n	Men Score	*p* value*	
Overall scoreBLFoTA	944938	1.91.5 (–0.4)	296290	1.71.2 (–0.5)	939927	1.91.2 (–0.7)	< 0.001	295285	1.81.1 (–0.7)	0.019
Stool symptomsBLFoTA	943938	2.41.9 (–0.5)	296290	2.21.7 (–0.6)	938927	2.41.6 (–0.8)	< 0.001	295285	2.31.5 (–0.8)	0.013
Abdominal symptomsBLFoTA	944937	1.91.4 (–0.4)	296290	1.51.0 (–0.5)	938928	1.91.2 (–0.7)	< 0.001	295285	1.61.0 (–0.6)	0.336
Rectal symptomsBLFoTA	943937	1.10.8 (–0.3)	293290	1.00.7 (–0.4)	937927	1.20.7 (–0.5)	< 0.001	295285	1.10.6 (–0.5)	0.061

*Placebo versus prucalopride. Based on a Cox proportional hazard regression including terms for treatment group, study, country, number of complete bowel movements at baseline (0 or > 0) and sex.

BL, baseline; FoTA, final on-treatment assessment; PAC-SYM, Patient Assessment of Constipation-Symptoms.

Aims & Methods: To evaluate clinical management of CC subgroups (FC, IBS-C, NRC) by 52 Italian gastroenterologists.
Results: Rome-criteria were routinely used by 45/52 of the gastroenterologists. Data from 918 CC patients were obtained (F: 80.5%; mean age: 51.1; FC: 61%; IBS-C: 31%; NRC: 8 %). The duration of CC was > 10 years in 48%. Dyspepsia, anxiety/depression, gastroesophageal reflux and sleep disturbances were the most frequent comorbidities. Bristol 1-2 was reported in 71.6% of CC (FC: 71.8%; IBS-C: 75.6%; NRC: 48.1%; $p < 0.001$). Digital rectal examination was performed in 56.7%. Psychological consultation was requested in 11.4%, urological in 8.3% and gynecological in 12.4%. Diagnostic tests were requested in 79.6%: blood tests in 53.4%, thyroid function tests in 45% (FC: 43.2%; IBS-C: 52.4%; NRC: 35.2%; $p < 0.005$), colonoscopy in 38.7% (52.8% ≥50 years; 25.2% < 50 years; $p < 0.0001$); anorectal manometry in 34.6% (FC: 38.6%; IBS-C: 29.8%; NRC: 22.2%; $p < 0.01$), colonic transit time in 25.8% and abdominal ultrasound in 21.8%. Dietary suggestions were prescribed in 80.4%; fibers in 54.9% (IBS-C: 60.7%; FC: 53.2%; NRC: 55.6%;), probiotics in 36.1%. Macrogol was suggested in 69% (FC: 70.9%; IBS-C: 71.6%; NRC: 42.6%). Antispasmodics were prescribed in 16.4% (IBS-C: 27.6%; FC: 11.6%; $p < 0.0001$). PAC-SYM (1.6 ± 0.7) was related to the duration of constipation ($p < 0.005$), to IBS-C and to an increased number of diagnostic tests ($p < 0.001$) and therapies ($p < 0.05$). PAC-QOL (1.78 ± 0.70) was related to IBS-C, to female sex ($p < 0.05$) and to an increased number of diagnostic tests ($p < 0.05$), specialist consultations ($p < 0.005$) and therapies ($p < 0.0001$).
Conclusion: NRC have a shorter history of disease, milder symptoms and require fewer diagnostic tests. PACSYM and PACQOL display higher values in IBS-C than in FC. Digital rectal examination is performed only in 57% of patients. Although not recommended by current guidelines, abdominal ultrasound is frequently requested. Macrogol is the most prescribed laxative both for FC and IBS-C.
Disclosure of Interest: None declared

P1070 AN AUDIT OF THE PREVALENCE OF FAECAL INCONTINENCE IN HOSPITAL PATIENTS

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Introduction: Faecal incontinence (FI) is a common and under-reported problem, with many patients too embarrassed to seek help. Optimal management relies on first identification of these patients and only then- a thorough diagnosis that identifies all contributory factors, and a systematic approach to treatment. Management options include drug therapy, topical applications, containment products, behavioural techniques and surgery. Many patients do not receive optimal care due to lack of identification. In-hospital identification when they are admitted for other reasons may be one method of improving the care of such patients.
Aims & Methods: We assessed the identification of continence problems in our hospital patients via a simple 'spot check' audit of the different wards; we used the case notes for checking the documentation by both nursing and medical staff. We looked at care plans, stool charts, follow up plans etc.
Results: Overall, 163 patient case notes were examined. 90% had nursing documentation about faecal continence documented in comparison to 48% for medical documentation. Of the 147 patients where nursing documentation was found, 10.8% were found to have FI. Only 31% of these patients would have been identified by medical documentation. If only medical documentation had been used, this would have dropped to 6.5%. Most of the patients that were identified as having FI were, as expected, elderly and on the stroke unit (44%), general elderly medical wards (37.5%), orthopaedic (12.5%) and gastroenterology (6%) wards. All patients (100%) were then referred appropriately for further management.
Conclusion: Faecal incontinence has considerable impact on patients' lifestyle and quality of life, and can cause profound distress. It is important to identify these patients with FI, establish the cause and initiate appropriate management, whilst maintaining their privacy and dignity. The impact of FI on the patient's quality of life needs to be assessed prior to planning management/specialist referral etc. Written documentation in the form of care plans, follow up arrangements, advice leaflets etc is vital to providing optimal care for our patients. We found that our nursing documentation was much better than the medical documentation which needs to be improved. Once identified, all our patients were managed appropriately.

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P1071 QUALITY AND EPIDEMIOLOGY OF CLINICAL PRACTICE GUIDELINES FOR CONSTIPATION: A SYSTEMATIC APPRAISAL

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Introduction: Clinical practice guidelines (CPGs) play an important role in healthcare. The guideline development process should be precise and rigorous to ensure that the results are reproducible and not vague. The main objective of our work was to identify published constipation guidelines and assess their quality with the Appraisal of Guidelines for Research and Evaluation instrument (AGREE) and their suitability regarding adaptation for future guidelines.
Aims & Methods: To assess the methodological quality and epidemiology of clinical practice guidelines on constipation. We performed a systematic literature search on constipation CPGs of five databases (included MEDLINE and EMBASE) and guideline websites were searched till to April, 2015. The methodological quality of the guidelines was assessed by four authors independently using the AGREEII instrument.
Results: From 1234 citations, 22 relevant guidelines were included. The overall agreement among reviewers was moderate (Intra-class correlation coefficient = 0.84; 95% confidence interval [CI], 0.56-0.86). The mean scores were moderate for the domains "scope and purpose" (51.77) and "rigor of development"(56.73), however, there were low for the domains "clarity of presentation" (23.73), "stakeholder involvement"(32.23),"applicability"(29.14) and "editorial independence"(29.59). Four sixths domains scores were lower when compared with international average level. According to the AGREE instrument, six guidelines can be strongly recommended, 10 with provisos and alterations while the remaining cannot be recommended for adaptation due to poor methodological quality.
Conclusion: Overall, the quality of the guidelines assessed was low when compared with the international CPGs average level. The quality and transparency

Abstract number: P1075
Table 1: Top 5 accuracy websites with corresponding scores and Google rank positions.

Website	Accuracy QEI(0-44)	Quality GQS(1-5)	DISCERN(16–80)	LIDA(0-100%)	Readability FRE	FKG	Google rank
www.cancer.org	41	5	65	67%	62	9th	6
www.bowelcanceraustralia.org	38	3	35	58%	58	10th	5
www.uptodate.com	37	5	69	85%	28	14th	27
www.macmillan.org.uk	35	4	49	69%	48	11th	19
www.nlm.nih.gov/medlineplus	34	4	57	81%	59	8th	4

of the development process and the consistency in the reporting of constipation guidelines need to be improved. Many other methodological disadvantages were identified. In the future, constipation CPGs should base on the best available evidence and rigorously developed and reported. Greater efforts are needed to provide high-quality guidelines that serve as a useful and reliable tool for clinical decision-making in this field.

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Disclosure of Interest: None declared

P1072 LONG-TERM OUTCOME OF INFANTS WITH SUSPECTED HIRSCHSPRUNG'S DISEASE BUT NORMAL RECTAL BIOPSY

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Introduction: Hirschsprung's disease (HD) must always be considered in very-early onset constipation. While HD has a well describes clinical course, little is known about those infants in whom HD was excluded.

Aims & Methods: We aimed to describe the long-term clinical outcomes of infants with clinical suspicion of HD which was excluded by rectal suction biopsy.

This is a single-center double-cohort comparative study. Infants who underwent rectal mucosa biopsy for suspected HD were age and gender-matched with healthy controls. A survey relating to clinical outcomes, stooling patterns and other gastrointestinal-related conditions was sent to parents. Pathology slides were re-reported by an experienced histopathologist blinded to the clinical data.

Results: A total of 51 infants were included (25 case, 26 control; median 51 months (IQR 32-83) months of follow-up). Nine (36%) of the case group required prolonged laxative use for constipation during the first year of life compared with 0 (0%) of controls ($P < 0.001$). Case infants were significantly more likely to be hospitalized or be diagnosed with a chronic gastrointestinal-related condition than controls (33% vs 12%, $p = 0.01$; and 19% vs 8% respectively, $p = 0.04$).

Conclusion: Constipation in infancy is associated with long term gastrointestinal related disorders and should be considered clinically significant even when the diagnosis of HD is excluded. Infants with early onset abnormal stooling patterns should be monitored with adequate pediatrician or pediatric gastroenterologist follow-up.

Disclosure of Interest: None declared

P1073 IMPACT OF SWITCHING FROM A BRAND TO A GENERIC MACROGOL ON PRESCRIPTIONS AND DOSES FOR PATIENTS WITH CHRONIC CONSTIPATION IN THE UK

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Introduction: Patients with constipation switching from a branded to a generic macrogol may require a higher number of prescriptions and doses (defined as packs of 20 sachets). Repeated switching on the basis of cost savings alone can irritate patients and can erode trust and compliance (GPC 2013[1]).

Aims & Methods: This analysis compares prescription numbers and doses (20 sachets/pack) for chronic constipation patients switched from branded macrogol (MOVICOL) to generic macrogol (LAXIDO), and those who switched back. Retrospective real-world, longitudinal patient and prescribing data from 397 UK GP practices (2,186 GPs, 13,567 patients; Jan-Dec 2013; Cegedim Strategic Data Ltd, a division of IMS Health) were analysed in two cohorts of chronic constipation patients: (1) patients prescribed branded macrogol, switched to generic; (2) patients prescribed branded macrogol, switched to generic (Switch-1) and returned to the brand (Switch-2). All patients were tracked from initiation to treatment end. Annualised prescriptions and doses/patient changes in each cohort were analysed (one- and two-sided t-test for two-sample assuming unequal variances).

Results: Males/females aged ≥13 years were analysed. In cohort (1), $N = 3109$, $M = 0.63$, $SD = 8.29$, prescription numbers (+8%) and doses (+13%) per patient/year showed an average increase. Absolute increase in prescription numbers (+0.6) and doses (+1.7) were significant ($p < 0.05$), and observed across all age groups (elderly [65+], middle-aged [36-64], young adult [19-35], adolescent [13-18]). In cohort (2), $N = 91$, $M = -3.41$, $SD = 1.65$, prescription numbers (-24%) and doses (-11%) per patient/year showed an average reduction during Switch-2. Additionally, absolute increase in prescription numbers (+5.0) and doses (+4.9) at Switch-1 was significant ($p < 0.05$).

Conclusion: Chronic constipation patients switched from branded to generic macrogol required a significantly higher number of prescriptions and doses than previously required. Patients who switched back from the generic to the branded macrogol required fewer. Factors impacting changes in prescription e.g. efficacy, convenience, and compliance require further investigation.

This analysis was funded by Norgine.

Reference

1. Prescribing in General Practice, General Practitioners Committee (GPC), BMA, May 2013.

Disclosure of Interest: V. Bajaj Conflict with: Employee of Norgine, A. Naidoo Conflict with: Employee of Norgine

P1074 EFFECT OF PRUCALOPRIDE ON SYMPTOMS OF CHRONIC CONSTIPATION IN MEN AND WOMEN: AN INTEGRATED ANALYSIS OF SIX RANDOMIZED CONTROLLED CLINICAL TRIALS

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Introduction: Prucalopride, a highly selective 5-hydroxytryptamine receptor-4 agonist, stimulates intestinal motility and is effective at alleviating symptoms of chronic constipation (CC).

Aims & Methods: This analysis aimed to compare the effect of prucalopride ≤ 2 mg on constipation symptoms in men and women, using the validated Patient Assessment of Constipation-Symptoms (PAC-SYM) questionnaire. An integrated analysis was performed on data from six phase 3 and 4, multicentre, double-blind, randomized, placebo-controlled, parallel-group trials investigating the efficacy and safety of prucalopride in CC. All six studies had similar study designs, allowing pooling of results and sex-specific sub-analyses. The treatment period was 12 weeks in five of the six studies, and 24 weeks in the sixth study.

Results: Overall, 2484 patients (597 men, 1887 women) were included in the analysis. Of these, 1237 received prucalopride and 1247 received placebo. The mean (standard deviation) age was 47.5 (15.3) years and duration of constipation was 17.3 (15.0) years. For both men and women at baseline, stool symptoms were rated greater in severity (moderate to severe) than abdominal and rectal symptoms (mild to moderate for both). The mean decrease in overall PAC-SYM score from baseline to final on-treatment assessment (FoTA) was significantly greater for men and women in the prucalopride group (both, –0.7) than in the placebo group (men, –0.5, $p = 0.019$; women, –0.4, $p < 0.001$) (Table). The proportion of patients with a change of ≥ 1 point in overall PAC-SYM score at FoTA was quantitatively greater for men and women in the prucalopride group (men, 31.1%; women, 33.9%) than in the placebo group (men, 24.5%; women, 23.7%); similar results were reported for all subscores.

Conclusion: The symptoms of CC improved in both men and women receiving prucalopride, as assessed using PAC-SYM scores.

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M. Camilleri: None declared, J. Tack Financial support for research: Abbott, Novartis and Shire, Lecture fee(s): Abbott, Almirall, AstraZeneca, Janssen, Menarini, Novartis, Shire, Takeda and Zeria., Consultancy: Almirall, AstraZeneca, Danone, GI Dynamics, GlaxoSmithKline, Ironwood Pharmaceuticals, Janssen, Menarini, Novartis, Rhythm, Shire, Takeda, Theravance, Tsumura, Will-Pharma and Zeria, E. Quigley Financial support for research: Rhythm and Vibrant, Lecture fee(s): Almirall, Ironwood, Metagenics, Procter and Gamble and Shire-Movetis, Consultancy: Alimentary Health, Almirall, Forest, Ironwood, Movetis, Rhythm, Salix, Shire and Vibrant, M. Ke Lecture fee(s): Janssen, S. da Silva Conflict with: employee of Shire, A. Levine Shareholder: Shire, Conflict with: employee of Shire, R. Kerstens Consultancy: Shire, Conflict with: employee at Shire at the time of the study

P1075 SYSTEMATIC REVIEW OF QUALITY OF PATIENT INFORMATION ON COLORECTAL CANCER SCREENING ON THE INTERNET

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Introduction: Efficacy of colorectal cancer (CRC) screening programs is dependent on screenees' participation. The internet is increasingly used by individuals for health information and can be an important tool to support decision making. The aim was therefore to evaluate the accuracy, quality and readability of patient-oriented websites on CRC screening.

Aims & Methods: Websites were identified by Google.com™ using the search term: ''colorectal cancer screening'' OR ''bowel cancer screening'' OR ''colon cancer screening''. To assess accuracy, a Quality Evaluation Instrument (QIE) was developed and pretested, which awards points (0-44) on various aspects of CRC screening. In addition, websites were evaluated using a validated five-point Global Quality Score (GQS), two validated internet quality instruments (LIDA; 0-100% and DISCERN;16-80) and two reading scores; Flesch Reading Ease (FRE) and Flesch-Kincaid Grade Level (FKG). Since internet searchers do not typically view more than one page and usually choose one of the first results displayed by the search engine, two raters independently assessed the first 3 Google pages totaling 30 websites. Portal links to other sites, duplicates and news articles were excluded. For QEI assessment, consensus in case of disagreement was achieved through discussion with a third reviewer. For other parameters the mean score of both website raters was used.

Results: Out of the first 30 hits, 20 websites met the inclusion criteria. The mean QEI score was 25.5 (range 9-41) and the median GQS was three (range 2-5). There was a strong positive correlation between the QEI and the validated GQS (Spearman's $r = 0.81$; $p < 0.001$). Also the validated LIDA and DISCERN had a moderate correlation with the QEI; $r_s = 0.45$ ($p = 0.05$) and $r_s = 0.65$ ($p < 0.01$) respectively. There was no correlation between the Google rank and QEI ($r_s = -0.36$; $p = 0.12$). The mean FRE was 48 (range 27–76). Only 30% of the websites had a reading level acceptable for the general public (FRE > 60). The mean FKG was 11 (range 5.4–15.9), indicating the text would be understandable to an average 11th grade US student. The mean LIDA overall score was 68% (range 25-86%) and the mean DISCERN score was 46 (range 27-68).

Conclusion: There is marked variation in quality of websites on CRC screening. The developed QEI was strongly correlated with previously validated quality instruments, making it a valuable tool to identify high-quality, accurate CRC screening websites. Notable is the poor correlation between quality and Google ranking. As people generally only read the first 10 hits, our findings suggest that they will miss out on high quality CRC screening websites. Improvements in quality and readability are required to provide patients with reliable information to make informed decisions on CRC screening participation.

Disclosure of Interest: None declared

P1076 GUAIAC-BASED FAECAL OCCULT BLOOD TESTS VERSUS FAECAL IMMUNOCHEMICAL TESTS FOR COLORECTAL CANCER SCREENING IN AVERAGE-RISK INDIVIDUALS

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Introduction: Faecal occult blood tests (FOBT) to screen for colorectal cancer (CRC) fall into two main categories: a guaiac-based FOBT (gFOBT) or the more recently developed faecal immunochemical test (FIT). More evidence has become available about FOBT screening which suggests that FIT may be superior to the commonly used gFOBT. The aim of this systematic review was to compare the diagnostic test accuracy of FIT and gFOBT screening for detecting advanced neoplasia (AN) and CRC in average-risk individuals.

Aims & Methods: This abstract is based on a pre-peer review of a formal Cochrane Review. Upon completion and approval, the final version of the manuscript is expected to be published in the Cochrane Database of Systematic Reviews. Studies were identified by searching electronic databases Medline, Embase, Cochrane Library, BIOSIS Citation Index, and SCI-expanded (31 January 2015) without restrictions on date or language. We included randomized and/or comparative studies in which asymptomatic average-risk individuals ≥ 40 years of age underwent gFOBT and/or FIT screening. Studies in which all participants underwent both a FOBT followed by colonoscopy were included. Data were analysed using a bivariate linear mixed model (Reitsma et al., 2005). Results of the tests reporting a cutoff of 10 mcg Hb/g faeces (FIT10) or 20 mcg Hb/g (FIT20) are shown.

Results: The search identified 5,355 titles, of which 526 were fully assessed and 23 studies were included. Seven studies compared more than one test and in 6/7 studies participants underwent more than one test; resulting in a total of 32 tests in 85,403 participants. For 11 FITs the data for FIT10 were retrieved, and for 8 FITs data for FIT20. All included gFOBT studies used a cutoff of at least one positive card. The sensitivity for detection of AN ranged between studies from 0% to 33% for gFOBT, from 5% to 67% for FIT10, and from 50 to 100% for FIT20. Sensitivity for AN was lower for gFOBT with a pooled sensitivity of 16%, compared to 32% for FIT10 ($p = 0.001$), and 27% for FIT20 ($p = 0.007$). Sensitivity for CRC ranged between studies from 57% to 67% for gFOBT, from 75% to 100% for FIT10, and from 63% to 94% for FIT20. Sensitivity for CRC was lower for gFOBT with a pooled sensitivity of 41%, compared to 80% for FIT10 ($p = 0.003$), and 72% for FIT20 ($p = 0.002$). No significant differences in specificity were found for AN between gFOBT (94%), FIT10 (95%) and FIT20 (96%), nor for CRC between gFOBT (94%), FIT10 (93%) and, FIT20 (93%).

Conclusion: This meta-analysis shows that FIT is superior to gFOBT in detecting advanced neoplasia and colorectal cancer in average-risk individuals. The specificity of both tests is similar. These results strongly support the current European guidelines for implementing FIT-based CRC screening programs and the switch from gFOBT to FIT testing for existing programs.

Disclosure of Interest: None declared

P1077 COMPARISON OF OC-SENSOR AND FOB-GOLD IN POPULATION BASED COLORECTAL CANCER SCREENING BASED ON FIT

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Introduction: Colorectal cancer (CRC) screening programs are implemented worldwide and many are based on fecal immunochemical testing (FIT). Data on participation and yield over consecutive rounds of FIT screening are limited. In the Netherlands, pilot-studies have been performed with OC-sensor (Eiken, Japan) and the recently started nationwide program is using FOB-Gold (Sentinel, Italy). Yet, little evidence is available how these two tests compare. The aim of this study was to evaluate the two tests on usability, participation and diagnostic yield.

Aims & Methods: The comparison was performed in the 4th round of a population-based FIT-screening cohort in the Netherlands. Demographic data of randomly chosen 20.000 individuals between 50-74 years living in the Amsterdam and Rotterdam regions of the Netherlands were obtained from municipal population registers (March 2014 to December 2014). All invitees in previous biennial rounds were re-invited except for those who tested positive in earlier rounds or those passing the upper age limit. Invitees were randomized to receive an OC-sensor or an FOB-Gold test. The test was considered positive if hemoglobin concentration was ≥ 10 μg Hb/g feces. Participation rate, positivity rate, and positive predictive value (PPV) for advanced neoplasia (AN) and CRC were calculated. The detection rate was defined as the proportion of participants being diagnosed with AN.

Results: In total 19,290 eligible persons (median age 61, IQR 57-67; 48% males) were invited: 9,669 invitees received the OC-sensor and 9,621 the FOB-Gold test: 62.4% returned the OC-sensor and 62.5% the FOB-Gold test (n.s.). Inappropriate use or unanalyzable tests occurred in 0.7% invitees using the OC sensor vs. 1.9% invitees using FOB-Gold test ($p < 0.001$). For OC-sensor, 7.9% were positive, compared to 6.5% for FOB-Gold ($p = 0.002$). The PPV for AN in the OC-sensor group was 31.2% (95% CI:27.1-38.5), versus 32.1% in the FOB-Gold group (95% CI: 27.5-37.3) (n.s.). The detection

rate was slightly higher for OC-sensor 2.2%, than for the FOB-Gold 1.9% (n.s.).

	Total	OC-sensor	FOB-Gold	*p*
Participation rate (%)	62.4	62.4	62.5	n.s.
Unanalyzable tests* (%)	1.3	0.7	1.9	< 0.001
Positivity rate (%)	7.2	7.9	6.5	0.002
Detection rate				
AN (%)	2.1	2.2	1.9	n.s.
CRC (%)	0.2	0.2	0.2	n.s.
Positive predictive value				
AN (%)	31.6	31.2	32.1	n.s.
CRC (%)	3.5	3.0	4.0	n.s.
True positives (AN) per 1000 invited (n)	12	13	11	

Conclusion: In this fourth round of biennial population based FIT-screening, both FITs OC-sensor and FOB-Gold seemed comparable regarding participation rate and positive predictive value. Significant differences between the tests were found on unanalyzable tests, with more additional FOB-Gold tests needed to be sent to invitees due to inappropriate use, and positivity rate, resulting in more colonoscopies to be performed for a positive OC-sensor.
Disclosure of Interest: None declared

P1078 HOW OFTEN DO THE PATIENT REPEAT SCREENING COLONOSCOPY? ; A STUDY FOR PERSONALIZED RECOMMENDATION OF SCREENING COLONOSCOPY INTERVAL

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Introduction: Colorectal cancer (CRC) is the third most common cancer and the second most frequent cause of cancer death of female and fourth most of male in South Korea. Most CRCs develop through the adenoma–carcinoma sequence, which allows for screening and prevention of CRCs by screening colonoscopic examination and polypectomy. However, there have been limited data on personalized optimal time interval of next surveillance colonoscopic examination. The aim of our study is to recommend personalized interval by analysis of various clinical factors obtained by health care examination.
Aims & Methods: We enrolled the patients who underwent two times more voluntary, complete screening colonoscopy at health care unit of Korea University Medical Center Anam Hospital from July 1, 2004 to July 31, 2010. The clustering analysis using the partitioning around medoids algorithm and Hierarchial cluster were conducted including the 32 clinical, geographic and laboratory data. For each cluster, we then performed survival analysis that provides the probability of having polyps according to the number of days until next colonoscopy.
Results: Totally 8332 patients underwent screening colonoscopy, among them 625 patients performed repeat colonoscopy exam. 625 patients divided four clusters by clustering analysis. Adenoma detection at first screening colonoscopy was the most potent risk factor of develop of adenoma at next screening. Male gender, triglyceride (>134 mg/dL), and age (>56 years old) were significant factor for decision of the personalized interval of next screening colonoscopy. For example, male patient, who had adenoma at fist screening, the predicted risk of adenoma is 50% after 25 months.
Conclusion: Our study can provide personalized time interval of next screening colonoscopy according to patients' individual clinical data. Further study are necessary for validation our results.

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P1079 URSODEOXYCHOLIC ACID AND RISK OF COLORECTAL CANCER: A POPULATION-BASED COHORT STUDY IN TAIWAN

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Introduction: Whether Ursodeoxycholic acid (UDCA) has a chemopreventive role or not for colorectal cancer (CRC) remains unclear. UDCA has been efficiently employed as a cytoprotective agent *in vitro* and is reported to prevent CRC in patients with primary sclerosing cholangitis and ulcerative colitis.[1,2] In contrary, a recent study showed that high doses of UDCA was associated with increased CRC risk for similar groups of patients.[3] Many patients with chronic hepatitis has been prescribed with off-label use of UDCA in Taiwan, a high endemic country for chronic viral hepatitis B.
Aims & Methods
Aims: We sought to investigate the association between UDCA therapies and CRC.
Methods: A nationwide cohort population-based study was performed using the Taiwan National Health Insurance Research Database. Patients who were taking UDCA from years 1998-2007 and were ≥ 20-year-old from one million beneficiaries were enrolled. Those patients with antecedent malignancy or taking insufficient UDCA (UDCA ≤ 28 prescribed daily dose (P.D.D.) or 300mg/day) were excluded. For a sensitivity analysis, those CRC patients found within 1 year of the first dose of UDCA were also excluded. Propensity scores were used to match the UDCA users (treated cohort) with UDCA-nonusers at a 1:1 ratio, based on age, gender, comorbidities and medications. Both groups were followed until CRC diagnosis or the end of year 2010.
Results: 7,328 UDCA users were identified to take more than 28 P.D.D. After matched by propensity score, 5,385 patients in treated and control cohorts were identified for final analysis. The median follow-up time was 7.3 ± 2.9 years. The hazard ratio of CRC development for UDCA-users over non-users after adjustment for propensity score was 0.772 (95% C.I. 0.222-2.685). For patients taking 28-84 P.D.D.,85-179 P.D.D., 180-364 P.D.D., and ≥ 365 P.D.D., the hazards ratio for CRC were 0.774 (95% C.I. 0.365-1.64), 0.717 (95% C.I. 0.247-2.087), 0.738 (95% C.I. 0.220-2.471), and 1.372 (95% 0.554-3.400), respectively. The results suggested that no dose-responsive curve could be observed between hazards ratio for CRC and UDCA dosage.
Conclusion: In this nation-wide survey, the largest cohort till now, there existed no evidence to support the chemopreventive role of UDCA in CRC. Routine use of UDCA to prevent CRC is not recommended.

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Disclosure of Interest: None declared

P1080 A RANDOMIZED CONTROLLED TRIAL OF AN EDUCATIONAL VIDEO TO IMPROVE QUALITY OF BOWEL PREPARATION FOR COLONOSCOPY

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Introduction: High-quality bowel preparation is necessary for colonoscopy. A few studies have been conducted to investigate improvement in bowel preparation quality through patient education. The reported methods for patient education on bowel preparation are various, however have not been well studied. The aim of this study is to evaluate the effect of our own educational video for bowel preparation.
Aims & Methods: A randomized and prospective study was conducted. All patients received regular instruction for bowel preparation during a pre-colonoscopy visit. Those scheduled for colonoscopy were randomly assigned to view an educational video instruction (video group) on the day before the colonoscopy, or to a non-video (control) group. Qualities of bowel preparation using the Ottawa Bowel Preparation Quality scale (Ottawa score) were compared between the video and non-video groups. In addition, factors associated with poor bowel preparation were investigated.
Results: A total of 502 patients were randomized, 250 to the video group and 252 to the non-video group. The video group exhibited better bowel preparation (mean Ottawa total score: 3.03 ± 1.9) than the non-video group (4.21 ± 1.9; $P < 0.001$) and had poorer bowel preparation (total Ottawa score ≥6: 91.6% vs.

78.5%; $P < 0.001$). Multivariate analysis revealed that males (odds ratio [OR] = 1.95, $P = 0.029$), diabetes mellitus patients (OR = 2.79, $P = 0.021$), and non-use of visual aids (OR = 3.09, $P < 0.001$) were associated with poor bowel preparation.
Conclusion: The addition of an educational video significantly improved the quality of bowel preparation.
Disclosure of Interest: H. Kim Financial support for research: SK phamaceutical company, J. Park: None declared, M. Kim: None declared, K. Kwon: None declared

P1081 ECONOMIC BURDEN AND QUALITY OF LIFE OF MODERATE-TO-SEVERE IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C) IN EUROPE: POOLED RESULTS FROM THE IBIS-C STUDY

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Introduction: This is the first study to assess the socio-economic burden of moderate-to-severe IBS-C in six European countries (France, Germany, Italy, Spain, Sweden and UK). Here we present the pooled economic and quality of life (QoL) results from all participating countries.
Aims & Methods: Observational, retrospective-prospective (6 months each) study of patients diagnosed in the last five years with IBS-C (Rome-III criteria) and with moderate-to-severe disease at inclusion (IBS-Symptom Severity Scale [IBS-SSS] score ≥ 175). The primary objective was to determine annual direct and indirect costs. Secondary objectives included assessing QoL at baseline: IBS-QoL and EuroQoL-5D (EQ-5D) questionnaires. Work productivity was assessed using the Work Productivity and Activity Impairment:IBS-C questionnaire (WPAI:IBS-C). All costs were calculated in local currency and adjusted (for inflation) to 2012 values. Post-hoc currency conversion was performed for cost comparison purposes.
Results: 525 patients were included in the study (60% severe by IBS-SSS); mean (±SD) age 45.3 ± 15.8 years, 86.9% female. The most prevalent symptoms at baseline were constipation (85.7%) and abdominal pain (85.1%). In the week prior to baseline, mean presenteeism (WPAI:IBS-C) was: 36.5%±29.0% of time; absenteeism: 8.4%±21.4%; work productivity loss: 39.4%±30.1%; daily activity impairment: 44.2%±28.6%. Mean IBS-QoL was 54.9 ± 22.7 (scale: 0-100 [worst-to-best]; 63.3 Italy–42.8 UK). Mean EQ-5D was 55.5 ± 21.7 (scale: 0-100 [worst-best]) and 89.4% and 62.3% of patients reported moderate-to-severe problems in pain/discomfort and anxiety/depression, respectively. Over the year, 73.1% patients consulted a primary care physician (88.4% UK–58.0% Italy), and 89.7% a gastroenterologist (100% France, Italy, UK–69.6% Germany); mean 4.9 (6.9 UK–2.1 Sweden) and 2.8 (4.0 Germany–1.7 Sweden) visits, respectively. 18.1% (24.0% UK–11.1% Sweden) patients required emergency department visits/hospitalisation (mean stay: 13.8 ± 24.0 days) and 62.1% had a diagnostic test (mean: 4.0 ± 2.7 [4.1 Spain–3.4 France, Italy]). 65.3% (90.4% UK–41.1% Italy) of patients took prescription drugs for their IBS-C and 67.2% (82.1% Italy–56.3% Spain) took non-prescription drugs. The mean annual direct costs per patient for national healthcare systems: €2,108 (UK) – €937 (Italy); cost for the patient: €568 (Spain) – €244 (France); indirect cost: €11,249 (Sweden) – €339 (Italy). Total annual cost: €12,827 (Sweden) – €1,761 (Italy).
Conclusion: Moderate-to-severe IBS-C symptoms have a high impact on QoL and work productivity of patients. With current management practices, both direct and indirect costs were high for all participating countries. Differences in annual direct costs were due to differences in healthcare resource utilisation, mainly diagnostic tests and medical consultations. Hospitalisations and/or emergency room visits was the largest direct cost driver for all countries.
Disclosure of Interest: J. Tack Conflict with: Grants / research support: Abbott, Novartis, Shire. Honoraria / consultancy fees: Almirall, AstraZeneca, Danone, GI Dyamics, GlaxoSmithKline, Ironwood, Janssen, Menarini, Novartis, Rhythm, Shire, Takeda, Theravance, Tsumura, Will Pharma, Zeria. Speaker fees: Abbott, Almirall, AstraZeneca, Janssen, Menarini, Novartis, Shire, Takeda, Zeria, V. Stanghellini Conflict with: Grants / research support: Alfa Wassermann, Almirall, Aptalis, Italchimici, Norgine, Shire, Takeda, Valeas. Honoraria / consultancy fees: Abbott, Alfa Wasserman, Almirall, Angelini, Aptalis, CM&D Pharma, Farmaderma, Ironwood, Norgine, Shire, Takeda, Valeas, Vibrant, Zeria., F. Mearin Conflict with: Speaker fees: Almirall., Y. Yannakou Conflict with: Grants: Shire; Medtronic. Speaker fees: Almirall; Shire; Sucampo., P. Layer Conflict with: Abbott / Solvay, Almirall, Aptalis / Axcan, Norgine, Shire., B. Coffin Conflict with: Honoraria / consultancy fees: Almirall, Mundipharma, Mayoly Spindler, Menarini., M. Simren Conflict with: Unrestricted research grants: Danone, AstraZeneca. Consultant/ Advisory Board member: Danone, Nestlé, Chr Hansen, Almirall, Albireo, Shire. Participation in a company-sponsored speaker's bureau: Almirall, Shire, Tillotts, Takeda., J. Mackinnon Conflict with: Employee of TFS Develop S. L, contracted by Almirall S. A to conduct the study., J. Bertsch Conflict with: Employee of TFS Develop S. L, contracted by Almirall S. A to conduct the study, J. Fortea Conflict with: Employee of Almirall, S. A

P1082 CORRELATION BETWEEN INFORMATION QUALITY IN REFERRAL LETTERS ASSESSED ON A NOVEL THIRTY POINT SCORE AND A VISUAL ANALOGUE SCALE: AN OBSERVATIONAL STUDY

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Introduction: Assessing referrals can be challenging if the content of the referral letter is inadequate. There is a lack of knowledge regarding which information is essential in referral letters to gastroenterologists.
Aims & Methods: The aim of the study was to create a score to assess the quality of information in referrals to gastroenterology departments in Norway. A secondary aim was to assess whether this score correlates to the gastroenterologists' subjective assessment of the referral. 25 gastroenterologists participated in a survey regarding important information in referral letters. They were asked to select the 15 most important variables for 9 common indications. Each variable was assigned either 3, 2 or 1 points according to importance. The result was used to create a thirty point score (TPS). Subsequently, 327 referral-letters were collected from 7 primary gastroenterology referral centers. The quality of the information in the referral-letters was subjectively assessed on a 10 cm Visual Analogue Scale (VAS) and then assessed using the TPS. Pearson correlation analyses were performed to measure the association between the VAS and the TPS.
Results: The 327 referrals had an average score of 13.2(range 1-25) and an average VAS of 4.7(range 0.2-9.5). The overall correlation between the TPS and the VAS was moderate($r = 0.42$)(table 1). However, it ranged from fair($r = 0.24$) to substantial($r = 0.70$) for the various indications.

Table 1: Comparison of referral information quality assessed by VAS and TPS.

Reason for referral	N. referrals (%)	Mean score(95% CI)	Mean VAS (95% CI)	Correlation coefficient	P
Abdominal pain	50 (15.3)	12.6 (11.0-14.2)	4.5 (3.9-5.2)	0.70	0.001
Dyspepsia	47 (14.4)	11.8 (10.6-13.0)	4.3 (3.7-4.9)	0.27	0.069
Hematochezia	34 (10.4)	15.4 (13.8-17.0)	5.1 (4.4-5.9)	0.48	0.004
Change of bowel habit	48 (14.7)	14.8 (13.4-16.3)	5.1 (4.4-5.8)	0.58	<0.001
Diarrhoea	38 (11.6)	11.3 (9.9-12.7)	4.6 (4.0-5.2)	0.38	0.019
Dysphagia	36 (11.0)	11.2 (9.6-12.8)	5.0 (4.3-5.8)	0.29	0.089
Constipation	27 (8.3)	13.6 (12.2-15.0)	4.5 (3.8-5.1)	0.23	0.255
Weight Loss	21 (6.4)	14.9 (12.5-17.2)	4.8 (3.9-5.8)	0.63	0.002
Jaundice	26 (8.0)	14.3 (12.4-16.2)	4.9 (3.9-5.8)	0.24	0.236
Total	**327**	**13.2 (12.6-13.7)**	**4.7 (4.5-5.0)**	**0.42**	**<0.001**

Correlation coefficient interpretation: 0-0.2 = slight, 0.2-0.4 = fair 0.4-0.6 = moderate, 0.6-0.80 = substantial, 0.8-1.0 = almost perfect.

Conclusion: The referral information quality was modest, with considerable variation. There was a fair-substantial correlation between the TPS and the subjective quality assessed by VAS. Referral structure and appropriateness may contribute to explain some of the remaining discrepancy between the two assessments.
Disclosure of Interest: None declared

P1083 INCREASED PARTICIPATION IN COLORECTAL CANCER SCREENING DURING A PILOT OF A FAECAL IMMUNOCHEMICAL TEST FOR HAEMOGLOBIN (FIT) IN ENGLAND

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Introduction: The NHS Bowel Cancer Screening Programme (BCSP) in England has used a guaiac faecal occult blood test (gFOBt) since 2006. In April 2014 the BCSP commenced a six-month FIT Pilot study to assess the clinical, financial and organisational implications of adopting FIT.

Aims & Methods: Two regional BCSP Hubs (Southern and Midlands & North West) and associated Screening Centres participated in the pilot study. One in 28 invitees was offered FIT rather than gFOBt. 30,000 FIT invitations provided adequate power for analysis of FIT uptake compared with gFOBt. The OC-SENSOR FIT system (Eiken Chemical Co. Ltd., Japan) was used with a cut-off for positivity of 20 μg haemoglobin [Hb]/g faeces (100 ng Hb/mL buffer).

Results: 40,930 subjects were invited to participate with a FIT and 1,126,087 with a gFOBt during the pilot period (April - October 2014). Uptake of FIT was significantly higher than gFOBt (66.5% vs. 59.4%; OR 1.36). The increase in uptake was significantly greater for previous non-responders (FIT 25.8% vs. gFOBt 14.2%; OR 2.09), compared with subjects invited for the first time (61.2% vs. 50.3%; OR 1.56) and those who had participated previously (90.3% vs. 86.1%; OR 1.50). The increase in uptake was higher in males (FIT 64.6% vs. gFOBt 56.4%; OR 1.41) than females (68.3% vs. 62.1%; OR 1.31) and was apparent for all quintiles of deprivation. Of particular note is the increase in uptake with FIT compared with gFOBt in the most deprived and traditionally 'hard-to-reach' quintile (53.7% vs. 45.8%; OR 1.37).

Overall positivity was 7.8% with FIT (cut-off 20 μg Hb/g faeces) and 1.7% with gFOBt (OR 4.83). The increase in positivity was similar in males and females and in all deprivation quintiles, but increased with age. Significantly more colorectal cancers (CRC) (0.27% FIT vs. 0.12% gFOBt; OR 2.19) and advanced adenomas (1.74% vs. 0.35%; OR 4.97) were detected with FIT. The PPV for all neoplasms was significantly higher with FIT (55.9% vs. 51.9%; OR 1.17). At a cut-off of 150 μg Hb/g faeces (750 ng Hb/mL buffer), which yielded a positivity for FIT (1.8%) similar to gFOBt, FIT had a higher detection rate and PPV for advanced adenomas and all neoplasms.

Conclusion: FIT significantly increased uptake of screening and provides an opportunity to adjust the faecal Hb concentration cut-off for positivity and thus the burden on colonoscopy resource. Further analysis will determine how the faecal Hb concentration measured by FIT could be incorporated into a multivariate risk score for CRC.

Disclosure of Interest: None declared

P1084 TRIAL OF THE NEW BOWEL PREPARATION METHOD FOR CT COLONOGARAPHY

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Introduction: CT colonography (CTC) is a useful examination of colorectal cancer screening, and accuracy verification of CTC has been promoted in Japan. When performing the CTC, bowel preparation method is used similar method as colonoscopy. However, taking a large volume of bowel cleansing solution has contributed to reduce the acceptability of the examinee in colonoscopy.

Aims & Methods: We propose a new bowel preparation method to take a laxative and a water-soluble contrast agent without taking a large volume of bowel cleansing solution. Using this method, we evaluated the acceptability of the examinees and the accuracy of the CTC image. The subject of this examination was 30 examinees, including 16 men and 14 women with a mean age of 53.8 years old, who received CTC at the Cancer Screening Center of Cancer Institute Hospital. Examinee received a one capsule of laxative (Amitiza) and 50ml of water-soluble contrast agent (Gastrografin) on the night prior to CTC. Morning of CTC, examinee received 50ml of water-soluble contrast agent again. The day prior of CTC, all examinee were allowed a low-residue meal kit. For evaluation, the colon was divided into six segments (rectum to cecum). The observed amount of residual stool regardless of tagging was assessed on axial images using a 4-point scale: 0 = no stool, 1 = small stool, 2 = moderate-size stool, and 3 = large stool. The observed presence of residual fluid was assessed on axial images using a 4-point scale: 0 = no fluid, 1 = minimal fluid, 2 = moderate fluid, and 3 = substantial fluid. The homogeneity of fecal tagging was assessed using a 5-point scale: 0 = no tagging, 1 = poor tagging, 2 = inhomogeneous tagging, 3 = good tagging, and 4 = excellent tagging. We performed an evaluation questionnaire of acceptability to examinees.

Results: The observed amount of residual stool was an average 0.5 points, the observed presence of residual fluid was an average 1.7 points, and the homogeneity of fecal tagging was an average 4.0 points. From the results of the questionnaire survey, it was 3 person answered ''preparation was unacceptable", and there was small impact on the daily life and work.

Conclusion: The main advantage of this preparation method is that it is not necessary to take a large amount of bowel cleansing solution. Furthermore, preparation conditions are also excellent. Since acceptability of the examinees for this preparation method is generally good, it is expected to contribute to the popularization of CTC.

Disclosure of Interest: None declared

P1085 A MULTI DISCIPLINARY TEAM APPROACH FOR COMPLEX BENIGN COLO RECTAL POLYPS: A TERTIARY REFERRAL CENTRE EXPERIENCE

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Introduction: Limited or no data is available on the impact of multidisciplinary team-(MDT) for complex benign colorectal polyps. Optimising the chance of successful and safe polyp resection at a single hospital visit is fundamental to offering a quality service.

Aims & Methods: A bi–weekly polyp MDT meeting was established in January 2013 to discuss the optimal management and resection strategies of all complex polyp referrals. The team comprises gastroenterologists/endoscopists, colorectal surgeons, pathologists, radiologists and a medical and nursing co-ordinator. The purpose of this pilot prospective study was to assess the impact of the MDT approach on the management of complex benign colorectal polyps.

Results: 96 polyp cases were discussed from January-2013 to October-2014. Inclusion criteria were defined as complex large polyps, those with difficult endoscopic access and recurrent fibrotic polyps after previous failed endoscopic excision. Most cases were tertiary referrals (78%). Reasons for referrals: very large complex polyps (55%)/difficult endoscopic access (54%)/previous unsuccessful polypectomy (36.4%). Majority of the polyps were in recto sigmoid (51%)/in caecal pole including ileocaecal valve or appendix (31.8%).

In 39.6% of cases the provisional management plan was changed after discussion at the polyp meeting. Apart from the conventional endoscopic techniques, the polyp MDT consensus proposed alternative approaches in 65% of cases to achieve a radical and complete excision of polyps. A single-hospital visit was recorded in 26% (25/96). The remaining cases (71/96) needed further diagnostic work-up and outpatient review (67/76), referral to the polyposis team (2/76), no polyp was found on two occasions.

Successful complete polyp removal was achieved in 85/96(88.5%) using conventional, novel and endo-surgical techniques; Endoscopic excision without surgical assistance in 39.6%(38/96), novel endo-surgical approaches in 25%(24/96 – Trans-Anal-Submucosal-Endoscopic-Resectio/TASER, Full-thickness-Laparo-endoscopic-EXcision/FLEX, Transanal-Endoscopic-Micro-Surgery/TEMS), laparoscopic-assisted-endoscopic-resection in 13.5%(13/96), surgical resection in 10.4%(10/96). Remaining 11 cases were managed as follows; surveillance in 4, no polyps found on examination of 2 cases, palliative care in one (carcinoma with metastases), 2 patients referred back to the base hospital for surgical resection, and one patient procedure is postponed due to co-morbidities and the other declined to have the procedure. 7 polyps were found to harbour carcinoma; all but one had surgical resection. The proposed MDT management plan was successfully followed in 82.3% of cases.

Conclusion: The polyp MDT provided a consensus on the key therapeutic issues for complex benign colorectal polyps and lead to a change in management plan in almost half of the patients. The multi-disciplinary approach helped to streamline patient care and avoid incomplete resection attempts.

Disclosure of Interest: None declared

Abstract number P1087 Table: Validation of scoring systems in predicting need for clinical intervention and 30-day mortality

1. Need for clinical intervention

Score*	Sensitivity(%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
RS > 0	95.68	36.09	64.58	100
CRS > 2	89.51	60.9	73.6	82.65
GBS > 0	100	2.26	55.48	100
mGBS > 0	100	3.01	55.67	100

1. **30-day mortality**

Score*	Sensitivity(%)	Specificity(%)	Positive predictive value (%)	Negative predictive value (%)
RS > 0	93.33	19.29	5.83	98.18
CRS > 2	86.67	34.29	6.6	97.96
GBS > 0	100	1.07	5.14	100
mGBS > 0	100	1.43	5.15	100

*Scores cutoff for 'high risk of intervention': RS > 0; CRS > 2; GBS > 0; mGBS > 0.

TUESDAY, OCTOBER 27, 2015 09:00–17:00

OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS II – HALL 7

P1086 DIEULAFOY'S LESION CLINICAL AND EPIDEMIOLOGICAL ANALYSIS OF A RARE CAUSE OF GASTROINTESTINAL HEMORRAGE

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Introduction: Dieulafoy's lesion, defined as submucosal tortuous artery of wide caliber, is a rare cause of gastrointestinal bleeding. As it's origen is an arterial bleeding, there is high risk of complications and morbimortality.

Aims & Methods

Aim: Analyze characteristics, risk factors, treatment and evolution associated to Dieulafoy s lesion.

Methods: Retrospective study since January 2000 and December 2013 of patients who underwent endoscopy resulting in Dieulafoy's lesion diagnosis. we have evaluated epidemiological varies, clinical presentation, risk factors, treatment and clinical outcome.

Results: We gathered data from 77 patients, medium age 74 years, 52% males. Dieulafoy's lesion supposed 1.4% of gastrointestinal bleeding admitted at our centre in this period. The most frequent locations were gastric (57%), duodenal (30%) and colon (12%). The common clinical presentation was melena (38%), followed by hematemesis (34%) and rectorragy (10%). The medium haemoglobin levels at diagnosis were 8.2 g dl and average admission was 8.4 days. The most prevalent risk factors were hypertension (60%), cardiovascular disease (53%), diabetes mellitus (31%) and paroxysmal atrial fibrillation (26%). One third of the patients had history of antiplatelet use, 28% were under anticoagulants and less than a half of them used proton pump inhibitors (PPI) (46%).

40% of patients needed more than one endoscopy for diagnosis. The more common treatment was sclerosis hemoclip (39%), needing a second treatment in 26% of the cases. Moreover, 70% of the patients needed blood transfusion (average 3.26 units patient). The recurrence was 18%. 9/77 patients deceased (11.7%), all with history of upper GI bleeding.

According to location, the colon and duodenum lesion were higher among women and gastric among men ($p < 0.05$). Colon lesions were associated in higher proportion with coronary heart disease ($p < 0.05$). Duodenal lesions debuted with more anaemia ($p < 0.05$), more transfusional need ($p < 0.01$), more blood units per patient ($p < 0.05$) and greater recurrence ($p < 0.05$).

Conclusion: Dieulafoy's lesion, nevertheless its low incidence, presents important morbimortality, with high transfusion rate. It is associated with cardiovascular disease. The duodenal location es the one with greatest repercussion. Even though there were endoscopical advances, Dieulafoy's lesion is still a diagnostic and therapeutic challenge nowaday.

Disclosure of Interest: None declared

P1087 CLINICAL IMPACT OF USING RISK SCORING SYSTEMS IN PATIENTS WITH SUSPECTED UPPER GASTROINTESTINAL BLEEDING

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Introduction: The clinical severity of an episode of upper gastrointestinal bleeding (UGIB) is highly variable. Numerous scoring systems have been developed to identify patients who have been affected adversely. Nevertheless, the use of these scoring systems in clinical practice is limited.

Aims & Methods: The aim of our study was to validate the application of different risk scoring systems in UGIB [Complete Rockall Score (CRS), clinical Rockall Score (RS), Glasgow-Blatchford Score (GBS) and modified Glasgow-Blatchford Score (mGBS)] within our country, and to compare in their utilities for prediction of clinical intervention and 30-day mortality. A retrospective and observational study was designed. 295 consecutive patients with acute UGIB admitted to a tertiary care hospital during a 1-year period were included. The primary outcome was the need for clinical intervention (blood transfusion, endoscopic, radiological or surgical intervention), and the secondary outcome included 30-day mortality. All of the above risk scoring systems were calculated for each enrolled patient. The validity of the tests was assessed using the receiver operated characteristics curve analysis (AUC), sensitivity, specificity, and positive and negative predictive values.

Results: The mean time until the requirement of upper endoscopy was of 12.76 ± 7.68 hours. 162 of the 295 patients (54.92 %) needed clinical intervention. 34 patients (11.53 %) developed recurrent bleeding and 30-day mortality was 5.08 % (UGIB-related mortality 3.73 %). The results in terms of sensitivity, specificity, and positive and negative predictive values for need for clinical intervention and 30-day mortality are shown in the table attached. The prognostic accuracy of GBS (AUC 0.849) and mGBS (AUC 0.854) were the highest achieved.

Conclusion: GBS and mGBS risk scoring systems are useful to select patients with low risk UGIB who could avoid hospitalisation. None of the scoring systems proved effective enough to predict mortality.

Reference

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Disclosure of Interest: None declared

P1088 COMPARISON OF AIMS65, GLASGOW-BLATCHFORD SCORE AND ROCKALL SCORE IN A EUROPEAN SERIES OF PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING

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Introduction: AIMS65 is a recently developed score designed to predict in-hospital mortality, length of stay and costs of gastrointestinal bleeding.

Aims & Methods: Our aim was to revalidate AIMS65 score as predictor of inpatient and 6-months mortality in a southern European population. Our secondary objective was to compare the AIMS65 score's performance with that of the GBS and RS with regard to mortality and the secondary outcomes of (A) a composite clinical endpoint of severity; (B) transfusion requirements; (C) rebleeding; (D) delayed mortality and (E) hospital length of stay. 309 patients with a diagnosis of upper gastrointestinal bleeding were included. AIMS65, Glasgow-Blatchford score and Rockall score were calculated to all of them. Every relevant clinical and biochemical data were collected, as well as transfusion requirements, endoscopic therapies, surgical or radiological treatments, and clinical outcomes for 6 months after admission. Clinical outcomes were in-hospital mortality, delayed mortality, rebleeding, composite endpoint, blood transfusion requirements, and hospital length of stay.

Results: Overall in-hospital mortality was 9.4%. On ROC analyses, AIMS65, GBS and RS were similar when predicting inpatient mortality (0.76 vs 0.78 vs 0.78). Regarding endoscopic intervention, AIMS65 and GBS were almost identical (0.62 vs. 0.62) but AIMS65 was useless when predicting rebleeding compared to GBS or AIMS65 scores (0.56 vs. 0.70 vs 0.71). The three scores proved to be very useful when predicting the need for blood transfusions. No patient with as AIMS65 = 0, GBS ≤ 6 or RS ≤ 4 died. When considering the composite endpoint of significant clinical outcomes, an AIMS65 score of 0 did not excluded patients which were considered high risk, but did a GBS ≤ 1 or RS ≤ 2. Considering the prediction of a prolonged in-hospital stay (>7 days), the three scores had similar AUROC. Delayed mortality was better predicted by AIMS65 than GBS or Rockall.

Table 1: Score components

Age (years)	65	51-78
Albumin (g/dl)	3.1	2.7-3.7
International normalized ratio	1.48	1.1-1.5
Sistemic blood pressure	111	95-126
Pulse	90	75-102
Hemoglobin	9.7	7.8-11.6
Urea	81.31	44.5-94.5
Hematemesis	151	48.9%
Melena	223	72.2%
Hematochezia	25	8.1%
Mental status change	25	8.1%
Syncope	45	14.6%

Conclusion: AIMS65 is a good score for patients with upper gastrointestinal bleeding, especially in predicting inpatient and delayed mortality, selecting high-risk patients and the ones who need intervention, similar to what has been reported with the Glasgow-Blatchford and the Rockall score, but more applicable to daily practice.
Disclosure of Interest: None declared

P1089 COMPLICATIONS OF FOREGUT POLYPECTOMY: A PROSPECTIVE, LONGITUDINAL AND MULTICENTER STUDY

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Introduction: Gastric and duodenal polypectomy is a common technique but there is little information about potential complications. However, an increased risk of bleeding has been reported in retrospective series with small number of patients.
Aims & Methods: To prospectively evaluate the complications that occurred during consecutive gastric and duodenal polypectomies.
This is a multicenter, longitudinal and prospective study of all patients undergoing polypectomy of gastric or duodenal polyps ≥ 5 mm using a polypectomy snare. Patients with PT $< 50\%$ and platelets $< 50{,}000$ or clopidogrel in the 7 days prior to the polypectomy were excluded. Prophylactic measures of hemorrhage were allowed in certain predefined cases. Intraprocedural hemorrhage was defined as bleeding that lasts more than 30 seconds and severity was graded from 1 to 4. Late hemorrhage was defined as melena or hematochezia since discharge from endoscopy unit and up to 30 days. Patients were followed during 30 days with serial phone calls. Predictive factors of complications were analyzed.
Results: 310 patients were included. The indications for gastroscopy were iron deficiency anemia in 94 (30.3%), gastric polyps control in 73 (23.5%), dyspepsia/GERD in 49 (15.8%), GI bleeding in 35 (11.3%), dysphagia in 6 (1.9%), pernicious anemia in 6 (1.9%) and others in 46 (14.8%). A total of 287 (92.6%) polyps were located in the stomach and 23 (7.4%) polyps in the duodenum. Most lesions were polypoid (46.1% 0-Ip and 40.1% Is). Histopathological diagnosis was: 215 hyperplastic polyps (69.4%), 39 adenomas (12.6%), 23 fundic gland polyps (7.4%), and others 33 (10.6%). A total of 113 patients (36.5%) had antiplatelet/anticoagulant regimen. The mean size of polyps was 14.8 ± 8.7 mm and 69% were hyperplastic. We found 46 complications in 45 patients (14.5%): hemorrhage (n = 33, 73.3%), abdominal pain (n = 10, 22.2%), perforation (n = 1, 2.2%), aspiration pneumonitis (n = 1, 2.2%), respiratory depression (n = 1, 2.2%). Most complications occurred during the procedure (n = 29, 64.4%). The severity of intraprocedural hemorrhage was grade 1 in 48.1%, grade 3 in 48.1 % and grade 4 in 3.7%. In 23 patients (69.7%) hemorrhage ocurred despite the use of prophylactic measures and in all cases hemostasis was achieved (15 with endoscopic treatment and 8 spontaneously). The only factor associated with bleeding was the type of polyp (hyperplastic 18/33 vs other types 197/277, $p < 0.04$).
Conclusion: The incidence of foregut polypectomy complications is higher than reported in the colon. Hyperplastic polyps are at increased risk of bleeding and prophylactic measures do not reduce the risk.
Disclosure of Interest: None declared

P1090 AIMS65 SCORE IS A USEFUL PREDICTOR OF MORTALITY IN PATIENTS WITH NONVARICEAL UPPER GASTROINTESTINAL BLEEDING: URGENT ENDOSCOPY IN PATIENTS WITH HIGH AIMS65

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Introduction: To validate the AIMS65 score for predicting mortality of patients with nonvariceal upper gastrointestinal bleeding and to evaluate the effectiveness of urgent (<8 h) endoscopic procedures in patients with high AIMS65 scores.
Aims & Methods: This was a 5-year single center, retrospective study. Nonvariceal, upper gastrointestinal bleeding was assessed using the AIM65 and Rockall scores. Scores were assessed under the receiver-operating characteristic curve (AUROC) for mortality. Patients with high AIMS65 scores (≥ 2) were allocated to either the urgent or non-urgent endoscopic procedure group. In-hospital mortality, success of endoscopic procedure, recurrence of bleeding, admission period and dose of transfusion were compared between the groups.
Results: A total of 634 patients were analyzed. The AIMS65 score successfully predicted mortality (AUROC = 0.943; 95% CI, 0.876-0.99) and was superior to the Rockall score (AUROC = 0.856, 95% CI, 0.743-0.969) in predicting mortality. The high AIMS65 scored group included 200 patients. The urgent endoscopic procedure group had reduced hospitalization periods ($P < 0.05$).
Conclusion: AIMS65 score may be useful in predicting mortality in nonvariceal upper gastrointestinal bleeding patients. Urgent endoscopic procedures in patients with high scores may be related to reduced hospitalization periods.

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Disclosure of Interest: None declared

P1091 URGENT BEDSIDE ENDOSCOPY FOR NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING IN INTENSIVE CARE UNITS

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Introduction: Urgent bedside esophagogastroduodenoscopy (EGD) for upper gastrointestinal bleeding (UGIB) in the intensive care unit (ICU) is essential for prompt identification and hemostasis of the source of hemorrhage. However, the clinical characteristics and outcomes of endoscopic hemostasis have not been well studied.
Aims & Methods: The aim of this study was to investigate clinical characteristics of hemorrhage and outcomes of endoscopic hemostasis in patients with nonvariceal UGIB (NVUGIB) after admission to the ICU.
A total of 62 ICU patients (ICU group) and 288 non-ICU patients (non-ICU group) with NVUGIB who underwent urgent EGD in Yonsei University Severance Hospital from January 2010 to April 2014 were included. We compared the demographics, clinical characteristics, technical success rate for endoscopic hemostasis, rate of rebleeding and mortality between two groups.
Results: The mean ages were 66.1 and 64.1 years (p = ns) and the number of comorbidities were 2.65 and 1.61 ($p < 0.05$) in ICU group and non-ICU group, respectively.
The most common initial clinical presentations were acute drop in hemoglobin level in ICU group (23/62, 37.1%) and melena in non-ICU group (180/288, 62.5%). ICU group presented higher blood urea nitrogen level (47.1 vs. 35.4 mg/dL), lower serum albumin level (2.5 vs. 3.2 g/dL), and higher Rockall score (7.01 vs. 5.37) with statistical significance.
The most common endoscopic finding was gastric ulcer with oozing hemorrhage (Forrest Ib) in both groups and initial technical success rates for endoscopic hemostasis were similar (91.5% vs. 94.6%, p = ns).
However, ICU group was significantly associated with higher 7-day rebleeding rate (37.1% vs. 10.4%, $p < 0.05$), shorter mean interval for rebleeding (1.4 vs. 3.4 days, $p < 0.05$), higher 30-day mortality rate (54.8% vs. 2.1%, $p < 0.05$), and higher bleeding-related mortality rate (16.1% vs. 1.4%, $p < 0.05$).
Conclusion: Despite similar technical success rate of endoscopic hemostasis, recurrent bleeding rate and bleeding-related mortality rate were significantly higher and interval for rebleeding was shorter in ICU patients. To reduce rebleeding rate and bleeding-related mortality rate, close monitoring and preemptive second-look endoscopic surveillance within 24 hours may be beneficial in the ICU setting.
Disclosure of Interest: None declared

P1092 THE MANCHESTER TRIAGE SYSTEM (MTS): A SCORE FOR EMERGENCY MANAGEMENT OF PATIENTS WITH ACUTE GASTROINTESTINAL BLEEDING

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Introduction: Suspicion of gastrointestinal bleeding (GIBLEED) is a prevalent diagnosis in emergency departments. Despite existing gastroenterological and endoscopic scores to estimate the risk of GIBLEED, the primary clinical assessment remains challenging for both, emergency doctors and interventional gastroenterologists. The five step Manchester Triage System (MTS) is an easy to use and validated score that is often applied for the initial assessment of patient in emergency rooms (ER). The MTS classifies patients into five priority levels, ranging from level 1 (emergency, should receive immediate medical attention) to levels 2-5, corresponding to a suggested medical evaluation within 10, 30, 60, and 120 minutes, respectively. The MTS was established to manage clinical risk of administrating medical attention. The aim of our retrospective analyse was, to determine if the MTS correlates with presence of a GIBLEED.
Aims & Methods: All patients who were admitted between January 2014 and December 2014 to our emergency department in a maximum care hospital (HSK Clinic Wiesbaden) were retrospectively analyzed. All relevant computer-based clinical patient records that included MTS priority levels were evaluated and associated with endoscopic findings.
Results: In summary 5689 gastroenterologic emergencies were treated at our emergency room. 284 patients (4.9%) (Mean age 64.3 years) were under suspicion of having GIBLEED. 47.5% of these patients were introduced to the emergency service. among these, 162 patients (57.04%) were admitted for immediate treatment. 160 patients (56.3%) received endoscopic diagnostic. 33.1% of patients who were transferred to the endoscopy by the emergency service team showed a confirmed endoscopic diagnosis of GIBLEED, compared to 49.1% who were self-referring to the ER ($p = 0.007$). Endoscopic intervention for hemostasis was needed in 22 patients (13.8%). The success rate of hemostasis was 96.6%. While 61.2% of all patients assigned to MTS levels 1, 2, and 3 received endoscopy, endoscopy rates in patients of levels 4 and 5 were only 26.3% ($p < 0.01$). Gastrointestinal bleeding was endoscopically confirmed in 40% of patients with level 1 to 2, 34% in level 3 and 5.3% level 4 to 5, which shows a significant correlation of MTS score and GIBLEED ($p = 0.043$, χ^2 test).
Conclusion: The MTS is an appropriate way to estimate the likelihood of GIBLEED for patients presenting in emergency departments. Patients at levels 1-3 should receive immediate endoscopic work up. Elective endoscopy can be performed in patients classified with levels 4-5.
Disclosure of Interest: None declared

P1093 THE USE OF CAPSULE ENDOSCOPY IN TRIAGING PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING: A RANDOMISED STUDY

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Introduction: Patients presented to hospitals with coffee ground vomiting or black-color stool may not be actually suffering from active upper gastrointestinal bleeding (UGIB). Hospital admission can be avoided if active UGIB or high-risk lesions are excluded at the emergency room (ER).
Aims & Methods: This is a prospective randomized study comparing the use of capsule endoscopy as a triage tool versus standard care in the management of UGIB at the ER of an acute hospital. Patients presented to the ER at an acute hospital with symptoms suggestive of UGIB were recruited into this study. Vital signs (blood pressure, pulse, conscious state), complete blood count and serum chemistry were monitored at the ER. Patients who were not in hemodynamic shock, coma or actively vomiting blood were randomized to receive either capsule endoscopy (CE) by using PILLCam ESO (GIVEN) or (ST) standard care of hospitalization and early endoscopy within 24 hours. Patients in the CE group with capsule video showing clean stomach (no fresh blood or coffee ground) and no signs of active bleeding or high-risk lesions were discharged home and followed by out-patient endoscopy within 3 days. CE patients showing the following signs : 1. >5 ml coffee ground or fresh blood in stomach; 2. active oozing or spurting blood from upper gastrointestinal tract; 3. visible vessel or blood clot at ulcer base; 4. esophageal or gastric varices with red wale sign or fibrin clot, would be admitted for endoscopy within 24 hours. Patients in the ST group were admitted to hospital for resuscitation, observation and endoscopy within 24 hours.
Results: 71 patients were recruited and randomized to CE ($n = 37$) or ST ($n = 34$). Three patients in CE group were excluded because of known history of variceal bleeding (1x), retained capsule in esophagus (1x) and fever which precluded early endoscopy (1x). There were 34 patients in both CE and ST groups for analysis. The basic demography, blood pressure and pulse rate, baseline blood count and chemistry of the CE and ST groups were comparable. 7 patients in CE group were considered high-risk and hence required admission, whereas all 34 in ST group were admitted. Among the 7 CE patients (20.6%) admitted, 3 were confirmed to have high-risk lesions or active bleeding (GV/EV 1x; GIST with coffee ground 1x; GU with fresh blood 1x). None of the 27 CE patients discharged home were subsequently found to have active bleeding, except one found to have GU with visible vessel. None of the patients in both CE and ST group had early recurrent bleeding or died.
Conclusion: Capsule endoscopy can select most of the high-risk patient presenting with coffee group vomiting or melena for hospital admission and urgent endoscopy. Capsule endoscopy is a feasible and safe triage method in the management of UGIB.
Disclosure of Interest: None declared

P1094 CHRONIC ANAEMIA DUE TO GASTROINTESTINAL BLEEDING, WHEN DO GASTROENTEROLOGISTS TRANSFUSE? A NATIONWIDE SURVEY IN THE NETHERLANDS

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Introduction: Transfusion strategies have become more restricted over the past decade. Most guidelines state that in patients with chronic anaemia, symptoms are the most essential trigger to transfuse. This might differ for acute gastrointestinal bleeding, where prophylactic transfusions might be necessary at an earlier stage. Our hypothesis is that decision-making for transfusion among gastroenterologists varies considerably.
Aims & Methods: Our aim was to identify preferences and predictors of transfusion decision-making in chronic anaemia due to gastrointestinal bleeding.
To achieve this aim, a computerized adaptive choice-based conjoint survey was administered between February and April of 2015 to gastroenterologists in the Netherlands. The survey quantified the relative importance of 7 patient attributes, including haemoglobin levels, haemoglobin stability, age, iron indices, the presence of anaemia related symptoms, cardiovascular comorbidities and the number of transfusions in the past half year. Triggers of transfusion were studied in a scenario of chronic anaemia due to bleeding from angiodysplasias.
Results: A total of 112 gastroenterologists completed the survey (response rate = 28%; mean age = 47 years; 24% women). Of 7 attributes assessed, absolute haemoglobin level was the most important incentive of transfusions, accounting for 42% of decision-making, followed by age (15%), haemoglobin stability (12%), anaemia related symptoms (10%), cardiovascular comorbidities (10%), the number of transfusions in the past half year (6%) and iron indices (5%). An inflection point was found at a haemoglobin level of 8.0 g/dL, above this value gastroenterologists would not prescribe a transfusion. The average part-worth utilities for the different haemoglobin levels (>9.5 g/dL, 8.0-9.5 g/dL, 6.4-7.9 g/dL, <6.4 g/dL) were respectively -161 (SD 23), -27 (SD 19), 55 (SD 20), and 133 (SD 23).
Conclusion: Independent of all other factors, absolute haemoglobin level was found as the most important clinical factor to transfusion decision-making. In contrast, the presence of anaemia related symptoms and iron indices was of relatively little importance. This contradicts the current Dutch transfusion guideline.
Disclosure of Interest: None declared

P1095 DIAGNOSIS OF CHRONIC ATROPHIC GASTRITIS IN PRIMARY CARE SETTING BY MEANS OF GASTROPANEL®: A POPULATION STUDY ON 10,000 CONSECUTIVE PATIENTS

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Introduction: Chronic atrophic gastritis (CAG) is a stomach precancerous condition, often related to *Helicobacter pylori* (*H.p.*) infection. This condition is characterized by hypo- or achloridria due to loss of appropriate gastric glands. Gastropanel® is a non-invasive test able to detect both CAG and *H.p.* infection. This test, which provides information on both morphological and functional status of the gastric mucosa, is often referred to as "serological biopsy".
Aims & Methods
Aim: The aim of the present study is to investigate, by means of Gastropanel®, the prevalence of CAG in a large primary care population.
Subjects and Methods: Ten thousand dyspeptic patients, from two different areas of North-East of Italy, were enrolled. The first one (Group A) included 7,400 patients (M:F = 1.2:2.0 mean age 53 years) from 2003 to 2014 while the second one (Group B) involved 2,600 patients (M:F = 1.5:2.3, mean age 56 years) from 2011 to 2013. Upper GI endoscopy with biopsies sampling, evaluated histologically according to the Sydney classification and the O.L.G.A. staging system, as well as Gastropanel® (Biohit Oyj, Helsinki, Finland) were performed in every patient.
Serological diagnosis of CAG was made when PGI serum levels were < 25 microg/L and G-17 concentrations > 14 pmol/L. Histological diagnosis of CAG followed the criteria of *both* Sydney system and O.L.G.A. staging.
Results: Overall, CAG was diagnosed by serology in 716 out of 10,000 patients. In Group A population, 608 patients (mean age 57 years old) has a CAG, 2,492 (mean age 54) a non-atrophic gastritis related with *H.p.* infection was performed

while 879 patients (mean age 44 years) presented with a normal gastric morpho-functional assessment. In Group B population, CAG was found in 108 patients (mean age 58 years) and *H.p.*-related gastritis in 643 (mean age 59) while a normal pattern was detected in 721 patients (mean age 47).
Conclusion: Overall, in a primary care setting, a picture of CAG was found in 7.2% of patients. The prevalence was higher in Group A than in Group B (8.2% and 4.2%, respectively) for unknown reasons. The mean age of subjects with CAG was higher than that of patients with NAG *H.p*-related and normal population in both areas.
These findings suggest that CAG is more prevalent than previously thought and confirm that Gastropanel® is an effective non invasive tool for the screening of this precancerous condition.
Disclosure of Interest: None declared

P1096 ESTABLISHING A PROMPT ENDOSCOPY PROGRAMME FOR PATIENTS WITH DYSPEPSIA AND ALARM FEATURES REDUCES THE NUMBER OF SECONDARY CARE CONSULTATIONS

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Introduction: Dyspepsia is commonly encountered by primary care providers (PCP) and motives a significant number of endoscopies and secondary care consultations. A guideline issued by both the Spanish Society of Gastroenterology and the Spanish Society of Primary Care recommends prompt endoscopy in subjects with alarm features (anaemia, weight loss, dysphagia, gastrointestinal bleeding or abdominal findings) or appearance of symptoms after 55 years of age. We present the development of a prompt endoscopy programme (PEP) for dyspepsia with alarm features in primary care.
Aims & Methods: In June 2013 a PEP for patients with dyspepsia and alarm features was created with the cooperation of a primary care clinic (PCC) attending 36577 people, with a median of 58 monthly new gastroenterological secondary care consultations. After data analysis in August 2014, the programme was made available to all PCCs related to our hospital, which attends roughly 225000 people.
Demographic, clinical, endoscopic and histological data were prospectively retrieved, as well as secondary care consultations after endoscopy. A satisfaction survey was undertaken in the PCC participating in the pilot programme. Proper indication of prompt endoscopy was defined in the presence of at least one red flag or age >55. Significant findings were defined as cancer, ulcers or severe esophagitis.
Results: In the pilot study 113 patients were included with a median age of 57.4 (IQR: 45.9-64.1), 61.1% of them were women. Symptoms had been present for a median 4.5 months (2.5-12.5). 84.2% (95% CI: 75.8-92.6%) of endoscopies had been properly indicated. Monthly secondary care consultations from the PCC during the pilot study period compared with previous years were reduced in 10.5 patients (5.6-15.5).
Including all subjects attended, a total of 296 patients have undergone endoscopy with a median age of 56.3 (45.4-64.4), 61.5% were women. Proper indications were made in 81.8% (77.3-86.2%) of patients. Most common alarm features were: age over 55 (55.7%), weight loss (25.5%) and anaemia (20.8%). 38.9% presented 2 or more red flags. Upper epigastric pain (72.8%) was the most common symptom, but 50% also fulfilled criteria of gastroesophageal reflux disease, which was more frequent than bloating (40.9%) and early satiety (31.6%).
Significant findings were encountered in 14.5% (11-19%); gastroesophageal cancer in 1% (3 gastric cancers), peptic ulcers in 11.1% and severe esophagitis in 2.7%. Other cancers were found during a 2 months follow-up in 1% (colon adenocarcinoma, metastatic cancer of unknown origin and multiple myeloma). *H pylori* was diagnosed in 38.9% and a normal endoscopic appearance was present in 30.5%. The positive and negative predictive values of alarm features were 17.4% (12.8-22.7%) and 98.1% (90.1-100%) respectively 17.6% of patients were submitted to the gastroenterology out-patient clinic.
The satisfaction survey was completed by 24 PCP. All of them considered the PEP useful for their daily practice, although only 66.7% had used it. Most non users (87.5%) referred having met no patients with alarm features.
Conclusion: Availability of prompt endoscopy for dyspepsia with alarm features is considered a valuable asset by PCP and reduces the number of secondary care consultations.
Disclosure of Interest: None declared

P1097 PREVALENCE AND SOCIO-DEMOGRAPHIC DETERMINANTS OF UNINVESTIGATED DYSPEPSIA IN THE CZECH REPUBLIC

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Introduction: Epidemiology of uninvestigated dyspepsia was studied in the Czech Republic for the first time in 2001 (1). The aim this current multicentre prospective study was to evaluate dyspepsia using the same methods in a representative sample of general unselected population from the same geographical areas 10 years later.
Aims & Methods: A total of 22 centres entered the study. They were spread over the whole country, corresponding well to the geographical distribution of the Czech population. A total of 1,836 subjects (863 males and 973 females; aged 5-98 years) took part in the study and responded to the question on prevalence of dyspepsia. Complete data on variables used in our analysis was available for 1,685 subjects. The proportion of subjects reporting dyspepsia did not differ significantly between the restricted sample and the group excluded from multivariable analyses. Helicobacter pylori (Hp) status was investigated in all subject by means of 13C-urea breath test.
Results: In subjects aged 5-24 years, when we analyzed determinants of dyspepsia by type (subgroup A: dyspepsia as the only long-lasting symptom vs. subgroup B: dyspepsia as a part of the complex of other complaints or previously recognized diseases), we noted somewhat stronger increase in risk of dyspepsia A with age (OR 1.15 per 1 year of age, 95% CI 1.05-1.26, adjusted for gender) and with current use of antibiotics (OR 3.23 in users vs. non-users, 95% CI 0.87-11.9). In subjects aged 25+ years, when analyzed by type of dyspepsia, a statistically significant negative association of age with dyspepsia of type A became apparent (OR 0.95 per 1 year of age, 95% CI 0.94-0.97) while the association between age and dyspepsia type B was also statistically significant albeit positive (OR 1.02 per 1 year of age, 95% CI 1.01, 1.04). Furthermore, subjects who were single were at lower risk of dyspepsia type B (OR 0.46 in single vs. married, 95% CI 0.21-0.99, adjusted for age and gender). The unexpected protective effect of elementary education appeared also to be stronger for dyspepsia type B (OR for elementary vs. university educated 0.25, 95% CI 0.07-0.86, adjusted for age and gender). Hp negative subjects reported dyspepsia in 4.1% (aged 5-24 years) and 18.1 % (aged 25+ years). In Hp positive subjects, dyspepsia was present in 7.1% (aged 5-24 years; OR 1.45, 95% CI 0.41, 5.16) and 16.3% (aged 25+ years; OR 0.85, 95% CI 0.60, 1.21, adjusted for gender and age).
Conclusion: Despite the substantial decrease of Hp infection in the Czech Republic over the past 10 years, the prevalence and basic socio-demographic determinants of uninvestigated dyspepsia did not change significantly.

Reference

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P1098 IN VITRO EFFECT OF LEVOSULPIRIDE ON THE MAIN CONTRACTILITY PATTERNS IN THE HUMAN JEJUNUM, GASTRIC ANTRUM AND FUNDUS

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Introduction: To assess the effect of drugs currently in use to ameliorate symptoms of functional dyspepsia and gastroparesis in human tissue it is important to evaluate their mechanism of action on isolated human samples. Therefore, the aim of the present study was to evaluate the effect of the prokinetic drug levosulpiride on the main in vitro contractility patterns of the human stomach and jejunum.
Aims & Methods: Circular muscle strips from stomach (antrum and fundus) and jejunum from patients undergoing bariatric surgery were studied using organ baths to evaluate: the effect of levosulpiride on the spontaneous contractility and on electrical field stimulation (EFS)-induced release of neurotransmitters from enteric motor neurons.
Results: Levosulpiride, a $5HT_4$ agonist/D_2 antagonist, caused an increase in the EFS-induced cholinergic contractions, in the gastric antrum ($37 \pm 15.18\%$ of increase at $100\mu M$, $pEC_{50} = 4.46 \pm 0.14$; $p < 0.05$, $n = 8$) and jejunum ($45.4 \pm 22.03\%$ of increase at $100\mu M$, $pEC_{50} = 3.78 \pm 6.81$; $p < 0.05$ $n = 5$), whereas it did not cause a significant increase in the gastric fundus. It also caused a slight tone decrease and frequency of the spontaneous contractions increase in the jejunum whereas it did not have any major effect on the spontaneous contractility in the stomach. It did not have any effect on EFS-induced relaxations caused mainly by nitric oxide (NO) in the stomach (antrum and fundus) and by NO and ATP in the jejunum.
Conclusion: Our results suggest that the prokinetic effects of levosulpiride are mainly due to facilitating the release of acetylcholine by enteric motor neurons in the gastric antrum and the jejunum.
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P1099 AN HERBAL MEDICINE FOR THE SYMPTOMATIC RELIEF OF MILD GASTROINTESTINAL DISCOMFORT, ALTHAEA ROOT EXTRACT, HAS PROTECTIVE EFFECTS ON HUMAN MUCOSA CELLS

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Introduction: The use of herbal medicinal products in gastrointestinal complaints is very common in Europe. To these belongs the extract of the root of the herb *Althea officinalis* L. (marshmallow root), which is traditionally used "for the symptomatic relief of mild gastrointestinal discomfort", an indication which has been confirmed by the European drug regulatory agency EMA [1], besides its more common use in the treatment of pharyngeal irritation and associated dry cough. As this use has been often rated as being merely symptomatic [1], a study has been conducted with the aim to identify mechanisms of action which point to an active, causal therapeutic effect in mucosal cells, beside its well-characterized protective physical effect [2].

Aims & Methods: Therefore the mechanisms of action of a well defined extract of Althea officinalis roots, STW 42, and of polysaccharides from the extract (RPS) were tested in a human mucosal cell line (KB-cells, origin: nasopharynx), and for comparison purposes, a human fibroblast cell line [3, 4].

Results: In KB-cells, RPS (1-10 µg/mL) significantly increased cell vitality, measured as reduction of the tetrazolium salt WST-1, in contrast, STW 42 had no significant effect at that time. Cellular proliferation, measured by ELISA in the BrdU-Test was significantly stimulated by STW 42 (10 µg/L), while RPS had this effect only at 100 µg/mL. RPS, labelled by fluorescein 5-isothiocyanat (FITC), was internalised by KB-cells, not fibroblasts, after incubation for 14 h.

Conclusion: According to these results, STW 42 may have an active influence on mucosal cells and fibroblasts. *Althaea* polysaccharides can even be internalised by mucosal cells. This points to a not merely demulcent, but actively protective effect on the mucosa. By stimulating mucosal regeneration, it potentially could even have a causal therapeutic effect in mucosal disturbances.

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P1100 STRUCTURAL CHANGES OF ENTERIC GLIAL CELLS AND MOTILITY DISORDERS OF THE STOMACH AS RESPONSES TO EARLY LIFE STRESS (MATERNAL SEPARATION) AND ACUTE STRESS IN ADULTHOOD IN RATS

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Introduction: Enteric glial cells (EGCs) play an important role in physiological neurotransmission. However, its regulatory mechanism(s) under various stresses (mental, physical, acute, and/or chronic) remains to be elucidated. We investigated changes in mRNA expression and structural changes in gastric EGCs in the time course of the stress intensity in a maternal separation (MS) model, a model of early life stress affecting central glial cells.

Aims & Methods: Male Wistar rat pups underwent MS for 3 hours starting on postnatal days 2-14. At 8 weeks of age, we used the water immersion method as an acute stress (AS) model and excised the whole stomach at 24 hours later. For the AS, MS, MS + AS, and control groups, we evaluated mRNA expressions of glial fibrillary acid protein (GFAP) using real time RT-RCR. Whole mount longitudinal muscle-myenteric plexus preparations were used for immunohistochemistry of EGCs (GFAP) with pan neuronal marker (HuC/D). We evaluated gastric emptying time using the phenol red method.

Results: GFAP mRNA expression was increased by 2-fold at 1 hour after AS compared to the controls ($p < 0.05$). However, in the MS + AS group, AS did not affect GFAP mRNA expression. The two-dimensional area with apparent overlap of these EGC processes with the neurons was expressed as a percentage of the area encompassing the HuC/D-positive neurons. The area ratio significantly increased according to the stress intensity (10.2%, acute stress; 10.0%, maternal separation; 26.4%, maternal separation with acute stress vs. 5.1%, control). The density of GFAP-positive EGC processes that apparently overlapped with the neurons and the extent of bulbous swelling of terminals increased according to the stress intensity. Two types of glial processes were observed: filamentous (no obvious neck or bulbous terminal swelling) and leaf-like (a neck region with a bulbous terminal swelling). Mean ratio of leaf-like processes to total processes per ganglion was 4% in the control group, which was increased to 17% by AS for 8 hours. The mean ratio was 13% in the MS group, and began to increase from 1 hour in a time dependent manner in the MS + AS group and reached up to 25% at 8 hours. In the MS group, gastric emptying was significantly delayed compared with those in control group in addition to aging. At 17 weeks, MS with AS induced the significant delay in gastric emptying.

Conclusion: Maternal separation with additional acute stress in adulthood caused structural changes in gastric EGCs, which may be critically important for glio-neural dysfunction of functional gastrointestinal diseases.

Disclosure of Interest: None declared

P1101 FUNCTIONAL DYSPEPSIA IS SUSCEPTIBLE TO CD14, GNB3, TRPV1 -BUT NOT MIF- GENE POLYMORPHISMS IN A WESTERN POPULATION

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Introduction: Functional dyspepsia (FD) might be susceptible to gene polymorphisms related to inflammation (CD14, MIF), motor (GNB3) and sensory dysfunction (TRPV1). Association studies have shown diverse results among different populations. Herein, we present the final results of our association study in a Western population; preliminary results were presented at UEGW 2012[1].

Aims & Methods: We aimed to examine the association between CD14, GNB3, MIF and TRPV1 gene polymorphisms and FD (Rome III criteria). We studied gene polymorphisms using polymerase chain reaction-based methods and we measured disease symptoms burden with a modified GSRS scale.

Results: We studied 100 dyspeptic (62 with epigastric pain syndrome; 41% *H. pylori* positive) and 119 healthy individuals. The frequencies of the TT genotype and T allele of the CD14 polymorphism were significantly associated (OR [95%CI], p) with FD (2.4 [1.16-5.01], 0.02 and 1.55 [1.05-2.28], p = 0.03, respectively). TT genotype and T allele frequencies of GNB3 showed also significant association with FD (4.73 [1.25-17.83], 0.02 and 2.14 [1.27-3.61], 0.006, respectively). While the distribution of GG, GC and CC MIF gene genotypes was similar between controls and FD patients, GC TRPV1 genotype and C TRPV1 allele were more common in controls (p = 0.06) and in FD patients (p = 0.07), respectively. Among dyspeptics, CD14 TT genotype was related to significantly lower epigastric pain burden score compared to the CC and CT genotypes (3.72 ± 0.18 vs. 4.36 ± 0.11 and 4.17 ± 0.12, p = 0.012). Similarly, the presence of CD14 T allele was related to lower epigastric pain burden score compared to the C allele (3.98 ± 0.1 vs. 4.36 ± 0.11, p = 0.012).

Conclusion: FD is susceptible to CD14, GNB3 and TRPV1 gene polymorphisms while CD14 gene polymorphisms are also associated with epigastric pain burden in our Western population.

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P1102 ASPARTIC ACID IS EFFECTIVE FOR EARLY SATIETY (FUNCTIONAL DYSPEPSIA): EFFECTS OF AMINO ACIDS ON THE GASTRIC EMPTYING EVALUATED BY BREATH TEST AND THE GASTRIC ADAPTIVE RELAXATION EVALUATED BY BAROSTAT IN RATS

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Introduction: Amino acid has been reported to have many physiological functions. Glutamic acid enhances contraction of the antrum and tryptophan inhibits gastric emptying. However, the effects of the other amino acid have not been clarified on the gastric function. On the other hand, Sanaka *et al.* (*Dig Dis Sci.* 2010) reported that PPI therapy enhanced the gastric adaptive relaxation and inhibited the gastric emptying, suggesting the relationship between gastric adaptive relaxation and gastric emptying. In addition, it has been known that gastric emptying and gastric adaptive relaxation closely relate to functional dyspepsia.

Aims & Methods: In the present study we evaluated 20 amino acids on the gastric emptying and gastric accommodation to find useful amino acid for the therapy of functional dyspepsia. Male SD strain rats were used after one night fasting. *Breath test:* Gastric emptying was evaluated by breath test (Uchida *et al., J Pharmcol Sci.* 2005). After the oral administration of liquid test meal containing [1-^{13}C]acetic acid, rats were placed in the chamber. The expired air was collected at 5-min intervals until 70 min after the test meal administration, with additional measurements at 90 and 120 min. The $^{13}CO_2$ levels in the expired air were measured by placing the breath-sampling bags into the sample joint of the UBiT-IR300 infrared analyzer. Gastric emptying was evaluated by the change of expired $^{13}CO_2$, Cmax, Tmax and AUC120min. Amino acids were administered orally 30 min before test meal administration. *Barostat study:* Gastric accommodation was evaluated by barostat. Balloon was introduced into the stomach through the mouth of anesthetized rats without the need for balloon surgery (Uchida and Shimizu, *J Smooth Muscle Res.* 2012). The balloon volume increased gradually just after an increment in the balloon pressure (1 to 8

mmHg), and reached a plateau within 1 min. This increased volume just after the increment of the balloon pressure was defined as adaptive relaxation. Amino acids were administered orally 30 min before barostat study.
Results: There were no amino acids enhancing the gastric emptying. Tryptophan significantly delayed the gastric emptying as compared with control and significant enhanced the gastric accommodation. Many amino acids inhibited gastric emptying and enhanced gastric adaptive relaxation. Significant positive correlation was observed between gastric emptying (Tmax) and gastric accommodation. Above findings show that amino acids delaying gastric emptying enhance the gastric accommodation. Only aspartic acid significantly enhanced the gastric adaptive relaxation, but did not influence the gastric emptying.
Conclusion: Functional dyspepsia is divided into postprandial distress syndromes and epigastric pain syndromes. Early satiety is one of the postprandial distress syndromes. This disease is supposed to be caused by the dysfunction of gastric adaptive relaxation. In this study, we found that aspartic acid significantly enhanced the gastric adaptive relaxation, but did not influence the gastric emptying. Therefore, aspartic acid may become useful material for the therapy of early satiety.
Disclosure of Interest: None declared

P1103 THE HERBAL PREPARATION, STW 5, PRESERVES GASTRIC FUNCTIONAL ACTIVITY IN A NOVEL SEQUENTIAL STRESS MODEL FOR FUNCTIONAL DYSPEPSIA

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Introduction: One of the main gastric disorders encountered in functional dyspepsia (FD) is a delay in gastric emptying and changes in gastric functional activity. The present study was designed to observe whether the established efficacy of the multi-component herbal preparation STW5 in FD[1-4] could owe its beneficial effects at least in part to preservation of gastric emptying and other parameters of gastric function. STW5 consists of standardized extracts of *Iberis amara, Melissa officinalis, Matricaria recutita, Carum carvi, Mentha piperita, Angelica archangelica, Silybum marianum, Chelidonium majus, and Glycyrrhiza glabra*. A novel stress model for FD has been devised to resemble the clinical situation where FD has been attributed to emotional stress in early life, followed by further exposure to stress in adulthood[5].
Aims & Methods: Weanling rats were separated from the mother cage for 3 hours/ day until day 21 from birth. After reaching adulthood 4 weeks later, they were restrained for 90 min / day for 1 week. During these sessions animals were given STW 5 orally in daily doses of 2 and 5 ml/Kg. One day after the last session, the gastric emptying time of the animals was determined using a phenol red meal. In a separate group of rats, blood samples were taken for assaying the stress hormones corticosterone and corticosterone releasing factor. Fundus strips were removed after sacrifice to test their sensitivity ex-vivo towards carbachol, serotonin, adrenaline and potassium chloride. Furthermore, duodenal homogenates were examined for expression of CSE, RelA, Nrf-2 and the tight junction proteins ZO-1 and occludin using qPCR.
Results: Rats subjected to the sequential stress procedure showed marked delay in gastric emptying, an effect which was counteracted dose dependently by STW5. Sensitivity of the fundus ex-vivo to the tested agents was markedly depressed by stress, but tended to be normalized after treatment with STW5. The stress hormone levels were elevated by the model but tended to be normalized by the herbal preparation. The expression of Nrf-2 and ZO-1 was reduced but that of occludin was raised by the model but normalized after treatment.
Conclusion: The results contribute to our understanding of the beneficial properties of STW 5 in FD. Thus the disturbance in gastric function often observed in patients with FD could be effectively prevented by the herbal preparation, STW5.

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P1104 ALDIOXA IMPROVES BOTH OF DELAYED GASTRIC EMPTYING AND IMPAIRED GASTRIC ACCOMMODATION, WHICH ARE PATHOPHYSIOLOGIC MECHANISM OF FUNCTIONAL DYSPEPSIA

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Introduction: Functional dyspepsia (FD) is a highly prevalent gastric functional disease defined as persistent or recurrent gastric discomfort and epigastric pain without underlying organic causes, in which delayed gastric emptying and impaired gastric accommodation play important roles. Although FD markedly reduces the patient's quality of life, its therapeutic protocol, including pharmacotherapy, has not been established.
Aims & Methods: In order to find candidate drugs for FD by drug repositioning strategy, we here screened compounds that could improve delayed gastric emptying from a library of medicines already in clinical use. Gastric emptying in mice was assessed by the phenol red method or the [^{13}C]-labeled acetic acid breath test. The intracellular cAMP level was determined by ELISA. Membrane fractions prepared from Chinese hamster ovary (CHO)-K1 cells expressing human α-2 adrenergic receptor and [^{3}H]-clonidine were used in filter-binding assay. Gastric accommodation in rats was examined using a barostat apparatus.
Results: Aldioxa (dihydroxyaluminium allantoinate) is a medicine used clinically to treat gastric ulcers and gastritis. Oral administration of aldioxa improved clonidine (α-2 adrenergic receptor agonist)-induced delayed gastric emptying. The dose of aldioxa required to suppress delayed gastric emptying was much lower than that required to suppress indomethacin-induced gastric lesions in mice. Other gastroprotective drugs (geranylgeranylacetone and sucralfate) had no effect on delayed gastric emptying. Aldioxa also suppressed the delayed gastric emptying induced by restraint stress, but did not affect the basal level of gastric emptying in intact mice. Administration of allantoin, but not aluminium hydroxide, restored the gastric emptying. Treatment of cells with clonidine decreases intracellular cAMP levels, which could be suppressed by the simultaneous treatment with aldioxa or allantoin. Both aldioxa and allantoin inhibited clonidine binding to the α-2 adrenergic receptor. We also found that aldioxa or aluminium hydroxide but not allantoin restored gastric accommodation in rats subjected to wrap restraint stress.
Conclusion: Results suggest that the oral administration of aldioxa restores gastric emptying activity via its antagonistic activity on the α-2 adrenergic receptor, with the allantoin moiety of this drug is involved in this restoration. The results also suggest that the aluminium hydroxide moiety of aldioxa is involved in the improvement of impaired gastric accommodation. We propose that aldioxa is a candidate drug for FD, because its safety in humans has already been confirmed clinically and its ameliorating effect on both of delayed gastric emptying and impaired gastric accommodation are confirmed here.
Disclosure of Interest: None declared

P1105 RIFAXIMIN FOR THE TREATMENT OF FUNCTIONAL DYSPEPSIA: A DOUBLE-BLINDED RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Introduction: Evidence suggests that gut dysbiosis may be partly causal in the genesis of pain and bloating in irritable bowel syndrome and treatment with the non-absorbable antibiotic rifaximin reduces these symptoms. Functional dyspepsia (FD), is another functional gastrointestinal disorder, where pain, bloating and belching can be particularly problematic. We evaluated a two-week course of rifaximin for the treatment of FD.
Aims & Methods: Consecutive subjects with a diagnosis of FD according to the ROME III criteria with a normal gastroscopy were recruited from two centres in Hong Kong. Subjects were randomized into two treatment arms, 400mg three times a day (TDS) of rifaximin or 400mg TDS of placebo. The investigators and study subjects were blinded to the allocation. Subjects were followed for 8 weeks in total. The primary end point of adequate relief of global IBS symptoms and the key secondary end points of adequate relief of bloating or belching, were assessed at week-2, week-4 and week-8. Lactulose hydrogen breath test was performed at baseline and at the end of the study.
Results: A total of 86 subjects were randomized to either rifaximin or placebo. Significantly more subjects in the rifaxmin than in the placebo group experienced adequate relief of global FD symptoms at the end of the study period, week 8 (76.5% vs. 52.6%, $P = 0.04$), with a strong trend in the preceding 6 weeks favouring rifaximin. Rifaximin was also superior to placebo in providing adequate relief of belching and bloating in subjects at week-4 however this improvement did not endure to week-8. Finally, a sub group analysis revealed that female subjects experienced earlier (79.2% vs. 40.6%, $P = 0.006$ at week 4) and more sustained improvements in their global dyspeptic symptoms (80.0% vs. 51.6%, $P = 0.048$ at week 8), as well as improvements in their belching and bloating at week-4. The oro-caecal transit time as measured by the lactulose hydrogen breath test was prolonged in subjects treated with rifaximin compared to baseline however there were no differences between subjects in terms of hydrogen production as measured by area under the curve calculations. The incidence of adverse effects were similar in both groups.
Conclusion: In subjects who met the ROME III criteria for FD, treatment with rifaximin led to adequate relief of global dyspeptic symptoms, belching and bloating. This was particularly marked in female FD subjects.
Disclosure of Interest: None declared

P1106 ACTIVATION OF DUODENAL BITTER TASTE RECEPTOR BY QUININE HYDROCHLORIDE EFFECTS ON INTRAGASTRIC PRESSURE PROFILES AND NUTRIENT TOLERANCE IN HEALTHY VOLUNTEERS

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Introduction: Bitter taste receptors are expressed in the stomach and the duodenum but their function is unclear. We previously reported inhibition of gastric accommodation and nutrient volume tolerance by intragastric administration of bitter tastants[1].
Aims & Methods: We assessed the effects of duodenal infusion of a potent bitter tastant, quinine hydrochloride (QHCl) on intragastric pressure (IGP, a measure of gastric accommodation), nutrient tolerance and satiation.
We conducted a single-blind cross-over trial in healthy volunteers (HVs) with intraduodenal administration (via a feeding catheter) of 10 μmol/kg QHCl or placebo 30 min before the experimental protocol started.
A high-resolution manometry (HRM) probe was placed via the nose till the duodenum in 12 HVs (age 27 ± 3; BMI 22 ± 1). A nutrient drink (ND; 30% fat, 42% carbohydrate, 28% protein) was intragastrically infused (60mL/min) until maximum satiation, when it was stopped. Satiation score was scored every minute on a 0-5 scale. Thereafter, IGP was measured for 2 hours after the meal. During the entire experiment, HVs were asked to their sensations of hunger, appetite and the epigastric symptoms (fullness, bloating, nausea, belching, cramps and pain), every 5 min on a 10-cm horizontal visual analogue scale (VAS).
IGP was measured as average pressure over 5 channels in the fundus at least 1 cm below the LES; 5 minutes before ND start was taken as baseline. All data are expressed as mean $\pm$ SEM. Outcomes of ND tolerance, total area above the curve (AAC) and max IGP drop during ND infusion, AAC of satiation score and VAS during both conditions were compared with a paired t-test.
Results: The intraduodenal administration of placebo or QHCL did not affect baseline IGP profile or symptoms. During the intragastric ND infusion, the IGP decreased initially and gradually increased thereafter in both conditions. QHCl administration failed to affect the max IGP drop (6.4 ± 0.6 mmHg for placebo vs 5.7 ± 0.7 mmHg for QHCl, ns), or the AAC (61 ± 11 mmHg*min for placebo vs 57 ± 12 mmHg*min for QHCl, ns) indicating a lack of an effect on gastric accommodation. Also the post-prandial IGP profile did not differ between both treatment arms. However, satiation scores after QHCl tended to be lower than in placebo (AUC 118 ± 6 ml vs. 107 ± 6 ml; $p = 0.09$) and the volume of ND ingested at maximum satiation was significantly higher after QHCl (835 ± 138 ml vs. 1031 ± 116 ml, $p = 0.05$).
Conclusion: In contrast to intragastric administration effects, intraduodenal administration of the bitter agonist QHCL did not affect gastric accommodation, but tended to inhibit meal-induced satiation and increased nutrient volume tolerance. The mechanism involved in this orexigenic action of intra-duodenal QHCL warrants further study.

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P1107 DOES AN IMPAIRMENT OF ANTIOXIDANT CAPACITY IN OBESE HUMAN GASTRIC ANTRUM CAUSE THE ALTERATION IN VASOACTIVE INTESTINAL PEPTIDE (VIP)- PATHWAY?

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Introduction: Genome-wide association analysis has identified a relation between obesity and the Vasoactive Intestinal Peptide (VIP) pathway. Obesity is characterized by systemic oxidative stress with an imbalance between the increase in reactive oxygen species (ROS) production and the decrease in cellular antioxidant capacity. Low levels of antioxidant capacity may impair cell signaling pathways in terms of membrane G proteins, second messengers (ie.cAMP) and transcripts encoding for endothelial nitric oxide synthase (eNOS). These signaling pathways and messengers are involved in vasoactive intestinal peptide (VIP), induced relaxation of human gastric antrum.
Aims & Methods: Aim of this study was to evaluate in obese patients oxidant capacity and its influence on antrum smooth muscle relaxation. Smooth muscle cells (SMC) and strips were isolated from human gastric antrum obtained from 14 normoglycemic-normocholesterolemic morbid obese patients (40.92; 372; 56 Antioxidant capacity was evaluated by antioxidant assay kit and the contribution of oxidative stress by the use of Apocynin (APO:1µg/ml) that inhibits NADPH oxidase the main producer of ROS. VIP (1μM) relaxant effects were tested on maximal cholecystokinin (CCK 1nM)-induced contraction on SMC and strips whilst the effect of adenylate cyclase activator forskolin (FSK,10 mM) and the 2nd messenger cAMP (0.1 mM) only on SMC. qPCR analysis was performed for transcripts for VPAC2, inflammatory cytokine (COX-2) and eNOS, the data were normalized to β-actin mRNA levels. Data are expressed as mean $\pm$ SE, $p < 0.05$ considered significant.
Results: Obese gastric muscle presented a low antioxidant capacity (30 ± 12 equivalent of trolox) associated to an hyporesponsiveness to VIP. In obese, VIP-induced relaxation was reduced both in SMC ($14.5 \pm 7.3\%$, $p < 0.05$) and strips ($13.8 \pm 5.2\%$, $p < 0.05$) in comparison to control (SMC:$79.96 \pm 5.78\%$; strips: $78.1 \pm 7.4\%$). This reduced VIP effect was associated in SMC with: 1) a decrease of VPAC2 messenger (obese: 3.63 ± 0.06 vs control: 6.27 ± 0.79, $p < 0.05$); 2) no transcripts for eNOS that was present in control (6.6 ± 0.4); 3) an increase of COX2 messenger (obese: 4.93 ± 0.63 vs control: 1.10 ± 0.08, $p < 0.05$); 4) an impairment of cAMP- and FSK- induced SMC relaxation, in comparison to control (cAMP: 44.9 ± 7.6 vs $73.4 \pm 5.8\%$; FSK: 54.95 ± 2.3 vs $71.80 \pm 11.8\%$, $p < 0.05$). The inhibition of NADPH oxidase by APO partially restores all these alterarations. A 2-fold increase of antioxidant capacity was observed (50 ± 0.5 equivalent of trolox), such as VIP-induced relaxation was restored (79.60 ± 11.84). VPAC2 messenger expression increase (4.02 ± 0.03, $p < 0.05$) as well as eNOS messenger (1.12 ± 0.08, $p < 0.05$).
Conclusion: An impairment of antioxidant capacity in human obese is are involved in alteration of VIP- induced relaxation of gastric antrum.
Disclosure of Interest: None declared

P1108 IMPACT OF TACRINE AND 7-METHOXYTACRINE ON GASTRIC MYOELECTRICAL ACTIVITY ASSESSED USING ELECTROGASTROGRAPHY IN EXPERIMENTAL PIGS

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Introduction: Tacrine was the first acetylcholinesterase inhibitor approved for therapy of Alzheimer's disease. Tacrine has dose-limiting side effects, including diarrhoea, nausea, vomiting and abdominal discomfort. It has currently been withdrawn in some countries mostly due to the risk of hepatotoxicity and been replaced by its derivate 7-methoxytacrine (7-MEOTA).
Aims & Methods: The aim of this study was to assess the impact of these two compounds on gastric myoelectrical activity by means of surface cutaneous electrogastrography (EGG) in experimental pigs.
Twelve pigs (*Sus scrofa f. domestica*, weighing 30-35 kg) entered the study. A single dose of tacrine (200 mg i.m., $n = 6$) or 7-MEOTA (200 mg i.m., $n = 6$) was administrated. Cholinesterase (acetylcholinesterase and butyrylcholinesterase) activity was determined in whole blood. Acetylcholine iodide was added as a substrate and liberated acetic acid was titrated with sodium hydroxide using an automatic titrator in potentiostatic mode. All EGG recordings were performed under general anaesthesia in the morning after 24 hours of fasting. Basal (30 minutes) and study recordings (150 minutes) were accomplished using an EGG stand (MMS, Enschede, the Netherlands). Running spectral analysis based on Fourier transform was used. Results were expressed as dominant frequency of gastric slow waves, power analysis (areas of amplitudes) and power ratio assessment (ratio of the areas of amplitudes after and before study drug administration).
Results: Maximal inhibition of blood cholinesterase activity was recorded after 10 minutes, being significantly stronger after administration of tacrine ($20.5 \pm 19.2\%$) compared to 7-MEOTA ($72.8 \pm 14.4\%$), $p < 0.001$. Tacrine decreased EGG dominant frequency 10 minutes after its administration (from basal 3.1 ± 0.6 to 2.8 ± 0.6 cycles per minute; $p = 0.014$). Tacrine induced a 60-minute but not significant increase of the power (with maximal value 493 ± 533 μV^2 at 20 minutes; $p = 0.300$) and power ratio (with maximal value 2.04 ± 3.4 at 10 minutes; $p = 0.330$). Tacrine caused significant gastric arrhythmia. 7-MEOTA did not influence dominant frequency of gastric slow waves significantly. 7-MEOTA caused a short-term late increase of the power (from basal 618.3 ± 747.3 to 2540.2 ± 6130.3 μV^2 at 90 minutes; $p = 0.079$) and power ratio at 60 minutes (6.3 ± 11.2; $p = 0.003$). Blood cholinesterase activity did not correlate with any EGG parameter either after tacrine or 7-MEOTA at any time.
Conclusion: Tacrine and 7-MEOTA have different impacts on EGG. Tacrine decreased dominant frequency and induced long-lasting gastric arrhythmia. 7-MEOTA caused a short-term late increase of the EGG power in experimental pigs.
Acknowledgements: the study was supported by an independent research grant (NT/14270).
Disclosure of Interest: None declared

P1109 THE EFFECT OF NEOSTIGMINE ON PORCINE GASTRIC MYOELECTRIC ACTIVITY ASSESSED USING ELECTROGASTROGRAPHY

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Introduction: Neostigmine is a parasympathomimetic agent that acts as a reversible acetylcholinesterase inhibitor. By interfering with the breakdown of acetylcholine, neostigmine indirectly stimulates both nicotinic and muscarinic receptors. However, there are no data on the direct effect of neostigmine on gastric myoelectrical activity.
Aims & Methods: The aim of this study was to assess the impact of neostigmine on the myoelectrical activity of the stomach by means of non-invasive surface cutaneous electrogastrography (EGG) in experimental pigs. Porcine EGG is fully

comparable with human EGG so it is suitable for various preclinical studies. Six adult female pigs (*Sus scrofa f. domestica*; 3 - 4 months old; mean weight 31.2 ± 2.1) entered the study. EGG recordings were performed under general anaesthesia (2% isoflurane in medicinal oxygen) in the morning after 24 hours of fasting. After the EGG baseline, neostigmine was administrated to the animals (0.5 mg i.m.; *Neostigmini metilsulfas*). EGG was followed by a 90-minute trial recording (MMS, Enschede, the Netherlands). Running spectral analysis based on Fourier transform was used for the evaluation. The results were expressed as dominant frequency of gastric slow waves and EGG power (areas of amplitudes).

Results: Neostigmine continuously increased the dominant frequency from basal EGG 2.6 ± 0.5 cycles per min. up to 2.9 ± 0.6 at the 60-90-minute interval ($p < 0.001$). Neostigmine continually decreased the EGG power from baseline values 1767.4 ± 2179.5 μV^2 (median 861.5) to 594.3 ± 853.8 μV^2 (median 151.0) at the 5-10-minute interval ($p = 0.036$), throughout until the 60 - 90-minute interval 117.6 ± 157.5 μV^2 (median 60.5; $p < 0.001$).

Conclusion: The standard dose of neostigmine significantly increased the dominant frequency of gastric slow waves and caused a continual long-lasting decrease of EGG power in experimental pigs.

Acknowledgements: the study was supported by an independent research grant (NT/14270).

Disclosure of Interest: None declared

P1110 ASSOCIATION BETWEEN THE TYPE OF ACHALASIA ESTABLISHED USING HIGH-RESOLUTION MANOMETRY (HRM) AND CHANGES OF PLASMA TOTAL CONCENTRATION OF NITRIC OXIDE METABOLISM END PRODUCTS

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Introduction: Previous studies have shown a decrease of nitric oxide (NO) metabolites level in patients with achalasia. However, the relationship between the type of achalasia and the level of plasma total concentration of NO metabolism (nitrates and nitrites) end products remains unknown.

Aims & Methods: to determine association between the type of achalasia and changes of plasma total concentration of end products of NO metabolism. 18 patients with achalasia (median age was 51.5 years (30-72) and 15 healthy volunteers were studied. We performed on every patient a high-resolution manometry (HRM) using a 22 channels silicone water-perfused catheter (Solar GI, MMS, Netherlands), and determined the total concentration of nitrates and nitrites. We analyzed HRM parameters: lower esophageal sphincter (LES) resting pressure (RP), integrated relaxation pressure (IRP), esophageal pressurization and distal contractile integral (DCI) according to the Chicago classification (version 3.0). The statistical analyses were performed using Statistica for Windows 6.0 (StatSoft Inc.).

Results: Type I achalasia was established in 10 patients (55.5%), type II in 5 patients (27.8%), and type III in 3 patients (16.7%). We detected an increase of IRP in all patients (21.0 mmHg (18.0; 35.2); $p < 0.001$), an increase of LES RP in 6 patients (33.3%) - 27.0 mmHg (19.0; 67.4), a decrease of DCI (290 mmHg (0-750)) in 14 (77.8%). Pan-esophageal pressurization revealed in 5 patients (27.8%), hypercontractile contractions in the distal part of the esophagus (DCI 5340 mmHg (3500; 6750)) - in 3 (16.7%). In patients with achalasia in comparison to healthy volunteers, we showed a decrease of NO metabolites (24.2 umol/l (20.5; 30.5) vs 36.8 umol/l (30.8; 48.6); $p < 0.05$). In patients with type II and III achalasia the level of NO metabolites was lower than in control group (25 umol/l (15.0; 33.5) and 22 umol/l (6.9; 30.5), respectively). Patients with type I had a normal trend (33.2 umol/l (29.9; 36.7)).

Conclusion: The level of NO metabolites depends on type of achalasia. Patients with type I achalasia have normal level of NO metabolites, while it is lower in patients with type II and to a greater extent with type III achalasia.

Disclosure of Interest: None declared

P1111 A NOVEL ROLE FOR THE EXTRACELLULAR MATRIX GLYCOPROTEIN-TENASCIN X IN GUT FUNCTION

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Introduction: Joint hypermobility syndrome (JHS) is a non-inflammatory connective tissue disorder commonly associated with gastrointestinal (GI) symptoms [1]. Ehlers-Danlos syndrome type III is a form of JHS where patients lack the Tenascin X (TNX) gene, an extracellular matrix glycoprotein. Clinically these patients manifest GI symptoms including constipation and rectal prolapse [2]. TNX knockout mice (KO) similarly suffer from rectal prolapse [3]. Previously we have shown TNX associates with vagal afferent calretinin+ nerve endings in wild type (WT) mouse stomach. In colon, TNX strongly associates with cholinergic, ChAT+ myenteric and submucous plexus neurones [4]. Therefore, localisation of TNX around nerve endings in stomach may affect gastric motor function, while association with cholinergic excitatory motor neurons suggests a role in contraction. We hypothesise TNX is important for regulating normal gastric and colonic function.

Aims & Methods: To establish the functional role of TNX in the stomach and colon using TNX KO mice. Methods: Gastric emptying rate was determined using ^{13}C octanoic acid breath test (WT:n = 13, KO:n = 9). From $^{13}CO_2$ curve, T½ (time for 50% of stomach emptying to occur) and T Lag (initial time delay in gastric emptying) were calculated. Colonic motility was assessed by manometry using a multi-lumen catheter, in an *ex vivo* colonic preparation (WT:n = 6, KO:n = 6). The number and amplitude of spontaneous contractions occurring throughout the colon over a 30 min study period were determined. Student's *t*-test was used to calculate statistical significance based on ± SEM for gastric emptying, and 2-way ANOVA for colonic motility.

Results: Gastric emptying was significantly accelerated in KO mice compared to WT (T½: WT = 158 ± 21.8 min vs. KO = 103 ± 12.9 min; $p = 0.0277$). Similarly, T Lag was significantly shorter in KO mice (T Lag: WT = 38 ± 5.7 min vs. KO = 24 ± 2.7 min; $p = 0.0194$). In the two groups colonic motility was measured in the following regions: Proximal, Mid-Proximal, Mid-Distal and Distal colon. Number of spontaneous contractions significantly decreased in all regions of the colon except for the proximal segment in KO mice compared to WT (Proximal: WT = 4.2 vs. KO = 5.6; Mid-Proximal: WT = 11.6 vs. KO = 3.17; Mid-Distal: WT = 11.6 vs. KO = 3.80; Distal: WT = 11.0 vs. KO = 3.20; $p < 0.05$). However, the mean amplitude of contractions significantly decreased only in the distal region of the colon in TNX KO mice (WT = 32mmHg vs. KO = 12mmHg; $p = < 0.05$).

Conclusion: In summary, we have identified two roles for the extracellular matrix glycoprotein-TNX. A loss of TNX causes accelerated gastric emptying which suggests that TNX is important in regulating gastric vagal afferent nerve activity. Also the absence of TNX causes a decrease in colonic contraction indicating TNX is needed to form the extracellular matrix around neurones important for neural communication, particularly in the cholinergic excitatory pathway. Collectively, the anatomical and functional data provide evidence that TNX is important in mediating normal gastric and colonic motor function.

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P1112 THE EXPRESSION OF NEUROTROPHINS AND NEUROTROPHIC FACTORS IN THE ACUTE MODEL OF EOSINOPHILIC INFLAMMATION OF THE ESOPHAGUS

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Introduction: Eosinophilic esophagitis is characterized by symptoms related to esophageal dysfunction (dysphagia, heartburn, and food impaction). Esophageal nerves regulate esophageal sensory and motor function, and alterations in these nerves are predicted to worsen esophageal dysfunction. However, it is unknown whether the eosinophilic inflammation in the esophagus leads to production of neurotrophins and neurotrophic factors that can induce profound alterations in peripheral nerves.

Aims & Methods: Here we aimed to characterize eosinophilic infiltration in the guinea pig model of acute allergic inflammation of the esophagus, and to evaluate changes in the expression of selected neurotrophins and neurotrophic factors in esophageal mucosa in this model. The antigen ovalbumin (OVA, 0.1% in saline) was injected into the surgically exposed cervical esophagus in the OVA-sensitized guinea pigs. The esophagus (middle portion) was harvested at various time points (2-14 days) and the eosinophil counts were evaluated in transversal sections (12μm) by using Giemsa staining. The expression of neurotrophins (NGF, BDNF) and neurotrophic factors (GDNF, artemin) was evaluated by quantitative RT-PCR. NGF, BDNF, GDNF and artemin were selected because esophageal nerves have receptors for these neurotrophins and neurotrophic factors.

Results: Eosinophils were rare in the esophagus of control naïve animals that received a vehicle injection or no injection. The maximal number of eosinophils per high power filed (hpf) was 5 ± 2 (n = 6). OVA injection into the esophagus in sensitized animals resulted in massive eosinophil infiltration of esophageal mucosa (97 ± 24 eosinophils per hpf, n = 10, $p < 0.05$ vs. control) on day 2 following the injection. The number of eosinophils was reduced on day 5 (27 ± 16, n = 4) and further reduced on day 14 (10 ± 6, n = 3), therefore the day 2 was selected for qRT-PCR analysis. The expression of BDNF was increased in the inflamed compared to control esophagus. dCT (detection threshold expressed relative to detection threshold of housekeeping gene b-actin) was 10.8 ± 0.5 vs. 9.8 ± 0.2 in control (n = 6) and inflamed (n = 7) esophagus, respectively, indicating twofold (ddCT = 1, 2^ddCT = 2) increase in BDNF mRNA ($p < 0.05$). In contrast the expression of artemin was moderately (to approximately 60%) reduced (dCT was 9.0 ± 0.2 vs. 9.7 ± 0.1, ddCT = -0.7, 2^ddCT = 0.6, $p < 0.01$). The expression of NGF (8.8 ± 0.4 vs. 8.7 ± 0.2, $p = 0.8$) and GDNF (12.5 ± 0.3 vs. 12.3 ± 0.2, $p = 0.5$) was not changed.

Conclusion: An acute allergen challenge in the esophagus leads to robust eosinophilic infiltration of esophageal mucosa that is associated with changes in the expression of neurotrophins and neurotrophic factors. This model is suitable

for the analysis of esophageal nerve plasticity in eosinophilic inflammation.
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P1113 OBJECTIVE BIOLOGICAL MARKERS OF MEAL-INDUCED PERCEPTION

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Introduction: We have previously shown that meal ingestion induces cognitive perception (sensations) with a hedonic dimension (well-being) that depend on the characteristics of the meal and the appropriateness of the digestive response.
Aims & Methods: The aim of the present study is to identify biomarkers of the cognitive response to meal ingestion.
In 18 healthy subjects, selected through a clinical questionnaire to determine the absence of gastrointestinal symptoms, the response to a test meal (Edanec, 1 kcal / ml) at an intake rate of 50 ml / min until maximum satiety were assessed. Perception measurements and blood samples for metabolomics analysis was taken at 5 min intervals before, during and 20 minutes after ingestion. Perception of hunger/satiety, desire of eating a food of choice, digestive well-being, abdominal fullness and discomfort/pain was measured on 10 cm scales. Metabolomic analysis was performed with MRI spectroscopy. Discriminative metabolites (determined by principal component analysis) were determined and quantified as the area under the peaks of the MRI spectra. Values of glucose, triglycerides, insulin, PYY and GLP-1 were measured using conventional laboratory techniques.
Results: During ingestion satiety progressively increased up to a maximum sensation (+5 score on a scale from -5 to +5) after ingestion of 976 ± 71 ml. Ingestion induced sensation of fullness and decreased digestive well-being. Twenty minutes after the meal, these sensations had partially recovered down to fasting levels. The total amount ingested by each subject correlated with basal sensation of hunger ($R = 0.8$; $p = 0.0001$), but not with other sensations or blood metabolites levels measured during fasting. Immediately after ingestion, satiation correlated with an increase in glucose ($R = 0.49$; $p = 0.038$) and valine levels ($R = 0.48$; $p = 0.043$), while well-being inversely correlated with CH3-lipids ($R = -0.72$; $p = 0.001$). Fullness sensation was associated with lower levels of GLP ($R = -0.77$; $p = 0.001$) and PYY ($R = -0.63$; $p = 0.015$). Twenty-minutes after finalizing ingestion, triglyceride levels had significantly increased and correlated with the decrease in desire to eat a food of choice ($R = -0.56$; $p = 0.016$). Throughout study, the increase in CH2-lipids correlated with lower discomfort ($R = -0.51$; $p = 0.032$).
Conclusion: Cognitive (sensations) and hedonic responses (well-being) to meal ingestion correlate with changes in circulating metabolites, that may serve as objective biomarkers of perception.
Disclosure of Interest: None declared

P1114 SHORT-TERM NON-INVASIVE AFFERENT VAGUS NERVE STIMULATION (NVNS) USING GAMMACORETM (GC) IN PATIENTS WITH TREATMENT REFRACTORY GASTROPARESIS

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Introduction: High-frequency, low-energy gastric neurostimulation(Enterra™) is indicated for compassionate treatment of patients with refractory gastroparesis. Symptom improvement is reported in 50-60% of patients but not accompanied by improved gastric emptying. It is likely that gastric neurostimulation affects the gut-brain axis influencing autonomic afferents (1). GammaCore(electroCore, LLC) is a non-invasive, afferent selective vagus nerve stimulator(nVNS) used for the treatment of migraine and cluster headache. We report the first use of gC in patients with refractory gastroparesis.
Aims & Methods: Thirty-five consecutive patients with intractable gastroparesis were invited to undergo a course of gC whilst awaiting funding for implantable gastric neurostimulation. The gC device delivers a high-frequency, low-energy stimulus to afferent vagus fibers as they cross the neck adjacent to the carotid arteries. The device is programmed to deliver doses of 120 seconds and patients were trained to deliver 2 doses (240 secs) to the left and right vagus nerve respectively. This dosing regimen was self-administered 8 hourly (12 doses/day) for 2 weeks, increasing in week 3 to 3 doses 8 hourly (18 doses/day). Patients were asked to grade their symptoms daily using the 9 item Gastroparesis Cardinal Symptom Index (GCSI)with a 5 point Likert scale. The GCSI was completed for 2 weeks prior to commencing treatment, and throughout the treatment period. Symptom change was evaluated in patients who complied with treatment and completed the daily symptom score. The mean aggregated GSCI score at baseline was compared with the aggregated score of the final week of treatment. Clinically meaningful improvement was defined as a GCSI Likert scale reduction of ≥ 1 (2).
Results: Twenty-three of the 35 patients (65.7%) used the gamma Core as instructed and completed the daily diary. The pre-treatment mean aggregated GCSI score in these patients was 2.85 (SD 0.90). At 3 weeks,8 patients (35%) had a ≥ 1 reduction in the aggregated GSCI score. Two compliant patients who continued stimulation for more than three weeks experienced a delayed response, giving a total response rate of 43%. In 8 of the responders, improvement was evident within 1 week of commencing treatment whilst a response was evident in the 2 patients who continued treatment for >3 weeks by week 5. All the responders experienced symptom recurrence within a week of stopping treatment. No serious adverse events device related were reported.
Conclusion: In this group of patients with treatment refractory gastroparesis, one third failed to engage with short term nVNS. In compliant patients, 43% recorded a fall of ≥ 1 in their aggregated GCSI score. As gC stimulates afferent vagus fibers, it is likely that the response is mediated at the level of the gut-brain axis. In refractory gastroparesis, nVNS delivered by gC might offer a new approach to symptom control. The dosing and duration of nVNS required to obtain an optimal response remains unknown and deserves further consideration.

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P1115 PHYSIOLOGICAL AND ELECTRICAL MODULATION OF VAGAL TONE ENHANCES ANTRODUODENAL MOTILITY IN HEALTHY HUMANS

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Introduction: The autonomic nervous system is a bidirectional hierarchically controlled brain body nexus that integrates the external environment with the internal milieu. The parasympathetic nervous system (PNS), whose main neural substrate is the vagus nerve, influences antro-duodenal motility. In animal models, the stimulation of vagal afferents have been shown to enhance antroduodenal motility. Hitherto, the influence of physiological and electrical modulation of vagal tone in humans on antroduodenal motility has not been objectively evaluated.
Aims & Methods: To investigate the synergistic effects of physiological (deep slow breathing (DSB)), and electrical (transcutaneous auricular vagal nerve stimulation (t-VNS)) modulation of vagal tone on antro-duodenal motility. 12 healthy subjects (9 female, median age 52.5 years, range 40-56) were randomized to receive either DSB/active t-VNS or sham-DSB/sham t-VNS in a crossover design. Cardiac vagal tone, a validated real time non-invasive parameter of efferent PNS tone from the brainstem (1), was measured at baseline and continuously thereafter. Antro-duodenal motility was assessed after 90 minutes of stimulation/sham using a validated real-time ultrasonographic method in response to a standardized liquid meal (2).
Results: In comparison to the sham condition, DSB/active t-VNS resulted in an increase in vagal tone (8.7 linear vagal scale +/- 3.8 vs. 6 +/- 3.9, $p = 0.02$). DSB/active t-VNS increased the frequency of antro-duodenal contractions (9.1 contractions/3 minutes +/- 2 vs. 7.1 +/- 1.9, $p = 0.04$) compared to sham. DSB/active t-VNS increased antroduodenal motility index (5.6 +/- 2.5 vs. 3.7 +/- 2.1, $p = 0.048$) compared to sham.
Conclusion: These findings provide preliminary evidence to suggest that DSB/active t-VNS increases cardiac vagal tone. Moreover, antroduodenal motility can be enhanced via physiological and electrical modulation of vagal tone. Such interventions warrant further exploration in patients groups such as those with functional dyspepsia.

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P1116 ROLE OF DELAYED GASTRIC EMPTYING AS PREDICTOR OF CARDIOVASCULAR EVENT IN PATIENTS WITH SYMPTOM OF GASTROPARESIS

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Introduction: Gastroparesis is a chronic disorder that significantly impairs the quality of life of affected individuals. However, little is known about the prognosis for morbidity or death of delayed gastric emptying. The aim of study was to evaluate the prognostic value of gastric emptying study on the prediction of morbidity including cardiovascular event.
Aims & Methods: We enrolled 139 patients (93 females, 105 patients with diabetes) with symptoms of gastroparesis, who underwent gastric emptying scintigraphy from 2004 to 2013. Comorbid condition, age, gender distribution were examined as potential risk factors. We evaluated the occurrence of cardiovascular events (coronary artery disease, stroke) and other morbid diseases after gastric emptying scintigraphy.
Results: There were 114 patients with normal gastric emptying (NGE) and 25 with delayed gastric emptying (DGE). The mean age, gender, BMI and distribution of comorbid conditions including diabetes were not significantly different between the two groups. There was more frequent occurrence of cardiovascular event in 'DGE' than 'NGE' (32.0 % vs. 10.5 %, $p = 0.011$). There was more

frequent occurrence of cardiovascular event and other neurologic disease in 'DGE' (40.0% vs. 14.9%, p = 0.009).
Conclusion: A delayed gastric emptying study may predict the occurrence of cardiovascular event and negative outcomes in patients with symptoms of gastroparesis.
Disclosure of Interest: None declared

P1117 GASTROPARESIS IN CHILDREN: CHARACTERIZATION AND CLINICAL PRESENTATION – A RETROSPECTIVE STUDY

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Introduction: Gastroparesis is commonly diagnosed on the basis of scintigraphy and is associated with symptoms of nausea, vomiting, early satiety and upper abdominal pain. The pathophysiology of this condition in adults and children is not clear and the literature describing the characteristics, aetiology, treatment and outcome of gastroparesis in the paediatric population is limited.
Aims & Methods: Aims of this study were to describe the clinical presentation and aetiology, comorbidities, diagnostic findings, treatments and outcomes in children with scintigraphic proven delayed gastric emptying.
A retrospective descriptive study at the Royal Children's Hospital in Melbourne was performed on patients (0-18 years) with scintigraphy proven delayed gastric emptying (DGE). We collected data from 2004-2008 on the clinical presentation, comorbidities, aetiologic factors, other diagnostic interventions, treatments and outcomes in these children. Sub-group analysis was performed to investigate (a) age and gender related differences in symptoms and comorbidities and (b) differences in outcome based on severity of delayed gastric emptying.
Results: One hundred and five patients were included in our study with 49% being boys and 51% being girls. Median age at presentation was 6.7 years (IQR 1.2 – 12.1). Boys tended to have a lower age at presentation compared to girls. The most common presenting symptoms were vomiting (61%), weight loss or failure to thrive (38%) and regurgitation (23%). Respiratory symptoms were more reported in males and infants. Nausea was more frequently seen in older children and females. Common comorbidities were gastro-oesophageal reflux (50%), respiratory (25%) and neurodevelopmental (21%). An idiopathic aetiology was seen in 74% of children and other causes were medication use, post viral and surgery. Additional investigations performed were a barium meal (71% of children) and endoscopy (66%). Treatment included diet (32%) and medications including a proton pump inhibitor (66%), a prokinetic (73%) and in 51% a combination of both. Over half the cohort had complete or partial resolution of symptoms. No differences in outcome were found with respect to severity of delayed gastric emptying.
Conclusion: Idiopathic gastroparesis was most common in our study group however, a substantial number of patients had a comorbidity. A variety of treatments were used and over half our cohort showed symptomatic improvement. It is important to note that there was no relationship between the severity of an objective test of gastroparesis and resolution of clinical symptoms. Future research is needed to develop a consensus on gastric emptying scintigraphy in children, to define subgroups and their disease mechanisms and to provide parents and doctors with more evidence based management approaches.
Disclosure of Interest: None declared

P1118 ESOPHAGEAL MOTILITY BEFORE AND AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL CANCER: A HIGH-RESOLUTION MANOMETRY STUDY

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Introduction: Endoscopic submucosal dissection (ESD) is a standard treatment for superficial esophageal cancer (EC). Postoperative stricture is one of the most common complications in esophageal ESD, and patients with postoperative strictures often suffer from dysphagia. Recently, procedures to prevent strictures, such as endoscopic balloon dilatation (EBD), endoscopic triamcinolone injection (ETI) and oral administration of prednisolone, have made it possible to avoid postoperative strictures more effectively. Nonetheless, some patients complain of dysphagia after ESD, although no postoperative strictures may be present. Although ineffective esophageal motility may be associated with dysphagia after ESD, levels of esophageal motility after ESD remain unknown.
Aims & Methods: The aim of this study was to elucidate the esophageal motility before and after ESD and the cause of dysphagia using high-resolution manometry (HRM).
Fifteen male patients (mean age: 69.8 years) who underwent ESD for superficial EC were enrolled in this study. Patients filled out a questionnaire about dysphagia and underwent HRM before and after ESD. The results of the HRM tests were analyzed according to the metrics and contraction patterns in the Chicago classification, version 3. All results were compared between before and after ESD.
Results: Data were obtained from 14 patients. The average size of the circumferential mucosal defect ratio at ESD was 52.1 ± 19.3% and 2 patients had more than sub-circumferential resection. The distal contractile integrity (DCI) before and after ESD and the frequencies of ineffective or fragmented contractions were not significantly different (1942.4 ± 1692.9 *vs.* 1907.8 ± 1515.9 mmHg-s-cm, $p = 0.826$ and 1.9 ± 2.4 *vs.* 1.9 ± 1.8 times, $p = 0.550$, respectively); however, the patient with sub-circumferential mucosal defect had a reduction in the DCI (before, 966.4 mmHg-s-cm; after, 587.8 mmHg-s-cm) and more frequent ineffective or fragmented contractions (before, 2 times; after, 5 times) after ESD. Furthermore, the patient with circumferential mucosal defects also showed a reduction in DCI (before, 3763.0 mmHg–s-cm; after, 2110.5 mmHg-s-cm) and more frequent ineffective or fragmented contractions (before, 0 times; after, 3 times).
Although no patients had noted dysphagia before ESD, four patients, including two cases with extensive ESD, developed dysphagia after ESD ($p = 0.030$).
Conclusion: Although there were no statistically significant differences between esophageal function before and after ESD, an extensive ESD could affect esophageal function and result in dysphagia. In this study, the number of patients with extensive ESD was small. Therefore, a further prospective study of patients with extensive ESD would be required for definitive conclusions.
Disclosure of Interest: None declared

P1119 SAFETY OF PER-ORAL ENDOSCOPIC MYOTOMY (POEM) IN PATIENTS WITH SEVERE CO-MORBIDITIES

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Introduction: Per-oral endoscopic myotomy (POEM) is an upcoming treatment modality for achalasia cardia. Results of POEM have been encouraging and are comparable to those after laparoscopic Heller's myotomy (LHM) or endoscopic balloon dilatation (EBD). The patients with severe cardio-respiratory diseases are relative contraindications for LHM or EBD. In this multi-center study, we analyzed safety and efficacy of POEM in sub-group of patients with severe co-morbid conditions.
Aims & Methods: Consecutive patients with achalasia cardia confirmed on endoscopy (EGD), high-resolution manometry (HRM) and barium swallow and undergoing POEM at three centers were included. Associated co-morbidities were recorded and graded according to American Society of Anaesthesiology (ASA) classification. Eckhardt dysphagia score was recorded before and after the procedure. Procedure time, technical success and complications were noted. Follow up was by EGD, HRM at 4 weeks and subsequently monthly by telephone.
Results: 61 patients were enrolled. 18 (29.50%) had severe systemic diseases classified as ASA class 3 or 4 and were analyzed. Mean age 57.41 years and females (6). Achalasia types: I – 4, II – 14, III – nil. Median symptom duration: 54 months. Comorbid diseases: cardiac 5 (ischemic heart disease – 4, permanent pacemaker – 1), pulmonary disease – 5 (COPD- 3, interstitial lung disease – 2, thoracic empyema - 1) essential hypertension (11), diabetes mellitus (4), morbid obesity (1). 8 patients (44%) had two or more co-morbid illnesses. Mean pre-procedure Eckhardt score – 7.2 (Range 6 – 9); mean LES pressure 36.78mmHg (Range 17.5 – 68mmHg). Mean procedure duration was 117.2 minutes (50 – 270). There were no intra or post procedural complications or deaths. Post-operative hospital stay was < 48 hours for all patients. Clinical success was 100%. At 4-weeks follow up, mean Eckhardt score was 1.42 (1 – 2, p = 0.001) and mean LES pressure 10.06mmHg (4.7 – 19) (p = 0.005). At a mean 9-month follow up, mean Eckhardt score remained at 1.48 (Range 1 – 2).
Conclusion: POEM is safe and effective treatment for achalasia cardia even in patients with severe systemic diseases that may preclude surgical intervention.
Disclosure of Interest: None declared

P1120 PROTON PUMP INHIBITOR AND SELECTIVE SEROTONIN REUPTAKE INHIBITOR THERAPY FOR THE MANAGEMENT OF NON CARDIAC CHEST PAIN

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Introduction: Although gastroesophageal reflux disease (GERD) constitutes the main cause of non cardiac chest pain (NCCP), administration of proton pump inhibitors (PPIs) benefits only a minority of patients. Our prospective study aimed to evaluate the effect of PPI and selective serotonin reuptake inhibitor (SSRI) therapy on the different subtypes of NCCP patients using multichannel intraluminal impedance and pH monitoring (MI-pH).
Aims & Methods: All patients with NCCP (i.e. at least 3 episodes of chest pain per week in the previous 3 months and exclusion of a cardiac source for the chest pain) underwent impedance and pH monitoring and the total distal esophageal acid exposure and the symptom index for chest pain were calculated. All patients also underwent esophageal manometry and upper endoscopy and were excluded if erosive esophagitis, Barrett's esophagus, eosinophilic esophagitis or motility abnormalities were found. According to the results of the impedance monitoring, patients have been prescribed PPIs twice daily if abnormal distal esophageal acid exposure was noted (group A), citalopram 20mg once daily and PPI once daily if a positive symptom index for chest pain was noted (group B) and citalopram 20mg once daily if a negative symptom index for chest pain was noted (group C). In all cases therapy has been administered

for 8 weeks and treatment success was defined as the complete disappearance of the chest pain.
Results: From March 2014 till March 2015, 66 patients with NCCP were screened for entry into the study. Three were excluded because of motility abnormalities during manometry (n = 1) and the presence of esophagitis (n = 2). Therefore the study sample consisted of 63 patients. From these patients 9 exhibited abnormal distal esophageal acid exposure and received PPIs twice daily (group A), 18 patients had a positive symptom index for chest pain and received citalopram 20mg once daily and PPI once daily (group B) and 36 had a negative symptom index for chest pain and received citalopram 20mg once daily (group C). After 8 weeks of therapy, complete resolution of chest pain was noted in 8 patients of group A (88.9%), in 13 patients of group B (72.2%) and in 24 patients of group C (66.7%).
Conclusion: Using combined impedance-pH monitoring different subtypes of non cardiac chest pain patients could be identified. According to the results of the monitoring patients can receive targeted treatment with PPIs and/or citalopram with a favorable outcome for the great majority of them.
Disclosure of Interest: None declared

P1121 SYMPTOMS AND ESOPHAGEAL MOTILITY BASED ON PHENOTYPIC FINDINGS OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Introduction: Scleroderma esophagus is defined as esophageal disease seen in patients with known scleroderma and is characterized by distal aperistalsis and LES incompetence because of fibrosis of esophageal smooth muscle. The association between scleroderma esophagus and different subgroups of the patients with systematic sclerosis (SSc) is still conflicting.
Aims & Methods
Aim: To assesses factors (cutaneous findings, pulmonary fibrosis, cutaneous ulcers, and computed tomography (CT) findings of esophageal lumen) that are associated with the clinical presentation and esophageal motor dysfunction of scleroderma esophagus.
Methods: Fifty-four SSc patients (48 women, mean age 50.61 ± 11.67) with esophageal involvement underwent clinical interview, medical records review and high resolution manometry (HRM) in a 2-year period study. Patients completed a symptom questionnaire. CT study enrolled totally 27 patients that underwent CT of the thorax at the time of scleroderma diagnosis and thereafter measurement of the diameter of the esophageal lumen at the level of the pulmonary veins origin (normal values were considered > 9mm).
Results: On esophageal manometry, findings revealed a pattern typical of scleroderma esophagus. In the symptom questionnaire responses, the most severe symptom reported was regurgitation, while the most frequent symptom conveyed was heartburn. Between different subgroups of SSc (diffuse *vs.* limited type, with *vs.* without pulmonary fibrosis, with *vs.* without cutaneous ulcers) there was no statistically significant difference in the severity and frequency of esophageal symptoms and in esophageal motility. The only statistically significant difference was observed in patients with esophageal diameter <9mm in CT who reported more severe dysphagia compared to patients with esophageal diameter >9mm in CT (51.2 ± 19.5 vs. 9.7 ± 13.8, respectively, $p < 0.0001$).
Conclusion: Our results did not support the idea that patients with different investigated factors are associated with the clinical and manometric presentations of scleroderma esophagus. Dysphagia is the only symptom that associated with esophageal diameter <9mm in CT. Dysphagia is likely to attribute to progressive fibrosis of esophagus causing stenosis of esophageal lumen.
Disclosure of Interest: None declared

P1122 PRUCALOPRIDE INCREASES BASAL LES TONE IN PATIENTS WITH ESOPHAGEAL MOTILITY DISORDERS

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Introduction: Esophageal hypomotility is a frequent finding in patients with upper GI symptoms, but to date there are not pharmacological options to improve esophageal motor activity. Prucalopride(PRU) is a selective agonist for 5-HT4 receptors, used for the treatment of chronic constipation that stimulates peristalsis and colonic transit. Recent studies suggest a potential role of PRU on esophageal motility, however the data available are limited to animal models. The only evidences in humans are related to a reduced number of reflux episodes in GERD patients and a faster gastric emptying in healthy subjects.
Aims & Methods: Aim of our study has been to determine whether Prucalopride has an action on esophageal body and LES motor activity in patients affected by esophageal weak or ineffective peristalsis. Patients and methods: 6 patients (2 Male, 4 Female) undergoing esophageal High Resolution Manometry (HRM) with detection of low amplitude esophageal body contractility and/or low basal LES tone entered into the study. After basal HRM they received 2mg/day (Q. D.) of PRU half an hour before lunch for 14 days. At the end of the treatment, a second HRM was performed. Waves amplitude and duration, Distal Contractile Integral (ICD) , Basal LES tone, Integrated residual pressure (IRP), distal latency were analyzed to identify possible changes as compared to baseline.
Results: PRU was associated to an increase in basal LES tone as compared to baseline (17.8 ± 4.9 basal vs 24.5 ± 6.8 mmHg after PRU, $p = 0.01$), while no change of esophageal body motility was computed. No side effects were reported.
Conclusion: A short course of Prucalopride 2 mg/day leads to an increase in LES basal tone with no changes in esophageal body motility. The drug was well tolerated. These preliminary data suggest a potential role by PRU in the treatment of patients with a deranged function of the esophago-gastric barrier. Further randomized controlled studies are needed to reinforce this hypothesis.
Disclosure of Interest: None declared

P1123 HIGH RESOLUTION ESOPHAGEAL MANOMETRY WITH A STANDARDIZED TEST MEAL INCREASES DIAGNOSTIC SENSITIVITY FOR CLINICAL RELEVANT ESOPHAGEAL MOTILITY DISORDERS

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Introduction: The Chicago Classification (CC) for esophageal motility disorders using high resolution manometry (HRM) is the accepted standard for the diagnosis of disorders of esophageal motility and is based on the analysis of ten 5ml water swallows (WS). It is uncertain if WS are representative of esophageal dysfunction during normal drinking and eating. Indeed, most patients do not receive any explanation for their symptoms with the current standards of using WS alone. Recent papers demonstrate a high rate of symptomatic dysmotility during solid test meal (STM) in patients with proton pump inhibitor (PPI) resistent reflux disease [1] and symptomatic dysphagia post-fundoplication.[2]
Aims & Methods: The primary aim was to compare the frequency of major and minor esophageal motility disorders using WS and STM. The secondary aim was to determine if observations during STM can establish esophageal dysfunction as a cause of dysphagia. Prospective series of patients referred for esophageal HRM between January 2010 and December 2013. WS and STM HRM studies were performed in the upright, seated position. Diagnosis of major and minor esophageal motility disorders were based on CC version 3.0 for water swallows[3] modified for use with solid swallows/test meal as appropriate [1].
Results: 750 consecutive patients (44% male; age 52.5 ± 16.9 years) referred for dysphagia (n = 360 [48%]), reflux symptoms (n = 329 [44%]) and other indications (n = 61 [8%]) were studied. Major esophageal motility disorders were present in 163/750 (22%) WS and 321/750 (43%) STM studies ($p < 0.001$). Conversely, we observed a matching decrease in the proportion of patients with minor esophageal motility disorder diagnosed with STM [152/750 (20%) compared to WS [335/750 (45%) ($p < 0.001$)]. Additionally, whereas symptoms were rare with WS (<1%), close association of dysphagia with dysmotility during STM established the clinical relevance of HRM findings in 245/360 (68%) patients. Patients with major motility disorders were more likely to have dysphagia associated with dysfunction than those with minor motility disorders or normal HRM findings (64% v. 26% v.13%; $p < 0.001$). The most common major dysmotility disorder detected by STM that were missed by WS was outlet obstruction, followed by spasm and hypercontractile dysmotility.
Conclusion: STM increases the diagnostic yield of treatable, major dysmotility by HRM studies compared to water swallows and can establish the association between esophageal dysfunction and symptoms.

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P1124 INCIDENCE AND PREVALENCE OF EOSINOPHILIC ESOPHAGITIS IN CHILDREN AND ADULTS IN POPULATION-BASED STUDIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: In recent years several studies have attempted to define the extent of EoE from estimating its epidemiology in different populations, by using different methodological approaches, from population-based studies to others that defined the frequency of EoE in series of endoscopies and esophageal biopsies. Although the results are widely variable, a trend to gradual increase in the prevalence of EoE has been described in recent years according to figures provided by different

authors. However, the epidemiology of EoE and its temporal trends in population-based studies have not been systematically evaluated to date, which prevents us to reliably and accurately estimate the magnitude of the problem.
Aims & Methods: A systematic review and meta-analysis was conducted to provide an accurate estimate of incidence and prevalence rates of eosinophilic esophagitis (EoE).
We search MEDLINE, EMBASE, and SCOPUS databases for population-based studies dealing with the epidemiology of EoE. The pooled incidence and prevalence rates, male-to-female and children-to-adult rate ratios, and geographical and temporal variations were calculated using a fixed or random-effects model.
Results: The search yielded 1,334 references; the final quantitative summary included 13 population-based studies from North America, Europe, and Australia, with the results showing high heterogeneity. The pooled EoE incidence rate was 4.8/100,000 persons/year (95% confidence interval [CI] 2.8–7.2) and was higher for adults (7; 95%CI 1–18.3) than for children (5.1; 95%CI 1.5–10.9).
The pooled prevalence of EoE was 24.7 cases/100,000 inhabitants (95%CI 15.3–36.2), rising to 32.7 (95%CI 18.4–51) in studies with a lower risk of bias. The prevalence was higher in adults than in children (43.4; 95%CI 22.5–71.2 *vs.* 29.5; 95%CI 17.5–44.7, respectively), and in American compared to European studies.
A steady rise in EoE incidence and prevalence rates was observed upon comparison of studies conducted before and after 2008. No significant publication bias was found.
Conclusion: EoE is a common disease that has significantly increased in North America and Europe in the last years. The population-based incidence and prevalence of EoE vary widely across individual studies, potentially because of variations in ascertainment of cases between centers and quality of research. Further large multicenter prospective research is needed to evaluate reported data.
Disclosure of Interest: None declared

P1125 NON-INVASIVE BIOMARKERS FOR MONITORING RESPONSE TO SHORT-TERM TREATMENT WITH BUDESONIDE IN EOSINOPHILIC ESOPHAGITIS

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Introduction: In eosinophilic esophagitis (EoE), treatment response is usually monitored by histological assessment of the esophagus, which requires repeated upper endoscopy. Instead, non-invasive biomarkers would be valuable. We thus examined absolute eosinophil count (AEC) and serum levels of Chemokine (C-C motif) ligand (CCL)-17, CCL-18, CCL-26, eosinophil cationic protein (ECP) and mast cell tryptase (MCT) for their utility to monitor treatment response in adult EoE-patients.
Aims & Methods: Venous blood samples of EoE-patients (n = 69) who had randomly received 14 days' treatment with budesonide (n = 51) or placebo (n = 18) were analysed. AEC and serum-CCL-17, -CCL-18, -CCL-26, -ECP and –MCT were measured before and after treatment and were correlated to patients' dysphagia score, endoscopy score and histological esophageal eosinophil density.
Results: Histological remission was achieved in 98% of the budesonide and 0% of the placebo recipients. AEC (380.2 vs. 214.7/cmm, P = 0.0001) and serum levels of CCL-17 (294.3 vs. 257.9 pg/ml, P = 0.0019), CCL-26 (26.7 vs. 16.2 pg/ml, P = 0.0058), ECP (45.5 vs. 27.5 µg/l, P = 0.0016) and MCT (5.3 vs. 4.5 µg/l, P = 0.0019) significantly decreased in budesonide, but not in the placebo recipients. There was no significant change of serum-CCL18. Only AEC significantly correlated with esophageal eosinophil density before (r = 0.28, P = 0.0236) and after (r = 0.42, P = 0.0004) budesonide treatment.
Conclusion: Response to short-term budesonide treatment of EoE can be reflected by AEC as well as by serum marker levels of CCL-17, CCL-26, ECP and MCT. AEC seems to be most valuable, being the only marker, which shows correlation to esophageal eosinophil density.
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P1126 PREDICTING ENDOSCOPIC AND HISTOLOGIC REMISSION IN ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS USING THE EESAI PRO SCORE

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Introduction: Long-standing eosinophilic esophageal inflammation leads to stricture formation with the inherent risk of food bolus impactions. It is currently unknown if clinicians can rely purely on symptom severity to estimate the endoscopic and histologic activity.
Aims & Methods: We aimed to evaluate the relationship between symptoms, endoscopic and histologic activity. Adult EoE patients were prospectively included (clinicaltrials.gov NCT00939263). Patients completed validated Eosinophilic Esophagitis Activity Index (EEsAI) Patient Reported Outcomes (PRO) instrument that measures symptom severity (7-day recall period). The EEsAI PRO score ranges from 0-100 points. A score from 0-20 points was defined as clinical remission. Patients underwent endoscopy with esophageal biopsy sampling. Endoscopic findings were recorded according to the Endoscopic Reference Score (EREFS). Endoscopic remission was defined as follows: 1) absence of white exudates; 2) absence of moderate and severe rings; 3) absence of strictures; 4) furrows and edema could be present but not in combination. Histologic inflammatory remission was defined as ≤5 eosinophils/high power field (hpf).
Results: A total of 120 adult EoE patients were recruited (61% males, 95% Caucasians, EoE symptom onset > 5 years in 67.2%). Fifty-one patients (42.5%) were in clinical remission. The following frequency of endoscopic findings was found: 13/51 (25.5%) patients had white exudates, 25/51 (49%) had furrows, 24/51 (47.1%) had edema, 23/51 (45.1%) had mild rings, 8/51 (15.7%) had moderate rings, 6/51 (11.8%) had a low grade stricture, and 1/51 (2%) had an intermediate stricture (passage of 8-9 mm-outer diameter endoscope not possible). Histologic remission was found in 23/51 (45.1%) of patients, 8/51 (15.7%) had 6-20 eos/hpf, 14/51 (27.5%) had 21-100 eos/hpf, and 6/51 (11.8%) had > 100 eos/hpf. Only 4/51 (7.8%) patients had eosinophilic microabscesses. Of the 51 patients in clinical remission 25 patients (49%) were in endoscopic remission and 23 patients (45.1%) were in histologic remission. The sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of a PRO score ≤20 points to predict endoscopic remission were 64%, 68%, 49%, 80%, 67%, respectively. The sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of a PRO score ≤20 points to predict histologic remission were 54%, 64%, 45%, 71%, 60%, respectively.
Conclusion: The EEsAI PRO score with a definition of ≤20 points for clinical remission has a moderate overall accuracy in predicting endoscopic and histologic remission. Thus, in addition to assessing PRO measures, assessment of objective signs of disease activity, including endoscopic and histologic alterations, remains to be an important element in the judgment of overall disease activity.
Disclosure of Interest: None declared

P1127 MODULATION OF CD8+CELLS INFILTRATION AND ACTIVITY IN EOSINOPHILIC OESOPHAGITIS BY SIX-FOOD ELIMINATION DIET

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Introduction: Eosinophilic oesophagitis (EoE) is an inflammatory disease of the esophagus histologically characterized by an infiltration of intraepithelial eosinophils. Clinical improvement and histological normalization through an exclusion diet support an allergic origin. However, similarities in the oesophageal transcriptome between allergic and non- allergic patients and the increase in intraepithelial $CD8^+$ leucocytes suggest the existence of additional mechanisms in the pathogenesis of EoE.
Aims & Methods: To identify the role of $CD8^+$ population in the pathophysiology of EoE.
EoE patients (n = 10; age: 33 ± 10 years old) who responded clinically and histologically to a six-food elimination diet (SFED: milk, wheat, egg, fish, legumes, nuts) and healthy controls (C, n = 10; age: 53 ± 20 years old) were selected. Clinical symptoms were assessed by a non-validated score and analysed before and after SFED, and food triggers were identified. The number of eosinophils per high power field (hpf) was quantified after haematoxylin and eosin stainning in oesophageal biopsies of the C group and in the EoE group before and after SFED. The number of $CD8^+$ and $CD2^+$ cells was quantified by area (mm^2). Furthermore, gene expression of specific CD8 molecules (granzyme A, granzyme B and granulysin) and of mucosal migration molecules (α4-integrin and MADCAM1) was evaluated by quantitative RT-PCR in esophageal biopsies of all subjects.
Results: The main symptoms reported by patients were dysphagia (100%), and food impaction (50%). Diet significantly reduced clinical symptoms in all patients. Milk was identified as the trigger food in 50% of the patients.

Oesophageal epithelium of EoE patients presented greater eosinophil (EoE:63 ± 40; C:0/hpf), $CD8^+$ (EoE:512 ± 360; C:84 ± 50/mm^2), $CD2^+$ (EoE:591 ± 342; C:108 ± 50/mm^2) and $CD8^+CD2^+$ (EoE:480 ± 356; C:79 ± 49/mm^2) counts than those in group C ($P < 0.05$). SFED significantly reduced the magnitude of these populations to C values in parallel with the clinical improvement of patients. Gene expression of cytotoxic molecules and markers of cell migration was higher in EoE than in C (1.6 to 26 fold-change; $P < 0.05$) and significantly decreased to C values after SFED treatment.
Conclusion: Reduction of $CD8^+$ number and activity, in association with clinical improvement after SFED, suggest that active cytotoxic mechanisms are present in the oesophageal epithelium and contribute to the physiopathology of EoE.
Disclosure of Interest: None declared

P1128 THE GERDQ QUESTIONNAIRE DISTINGUISHES PROTON PUMP INHIBITOR-RESPONSIVE ESOPHAGEAL EOSINOPHILIA FROM EOSINOPHILIC ESOPHAGITIS PATIENTS

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Introduction: Eosinophilic esophagitis (EoE) and Proton Pump Inhibitor-response esophageal eosinophilia (PPI-REE) present similar phenotypic appearance, similar histopathology but different response to antisecretory therapy. Indeed, current studies failed to observe clinical features able to distinguish the two entities. However, previous investigations did not systematically assess reflux-related symptoms by means of validated questionnaires. Recently, the GerdQ questionnaire has been validated in comparison with endoscopy and/or pH-testing for the diagnosis of gastro-oesophageal reflux disease (GERD).
Aims & Methods: We aimed to apply GerdQ questionnaire in patients with EoE and PPI-REE to assess whether a prospective and systematic evaluation of reflux symptoms may be helpful to distinguish patients with PPI-REE from those with EoE. Consecutive patients diagnosed with EoE and PPI-REE according to international criteria [a) presence of at least one typical symptom of esophageal dysfunction; b) at least 15 eosinophils per high-power field at mid/proximal esophagus; c) persisting or nor of eosinophils at mid/proximal esophagus after an 8-week PPI trial] prospectively completed a specific GERD-related questionnaire (GERDQ). The GerdQ questionnaire is a simple, self-administered and patient-centered questionnaire including six items[1]. A cut-off value higher ≥ 9 (range of 0–18) was considered diagnostic for GERD. For comparisons, a group of 27 patients with proven reflux disease was used.
Results: Fifty-two consecutive patients with histologically-detected eosinophilic infiltration (>15 eos/hpf) at mid-proximal oesophagus and with symptoms of esophageal dysfunction were included in the study. At the follow-up endoscopy plus biopsy, after 8 weeks treatment with twice-daily PPI, thirty-five (67%) patients were identified as having EoE, whereas 17 (33%) patients were diagnosed with PPI-REE. The two cohorts had similar dysphagia for solids (EoE 74% vs. PPI-REE 76%, $p = 0.651$), bolus impaction (66% vs. 70%, $p = 0.655$), but different heartburn (26% vs. 70%, $p < 0.001$), regurgitation (17% vs. 41%, $p = 0.014$) and chestpain (20% vs. 41%, $p = 0.012$). The overall GerdQ score was statistically lower in EoE vs. PPI-REE [1 (0-6) vs. 8 (2.5-11.25), $p = 0.004$]. When compared to control patients with GERD, both EoE and PPI-REE patients showed increased rate in dysphagia parameters, whereas EoE individuals reported less frequently heartburn (26% vs. 85%, $p = 0.001$), regurgitation (17% vs. 74%, $p = 0.001$) and overall GerdQ scores [1 (0-6) vs. 8 (6-12), $p = 0.001$] than control patients with GERD. In contrast, no difference was found comparing PPI-REE and control patients with GERD for heartburn, regurgitation and overall GerdQ score ($p = 0.176$, 0.192 and 1.000, respectively). Two EoE patients (6%), 8 PPI-REE patients (47%) and 15 control patients with GERD (55%) had a total score equal or above 9 (EoE vs. PPI-REE $p = 0.0001$, EoE vs. GERD $p = 0.002$ and PPI-REE vs. GERD $p = 0.757$).
Conclusion: The GerdQ is a useful complementary tool to distinguish patients with PPI-REE from those with EoE. The implementation of GerdQ could reduce the need for more aggressive therapies (i.e. topical steroids and specialised diets) and improve resource utilisation.

Reference

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P1129 MOTILITY ABNORMALITIES IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Patients (pat.) with eosinophilic esophagitis (EoE) often present with dysphagia and bolus obstruction. Whereas previous investigations using conventional manometry showed no significant changes, data about motility patterns from high resolution manometry (HRM) are rare.
Aims & Methods: To investigate motility patterns of pat. with EoE using HRM in correlation with clinico-pathological subtypes and in comparison controls without dysphagia and normal findings in HRM.
26 (10 female, 16 male, median age: 46.2 range 24-72 years) EoE pat. were included and investigated endoscopically, histopathologically and by HRM while on PPI medication. Diagnosis of EoE was confirmed according to the consensus guidelines 2011. HRM was performed in the upright position according to the Chicago classification system using 10 ml swallows.
26 controls were included (7 female, 19 male, median age: 51.0; range 22-78 years) from the GI lab database. Reason for HRM investigations was mainly clinically suspected GERD. Pat. with large hiatal hernia (>1.5 cm) were excluded. Results from HRM analysis were further correlated with the clinico-pathological EoE subtype (inflammatory (n = 17) vs. fibrotic (n = 9)).
Results: Pat. with EoE presented with significant higher resting pressure of the lower esophageal sphincter (LES) and upper esophageal sphincter (UES) (LES 34.0 vs. 26.3 mmHg, $p < 0.01$; UES: 160.3 vs. 98.3 mmHg, $p < 0.01$) compared with the control group. Further, pat. with EoE frequently showed larger breaks in the 20 mmHg isobaric contour (breaks 20 mmHg 2.5 vs. 0.7 cm, $p = 0.03$). Differences were seen especially within breaks according to the transition zone and to the middle of the peristaltic wavefront (breaks 20 mmHg transition zone 1.2 vs 0.5 cm, $p < 0.01$; breaks 20 mmHg middle 0.8 vs. 0.5 cm, $p < 0.01$. Larger breaks in the transition zone and in the middle of the peristaltic wavefront were also seen in the 30 mmHg isobaric contour by in pat. with EoE (breaks 30 mmHg 2.3 vs. 1.5 cm, $p = 0.01$; breaks 30 mmHg middle 1.1 vs. 0.3 cm, $p < 0.01$). These findings were not associated with a specific clinico-pathological subtype of EoE. For other parameters of HRM (IRP4s, intrabolus pressure, distal contractile integral, contractile front velocity, distal latency) no significant changes were found in pat. with EoE.
According to the Chicago classification system, the diagnosis in HRM varies between normal appearance (n = 11) to hypomotility (n = 10) and EGJ outflow obstruction (n = 5).
Conclusion: Esophageal motor dysfunction is a common phenomenon in pat. with EoE. Breaks of the contractile integrity with hypomotility and impaired bolus transit might explain the appearance of dysphagia in these pat., independant from clinico-pathological subtype.
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P1130 THE PREVALENCE OF GASTROESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS IN KOREA

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Introduction: In the western population, gastroesphageal reflux disease (GERD) is highly prevalent in patients with idiopathic pulmonary fibrosis (IPF). It has been hypothesized that chronic microaspiration due to GERD may cause repetitive subclinical injury to the lung leading to pulmonary fibrosis. Although some studies suggest proton pump inhibitor (PPI) was associated with slower decline of forced vital capacity (FVC), fewer acute exacerbation, decreased radiologic fibrosis and longer survival time in patients with IPF, these effects of PPI remain unclear.
Aims & Methods: The aims of this study were to investigate the prevalence of GERD in patients with IPF in Korean population and evaluate the relation with IPF and GERD or PPI. We retrospectively reviewed a chart of 917 consecutive adult patients with IPF at Seoul National University Bundang Hospital between April 2003 and March 2015.
Results: Mean age ± standard deviation (SD) was 75.5 ± 22.7 years, and 662 (72.2%) were males. Mean duration of follow up was 2.6 ± 2.8 years. Of the 917 patients with IPF, 145 (15.8%) were diagnosed with GERD. Of these 145 patients with GERD, 38 (26.2%) were diagnosed with erosive reflux disease by mucosal breaks and 107 (73.8%) had typical heartburn and/or acid regurgitation with minimal change or normal finding on esophagogastroscopy. In the univariate and multivariate COX regression harzard model, GERD (HR, 0.51; 95% CI, 0.28 – 0.94; $P = 0.030$), including azathioprine (HR, 1.71; 95% CI, 1.05 – 2.77; $P = 0.030$), age (HR, 1.04; 95% CI, 1.02 – 1.06; $P = 0.001$), initial FVC (HR, 0.98; 95% CI, 0.97 – 0.99; $P = 0.001$), hypertension (HR, 0.45; 95% CI, 0.27 – 0.76; $P = 0.003$) and pulmonary hypertension (HR, 4.48; 95% CI, 1.06 – 18.89; $P = 0.041$) was significantly associated with IPF-related mortality. However, there was an inversely association between GERD and IPF-related mortality. In the multivariate logistic regressive analysis, PPI (OR, 1.51; 95% CI, 1.00 – 2.28; $P = 0.048$), including peptic ulcer (OR, 1.71; 95% CI, 1.01 – 2.88; $P = 0.046$), prednisolone (OR, 1.64; 95% CI, 1.10 – 2.44; $P = 0.015$), N-acetylcysteine (OR, 2.32; 95% CI, 1.66 – 3.23; $P < 0.001$), initial FVC (OR, 1.03; 95% CI, 1.02 – 1.04; $P < 0.001$) and period of follow up (OR, 1.09; 95% CI, 1.02 – 1.15; $P = 0.006$) was associated with the aggravation of FVC. In a subgroup of patients with GERD and no history of peptic ulcer, PPI was also significantly associated with the aggravation of FVC (OR, 1.91; 95% CI, 1.32 – 2.76; $P = 0.001$).
Conclusion: In Korean patients with IPF, the prevalence of GERD was relatively lower than in western. Conversely, the IPF related mortality rate was significantly lower in patients with GERD than in patients without GERD. In contrast to prior researches, PPI maybe has no protective effect for aggravation of lung function and mortality.
Disclosure of Interest: None declared

P1131 WHAT IS THE FREQUENCY AND IMPACT OF GER AND MOTILITY DISORDERS IN COPD EXACERBATIONS?

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Introduction: Gastro-esophageal reflux disease (GERD) has been shown to worsen asthma control. But, the relationship between chronic obstructive pulmonary disease (COPD) exacerbations and GERD is less investigated, and there are conflicting results in literature.
Aims & Methods: We aimed to evaluate the presence of GERD and its symptoms in patients with COPD, and its impact on frequent exacerbation of COPD. We included 24 patients with stable mild-moderate stage COPD and 19 healthy volunteers as the control group. The patients using anti-reflux medication, non-invasive mechanical ventilation, and having acute exacerbation of COPD during previous 4 weeks were excluded. To all patients, we applied GERD symptom questionnaire, gastroscopy, high-resolution manometry (HRM) and ambulatory 24-hour pH-impedance study.
Results: Out of 24 patients with COPD, 23 were male. In control group, there were 12 male ($p = 0.14$). The mean age of the patients with COPD was 63 ± 10 years and 44 ± 10 years for the controls ($p < 0.001$). According to GERD questionnaire, only 5 (21.7%) patients had typical GERD symptoms**.** According to 24-hour pH-impedance study, mean DeMeester score was 38.1 in COPD group and 13.3 in the control group ($p = 0.005$). Seventeen (73.9%) patients in COPD group versus 5 (26.3%) patients in control group had pathologic acid reflux ($p = 0.002$). Symptom association probability (SAP) positivity rate was 17.4% ($n = 4$) in COPD group and none of the controls had SAP positivity ($p = 0.11$). Mean proximal extent rate of reflux (Z 17.cm) was 26.4 ± 12 % in COPD group. According to motility results, only 2 (20%) patients in the control group had minor motility disorder, the remainder was normal. On the contrary, 17 (70.8%) patients in COPD group had minor motility disorder, and 4 (16.7%) patients had major motility disorder ($p = 0.001$). Three (12.5%) patients in the COPD group were normal. In COPD group, 14 (58.3%) patients had weak peristalsis with large defects, 3 (12.5%) patients had weak peristalsis with small defects, 2 (8.3%) patients had jack hammer disorder, and 2 (8.3%) had distal esophageal spasm. Proximal extent of reflux was positively correlated with total number of exacerbation of COPD during a year time ($p = 0.039$, $r = 0.443$). Seven patients (30.4%) experienced frequent exacerbations of COPD in the previous year.
Conclusion: Gastroesophageal reflux is frequent in COPD, but only a qaurter of them did have typical reflux symthoms. Motility disorders and GERD was more common in COPD group compared with the controls. Proximal extent of reflux may trigger frequent exacerbation of COPD.
Disclosure of Interest: None declared

P1132 CHANGES IN BODY MASS INDEX ARE ASSOCIATED WITH RESOLUTION OF EROSIVE ESOPHAGITIS: A 5-YEAR RETROSPECTIVE COHORT STUDY

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Introduction: Obesity has been recognized as a risk factor for gastroesophageal reflux disease (GERD) and several studies demonstrated positive association between the body mass index (BMI) and GERD symptoms. However, literatures on whether BMI is related to the erosive esophagitis are scant.
Aims & Methods: This study aimed to investigate the effect of BMI changes on the erosive esophagitis. A retrospective cohort study was performed to assess the natural course of erosive esophagitis according to the changes in BMI. A total of 1126 cases of erosive esophagitis were included in this study. The degree of erosive esophagitis was measured by esophagogastroduodenoscopy and serially checked during the follow up period. A Cox proportional hazards model was used to investigate the hazard ratios (HRs).
Results: Of the total 1126 subjects, 906 (80.5%) cases were classified as LA-A, 209 (18.6%) as LA-B, and 11 (1%) as LA-C or LA-D at baseline. During the 5.6 years of mean follow up period, 645 (57.3%) cases showed resolution of erosive esophagitis. Subjects with decreased BMI were associated with resolution of erosive esophagitis compared to those with increased BMI (Hazard ratio [HR] 1.19, 95% confidence interval [CI] 1.02-1.39). Even after adjusting for sex, age, smoking, alcohol consumption, fatty liver status, level of education, and physical activity, the association between the BMI and erosive esophagitis was not attenuated (HR 1.22, 95% CI 1.01-1.46).
Conclusion: Decreasing BMI was significantly and independently associated with resolution of erosive esophagitis.
Disclosure of Interest: None declared

P1133 RISK OF ACUTE MYOCARDIAL INFARCTION IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE: A NATIONWIDE POPULATION-BASED STUDY

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Introduction: Gastroesophageal reflux disease (GERD) is a common disease which can cause troublesome symptoms and affect quality of life. In addition to esophageal complications, GERD may also be a risk factor for extra-esophageal complications. Both GERD and coronary artery disease can cause chest pain and frequently co-exist. A link between the two diseases has been suggested. However, the association between GERD and acute myocardial infarction (AMI) remain unclear.
Aims & Methods: The purpose of the study was to investigate the incidence of acute myocardial infarction in GERD patients and to compare it with that in an age- and sex-matched general population free of GERD. We also investigate the association between the risk of myocardial infarction and the use of acid suppressing agents in the cohort of GERD patients.
We identified patients with GERD from the Taiwan National Health Insurance database. The study cohort comprised 57,189 newly diagnosed GERD patients; 271,862 randomly selected age-, gender-, comobidity-matched subjects comprised the comparison cohort. Patients with any known prior coronary or peripheral arterial disease were excluded. Incidence of new AMI was studied in both groups.
Results: A total 1236 (0.5%) of the patients from the control group and 371 (0.7%) patients from the GERD group experienced AMI during years of follow-up. After Cox proportional-hazard model analysis, GERD was independently associated with increased risk of developing AMI (hazard ratio, 1.48; 95% confidence interval, 1.31–1.66, $p < 0.001$). Within the GERD group, subjects who were prescribed proton pump inhibitors (PPIs) for more than one years had decreased the risk of developing AMI, compared with those without taking PPIs (hazard ratio, 0.57; 95% confidence interval, 0.31–1.04, $p = 0.066$).
Conclusion: The large population-based study demonstrates an association between GERD and future development of acute myocardial infarction. Further prospective studies are needed to evaluate if anti-reflux medication may reduce the occurrence of acute ischemic event in GERD patients.
Disclosure of Interest: None declared

P1134 REFLUX ESOPHAGITIS IS POSITIVELY CORRELATED WITH FUNDIC GLAND POLYPS——A CASE-CONTROL STUDY

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Introduction: Fundic gland polyps (FGPs) is the most common type of gastric polyps, and was associated with chronic proton pump inhibitor (PPI) therapy. Most patient receive long-term PPI because of GERD, so whether FGPs is associated with PPI or GERD itself is a question.
Aims & Methods: This study aimed to elucidate the correlation between FGPs and GERD.
This case-control study included patients with FGPs (cases) and those without FGPs (controls). Consecutive patients (≥16 years of age) who agreed to complete a self-reported questionnaire and then undergo an upper endoscopy were enrolled. Patients who had undergone proton pump inhibitor (PPI) treatment for >8 weeks, had a history of familial adenomatous polyposis (FAP), or did not undergo the biopsy were excluded. The risks of sex, age, reflux symptoms, *Helicobacter pylori* infection, non-atrophic gastritis, reflux esophagitis, peptic ulcer disease, or upper gastrointestinal malignancy were assessed (odds ratio [OR] and its corresponding 95% confidence interval [CI]).
Results: A total of 4,250 patients were analyzed, including 288 with FGPs (cases) and 3,962 (controls) without FGPs. The patients with sporadic FGPs had an OR of 2.178 (95%CI, 1.613-2.941, $P < 0.001$), 1.037 (95%CI, 1.027-1.046, $P < 0.001$), 1.039 (95%CI, 0.998-1.082, $P = 0.065$), 0.970 (95%CI, 0.713-1.321, $P = 0.848$), 0.197 (95%CI, 0.121-0.321, $P < 0.001$), 1.993 (95%CI, 1.498-2.651, $P < 0.001$), 1.451 (95%CI, 1.031-2.043, $P = 0.033$), 0.782 (95%CI, 0.410-1.491, $P = 0.455$), and 0.265 (95%CI, 0.036-1.953, $P = 0.192$) for female gender, advanced age, BMI, GerdQ score ≥ 8, *H. pylori* infection, non-atrophic gastritis, reflux esophagitis, peptic ulcer disease, and upper gastrointestinal malignancy, respectively.
Conclusion: Reflux esophagitis is positively correlated with FGPs development. Female gender, advanced age, and non-atrophic gastritis are all risk factors of FGPs development. *H. pylori* infection is negatively correlated with FGPs development.
Disclosure of Interest: None declared

P1135 TUMOR MICROENVIRONMENT IN ESOPHAGEAL ADENOCARCINOMA: NUCLEAR P53 OVER-EXPRESSION IS ASSOCIATED TO LOW LYMPHOCYTE ACTIVATION

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Introduction: Esophageal adenocarcinoma (EAC) microenvironment is characterized by lack of cytokines with anti-cancer effect and by high expression of immuno-suppressive factors. HER2 over-expression is associated to worse

prognosis in esophageal adencarcinoma and it is related to the depth of invasion, nodal and distant metastasis. Similarly, p53 overexpression is associated to poor disease free and overall survival.
Aims & Methods: Our aim was to evaluate the possible relationships between HER2 and p53 overexpression in esophageal cancer and the antigen presenting cells (APC) and lymphocyte function in esophageal cancer.
Mucosa samples from cancer and from healthy esophagus were obtained during esophagectomy from 64 adenocarcinoma. Frozen samples were analysed with Real Time qPCR for costimulatory molecules (Cd80, Cd86), and lymphocytes activation (Cd38, Cd69) genes expression. Immunohistochemistry for HER2 and nuclear p53 expression, CD8 and NK cells cytolytic activity (CD107a) of tumor infiltrating lymphocytes and for CD80 was performed. Non parametric statistics was used.
Results: In patients with EAC, HER2 overexpression, CD80 and CD86 expression and CD8 + lymphocyte infiltration and activation were not different than in those who without it. HER2 overexpression correlated inversely with the presence of necrosis within the tumor (tau = -0.18, p = 0.46). In patients with EAC nuclear p53 overexpression, CD69 mRNA expression within the tumor was lower than in those without it (p = 0.038 and p = 0.014, respectively). On the contrary, CD80 and CD86 expression and CD8 + lymphocyte infiltration were not different in the two groups.
Conclusion: In EAC, HER2 overexpression does not seem to affect immune surveillance mechanisms based on CD80-CD28 signaling and CD8 lymphocyte activation. Its effect on invasiveness seemed to be more related on tumor cell immortalization. On the other hand, nuclear p53 overexpression within the tumor seem to inhibit lymphocyte activation suggesting a possible role in tumor immune modulation.
Disclosure of Interest: None declared

P1136 THE DEVELOPMENT OF A NOVEL ENDOSCOPIC ORTHOTOPIC TUMOUR MODEL FOR OESOPHAGEAL CANCER

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Introduction: The incidence of oesophageal adenocarcinoma (OAC) continues to rise rapidly. A clinically relevant animal model of OAC is needed to help study the effectiveness of novel therapeutic strategies for OAC. Current animal models have many limitations. Models that involve the injection of cells into the flanks of rodents do not replicate the native environment of OAC. Surgical models producing permanent biliary reflux that can lead to cancer are limited by the need for highly skilled surgical techniques, difficult reproducibility and significant morbidity to the animals involved. We describe a novel orthotopic tumour model for OAC. Our model is based upon the injection of tumour cells into the rodent oesophagus under direct endoscopic visualisation.
Aims & Methods: Two human tumour cell lines were used – OAC (OE19) and colon adenocarcinoma (HT29). Both lines were stably transfected to express luciferase and maintained in 5% CO2 at 370 C. 6-8 week-old female nude athymic rats (RNU Rat) were used for all experiments. A high-resolution diagnostic endoscope was used to perform all endoscopic procedures. Animals were anaesthetised using Isoflurane with concomitant oxygen given. Under direct visualisation, OE19 or HT29 tumour cells were injected. Immediately after endoscopy, 1ml of D-Luciferin (20mg/ml) was injected i.p. to follow luciferase-expressing OE19/HT29 tumour implantation. After 15 minutes, rats were inserted into a whole body cooled charged-coupled device (CCD) camera Photon Imager system and images obtained. All animals had Bioluminescent imaging (BLI) and endoscopy performed regularly to look for evidence of tumour growth.
Results: Implanted tumour cells were detected immediately after injection using BLI. Weekly, non-invasive BLI and regular endoscopic observation detected successful orthotopic tumour growth. Histological tissue samples confirmed the presence of tumour ulcerating the overlying squamous mucosa and infiltrating into, and through, the muscularis propria. This mirrors closely the behaviour of a primary human OAC.
Conclusion: We have developed a novel, more clinically relevant, orthotopic tumour model for OAC. By utilising rodent gastroscopy, our model replicates the native environment in which OAC grows and provides an opportunity for us to better understand the natural history of OAC in a manner that confers considerably less morbidity to animals than current models allow.
Disclosure of Interest: None declared

P1137 HOW OFTEN IS UPPER GASTROINTESTINAL CANCER MISSED DURING ENDOSCOPY? DATA FROM A DISTRICT GENERAL HOSPITAL (DGH)

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Introduction: Recent studies report between 6 to 14% of patients with a gastric and oesophageal cancer had an oesophagogastroduodenoscopy (OGD) up to three years prior to diagnosis that did not report malignancy. This has prompted a national effort to improve the quality of OGD. We have examined our records from a DGH which serves a population of 500,000 patients to assess how often cancers could be missed and whether there are any factors which are associated with this. We define a possible missed cancer as one where there was a previous endoscopy within the last 3 years.
Aims & Methods: Our aim is to achieve quality improvement to OGD via the analysis and modulation of contributing variables. We retrieved computerised records of 65 patients diagnosed with gastric and oesophageal cancer over a year from between April 2013 and April 2014. We investigated our endoscopy database for whether the patients had endoscopies within the last 3 years. We reviewed the previous endoscopies for a number of factors including the age of the patient, the grade of the endoscopist, the finding at prior endoscopy, the number of biopsies taken and the pathology report at any noted abnormal sites, the use of sedation for the patient, the comfort scores and the urgency of the procedure. We then compared the results of this analysis with a comparison group of all the patients who had been diagnosed as having oesophageal or gastric cancer at their first endoscopy.
Results: There were 48 oesophageal cancers and 17 gastric cancers. In 6 (9.2%) of these cases there had been an endoscopy within the preceding 3 years. The average age of patients in the missed cancer group and comparison group were 71 and 69.6 respectively.
A greater proportion of patients in the missed cancer group were sedated (100% vs 69%). A smaller proportion of patients in the missed cancer experienced moderate or severe discomfort (0% vs 13.6%). In the missed cancer group a greater proportion of patients were on the emergency endoscopic bleed list (33% vs 7%). In both the missed cancer and the comparison group the proportion of endoscopies performed by Consultant Gastroenterologist was approximately 67%.
An analysis of the missed cancer cases found that in all 6 cases an abnormality had been noted in the area where the cancer was subsequently found. 3 of these cases had Barrett's oesophagus in all cases multiple biopsies were performed and interval repeat endoscopy was arranged. In one case the endoscopist described a benign oesophageal stricture and did not biopsy, repeat biopsy 8 month later demonstrated malignancy. In 2 cases inflammation was noted at the lower oesophagus and stomach; firstly in the form of a malignant 4cm GOJ polyp and secondly in the form a malignant gastric ulcer. In the oesophagitis case no biopsies were taken and in the gastritis case biopsies suspected Iron pill gastritis.
Conclusion: In a small but important number of patients we potentially miss cancer at OGD. In our analysis the performance of the OGD for acute haemorrhage and not taking a biopsy were associated with missing cancers. There did not seem to be a negative association with the use of sedation, the discomfort of the patient or seniority of endoscopists. We will be continuing to monitor our 'missed cancer' rate and promote quality OGD by emphasising the importance repeating endoscopies limited by bleeding and the sampling of abnormal sites.
Disclosure of Interest: None declared

P1138 COMPARISON OF THE CLINICOPATHOLOGICAL CHARACTERISTICS AND THE SURVIVAL OUTCOMES BETWEEN THE SIEWERT TYPE II/III ADENOCARCINOMAS

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Introduction: In the recent decades, the incidence of adenocarcinomas of the esophagogastric junction (AEGJ) has significantly increased. There are some disagreements regarding its pathogenesis, classification and approach. According to the Siewert classification, there are 3 types of AEGJ, depending if the lesion's epicenteris located 5cm above the esophagogastric junction (EGJ) (I), in the EGJ (II) or 5cm below it (III). The protocol of our institution establishes that AEGJ type I should be treated as esophageal cancer and the AEGJ II/III as gastric cancer, with similar treatment protocol.
Aims & Methods
Aim: To analyze the clinical characteristics and survival outcomes in AJEG II and AJG type III tumours.
Methods: Retrospective analysis of consecutive patients with EGJ II/III tumours referred from Mar/2009 to Jun/2014 followed by our institution's multidisciplinary team. Clinicopathological characteristics and survival were analyzed. Statistics: chi-square test (categorical data). Kaplan–Meier curves/log-rank test (survival outcome), and log-rank test (statistical significance).
Results: A total of 109 patients (EGJ II n = 50; EGJ III n = 59) were included , 75 men, with a mean age of 66 ± 13 years. Demographic features were comparable between the two groups.
Eighty five patients had intestinal type adenocarcinoma and 24 had poorly cohesive carcinoma. This last histologic pattern was more frequent in EGJ III tumors (p = 0.037). AEJG cancer staging: I (7/109), II (46/109), III (20/109) e IV (36/109). Eleven patients were submitted to surgery only, 26 underwent surgery plus perioperative chemotherapy, 16 completed neoadjuvant chemotherapy before the surgery and palliative treatment in 54 patients. There were no differences regarding staging and treatment between the two groups.
The degree of tumor regression induced by chemotherapy and evaluated in the surgical specimen was similar between the groups (p = 0.589). For EGJ II and EGJ III tumors, the 36 months overall survival rate was 28.9% versus 29.4 %, respectively (p = 0.733). In the subgroup of patients treated with curative intention, the 36 months overall survival rate was 46.7% versus 49.8 %, respectively (p = 0.90).
Conclusion: In our series, there were no differences in clinicopathological characteristics and survival outcomes in EGJ II and EGJ III tumors, except for histological pattern with poorly cohesive carcinoma being more frequently

found in EGJ III tumors. We consider that despite a possible distinct pathogenesis, these tumors have similar clinical behavior.
Disclosure of Interest: None declared

P1139 EFFICACY AND TOXICITY OF SECOND-LINE CHEMOTHERAPY IN PATIENTS WITH ADVANCED OESOPHAGEAL SQUAMOUS CELL CARCINOMA PROGRESSING AFTER A FIRST LINE OF 5-FLUOROURACIL AND PLATINUM-BASED THERAPY: AN AGEO RETROSPECTIVE MULTICENTRIC STUDY

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Introduction: 5-fluorouracil (5-FU) and platinum-based chemotherapy (CT) is considered as a standard of care in first line treatment of metastatic oesophageal squamous cell carcinoma (SCC). Few data, essentially with taxane regimens, are available on the efficacy and toxicity of a second-line treatment. We therefore conducted a study to assess the efficacy and toxicity of second-line CT in such patients after progression during first line CT with 5-FU plus platinum.
Aims & Methods: Between January 2003 and December 2013, every patient from eleven medical centers with a metastatic or unresectable locally advanced oesophageal SCC who received a second line therapy after progression while on 5-FU and platinum (Cisplatin or Oxaliplatin) CT were retrospectively included. We collected and compared the data on overall survival (OS), progression free survival (PFS) and toxicity, using the NCI classification, from the beginning of the second-line for all patients and specifically for patients treated with Taxane (Paclitaxel or Docetaxel) or Irinotecan-based regimens.
Results: 68 patients (OMS 0-1 : 87%) were included : 51 (75%) received a second line CT with a taxane-based (22) or irinotecan-based regimen (29), and 17 received another CT regimen. Among these 51 patients, the median OS was 7.9 months and median PFS were 4.9 months. The 22 patients treated with Taxane had an OS and PFS of 7.5 months and 3.9 months respectively. The patients treated with Irinotecan-based chemotherapy had an OS and PFS of 8.7 months and 5.4 months respectively. The difference was not statistically significant between the two groups of patients ($p = 0.28$). One year survival rates was 32% for all patients (41.3% for Irinotecan-based CT group and 14.4% for Taxane group). The rates of severe toxicity (grade 3-4) and discontinuation of treatment related to toxicity were similar in the two groups. No toxic death was observed.
Conclusion: In this study, patients treated with a second-line therapy after progression under 5-FU and platinum CT, achieved a median OS of 7.9 months. Irinotecan and taxane based regimens showed no major differences in terms of toxicity and efficacy. These two types of regimen could be used in patients with good performance status. Prospective studies are necessary to determine which treatment would be the most appropriate.
Disclosure of Interest: None declared

P1140 A COMPARATIVE STUDY COMPARING A NEW ANTI-REFLUX STENT TO A CONVENTIONAL OPEN STENT IN THE PALLIATION OF DISTAL OESOPHAGEAL CANCER

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Introduction: Oesophageal cancer is the sixth most common cause of death from cancer in the United Kingdom and worldwide. It accounts for 7,701 deaths in the UK in 2012.[1] Oesophageal cancer has a poor prognosis with a 5 year survival rate of 10-15%.[2,3] Unfortunately, greater than 50% of patients have unresectable cancers at presentation and most of these will go onto develop progressive dysphagia.[4]
There are various therapies to palliate dysphagia, oesophageal stenting has now become the main treatment option of choice for palliative oesophageal malignancy. Oesophageal intubation with a self-expanding stent is the treatment of choice for stenosing tumours, where rapid relief of dysphagia in a one stage procedure is desirable.[5] There have been various stent designs marketed that incorporate an anti-reflux valve stent with a view to reducing this complication. Currently the British Society of Gastroenterology concluded that anti-reflux stents confer no benefit above standard stents.[5]
Aims & Methods: To compare a new anti-reflux stent with a conventional open stent in the palliation of patients with distal oesophageal cancer. This is a prospective study involving 40 patients with cancer involving the gastro-oesophageal junction. All patients will have been deemed inoperable within the local multi-disciplinary team meeting. Patients will receive either an anti-reflux stent (cardia-valve stent, Premier endoscopy) or a conventional open stent (ultraflex, Boston Scientific). All stents will be partially covered and placed across the gastro-oesophageal junction.
Quality of life will be measured and analysed using the oesophageal module European Organisation into Research and Treatment of Cancer questionnaire (EORTC QLQ-OES18). The questionnaires will be recorded by the attending endoscopist/physician at weeks 0 and 1. Differences between groups will be statistically evaluated by the Mann-Whitney test.
Results: There were 15 Ultraflex stents and 8 Cardiovalve stents that were followed up. Baseline EORTC QLQ-OES18 showed no significant differences in baseline scores (the Z-Score is -0.7423, the p-value is 0.4593).
At week one follow up there was no significant differences in the EORTC QLQ-OES18 between the two groups. The Ultraflex group had a EORTC QLQ-OES18 increase score of 38 compared with a 0 increase in overall score in the Cardiovalve group (The Z-Score is -0.3151. The p-value is 0.74896).
Conclusion: There was no significant differences in EORTC QLQ-OES18 scores between the two groups at week one suggesting that the stents appeared have similar quality of life profiles at week one post insertion. This is a small study and longer time follow up data is currently ongoing with 3 month follow up data of 40 patients currently being analysed.

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P1141 COMPARISON BETWEEN ARGON PLASMA COAGULATION AND SELF-EXPANDABLE METAL STENT PLACEMENT IN THE PALLIATIVE TREATMENT OF INOPERABLE OESOPHAGEAL CANCER

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Introduction: Self-expanding metal stents (SEMS) are the main palliative modality used in inoperable oesophageal cancer[1]. Other palliative options, including Argon plasma coagulation (APC), have been used and found effective[2]. Comparative studies between those modalities are scarce and the preference of SEMS as the palliation modality of choice is not based on solid evidence.
Aims & Methods: The aim of this study was to assess the relative efficacy of SEMS and APC in inoperable oesophageal cancer palliation, in terms of survival. This was a single centre, retrospective analysis of all patients ($n = 233$) with inoperable oesophageal cancer not receiving chemo-radiotherapy, treated with SEMS ($n = 163$) or APC ($n = 70$) as primary palliation modalities, between January 2000 and July 2014. Patient characteristics were retrieved from hospital records and Charlson Comorbidity Score (CCS) was calculated. Kaplan-Meier curves were created for each treatment modality and survival intervals were compared by the log-rank test separately for stage III and IV disease. A further analysis was performed after excluding patients surviving less than a month in order to minimize any potential selection bias.
Results: Patients having APC as primary treatment were older (median: 80 Vs 76 years, $p = 0.01$) and had a higher CCS (median 1 Vs 0, $p = 0.02$) compared to SEMS, but still had a significantly better survival. Median survival for patients treated with APC and SEMS was 257 (Interquartile range-IQR: 137, 414) and 151 (IQR: 61, 241) days respectively in stage III disease while it was 135 (IQR: 43, 238) and 70 (IQR: 32, 148) days respectively in stage IV disease. Both differences were statistically significant (0.02 and 0.05 respectively). After excluding patients not surviving more than a month, median survival in stage III patients was 257 (IQR:137,414) days for APC, compared to 162 (IQR: 100,285) for SEMS and in stage IV disease, median survival was 166 (IQR: 111,243) days for APC compared to 97 (IQR: 59,164) for SEMS. The difference was statistically significant in stage III ($p = 0.04$), whereas it was not in stage IV ($p = 0.07$).
Conclusion: Thsi study provides evidence that using APC as the primary palliation modality may significantly improve survival compared to SEMS in inoperable oesophageal cancer when patients are not candidates for chemo-radiotherapy. Further prospective studies to confirm those findings are needed.

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P1142 LEARNING CURVE FOR DETECTING SUPERFICIAL HEAD AND NECK CANCER DURING SURVEILLANCE USING NARROW BAND IMAGING ENDOSCOPY

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Introduction: Narrow-band Imaging (NBI) is effective in detecting superficial head and neck squamous cell carcinoma (HNSCC) in patients with esophageal squamous cell carcinoma (ESCC), and we introduced the surveillance for HN region using NBI for all patients with ESCC before treatment. However, skilled endoscopic technique is necessary to survey pharyngo-laryngeal region and detect the superficial cancer during upper GI endoscopy, and detection rate of superficial cancer by beginner endoscopists is unknown. The aim of our study was to compare the performance in detecting HNSCC between beginner endoscopist and expert, and investigate detection leaning curves in beginner.
Aims & Methods: ESCC patients who fulfilled the following criteria, and underwent surveillance for pharyngo-laryngeal region using per oral endoscopy with NBI between January 2011 and March 2015 were recruited from our database, (1) initially diagnosed ESCC; (2) initial endoscopic examination with NBI in our hospital; (3) no history of any HNSCC; (4) no synchronously HNSCC was detected in previous hospital. All patients provided written informed consent before examination.
We compared the detection rate of HNSCC during initial endoscopic examination between beginner (less than 1 years' experience of surveillance) and expert (at least 3years' experience), and between the first 3 months of beginner 's first year (period A) and 3 to 12months (period B).
Results: 747 patients (median age 68) were enrolled, and total 36 endoscopists (26 beginners and 10 experts) performed the surveillance endoscopic examination. A total of 63 HNSCCs were detected in 47 patients (6.3%) and all of the lesions were superficial cancer. The lesions were located in hypopharynx ($n = 39$), oropharynx ($n = 19$), and larynx ($n = 5$). HNSCC detection rate was 4.4% in beginner and 7.1% in expert, ($p = 0.19$). No beginner could detect superficial HNSCC in the first 3 months (period A), but detection rate was 5.9% during period B ($p = 0.069$). In period A, detection rate of beginners was significantly lower than that of expert (0% vs 7.1%, $p = 0.040$), however, there was no significantly deference between beginners and experts during period B (5.9% vs 7.1%, $p = 0.73$).
Conclusion: Detection of superficial HNSCC during endoscopic surveillance with NBI might be difficult for novice endoscopists. However, detection rate was improved and almost as same as an expert after 3 months of intensive endoscopic training.
Disclosure of Interest: None declared

P1143 CLINICAL OUTCOMES OF PERORAL ENDOSCOPIC MYOTOMY FOR ACHALASIA DEPEND ON MANOMETRIC SUBTYPE

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Introduction: Peroral endoscopic myotomy (POEM) is known to be safe and effective endoscopic surgery compared with surgical myotomy for achalasia patients. A higher percentage of patients with type II achalasia successfully treated with laparoscopic Heller myotomy than patients with types I and III achalasia.
Aims & Methods: We evaluated whether manometric subtype was associated with response to treatment in a patients treated with POEM. Esophageal pre-treatment manometry data were collected from 53 cases that was performed POEM from November 2011 to August 2014 at two tertiary referral centers. Manometric tracings were classified according to the 3 Chicago subtypes.
Results: Among 53 cases, 35 type 1, 8 type 2 and 10 type 3 achalasia were included. There was no difference in pre-POEM Eckardt score, basal LES pressure, and integrated relaxation pressure (IRP) between type 1, type 2 and type 3 group (6.1 ± 3.9 vs. 8.4 ± 3.6 vs. 6.6 ± 3.4; $p = 0.215$, 27.3 ± 29.8 vs. 39.7 ± 12.3vs. 34.1 ± 32.8mmHg; $p = 0.089$, and 23.4 ± 29.6 vs. 30.1 ± 14.9vs. 19.2 ± 28.8mm Hg; $p = 0.709$). All patients showed a significant improvement in Eckardt score after POEM during median follow-up of 16 months (6.1 ± 3.9vs. 0.6 ± 2.4; $p < 0.001$, 8.4 ± 3.6 vs. 0.6 ± 1.4; $p = 0.008$, 6.6 ± 3.4vs1.0 ± 2.0; $p < 0.001$). But there was difference in decreased degree of Eckardt score between type 1, type 2 and type 3 group ($p = 0.637$), LES pressure was significant decrease only for type 2 group (23.5 ± 16.3 vs.16.1 ± 12.4; $p = 0.113$, 39.7 ± 12.3 vs. 19.5 ± 4.4;$p = 0.029$, 34.1 ± 32.8 vs. 16.8 ± 17.2; $p = 0.421$). IRP score was significant decrease only fortype 1 group (23.4 ± 18.3vs.11.0 ± 9.5;$p = 0.014$, 30.1 ± 14.9vs. 12.50 ± 7.5; $p = 0.057$, 19.0 ± 29.0vs. 11.6 ± 12.3; $p = 0.886$).
Conclusion: POEM showed good clinical outcomes in any manometric subtype. In the future, large prospective study is needed to confirm that POEM can be considered as standard treatment in any subtype of achalasia patients.

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P1144 METABOLIC TUMOUR WIDTH PREDICTS POSITIVE CRM IN OESOPHAGEAL CANCER

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Introduction: Circumferential resection margin (CRM) involvement is universally regarded as a poor prognostic indicator in both oesophageal and rectal cancer surgery, but prediction of threatened CRM in the former is challenging. MRI accurately predicts CRM involvement in rectal cancer, but has proved technically difficult in oesophageal cancer.
Aims & Methods: The study aims to test the association between PET/CT defined tumour variables and CRM positivity. Prospectively collected data on 95 consecutive patients (median age 65 (range 24-82), 74 male, 85 adenocarcinoma, 9 SCC, 1 HGD) with FDG-avid oesophageal and junctional tumours, initially treated with surgical management +/- neo-adjuvant therapy were included. Five PET/CT defined variables; SUVmax, metabolic tumour length (MTL), metabolic tumour width (MTW), metabolic tumour volume (MTV) and total length of nodal disease (NLoD), were entered into a binary logistic regression model. Primary outcome was CRM positivity.
Results: Twenty-five patients had surgery alone, 65 received neo-adjuvant chemotherapy and 10 received neo-adjuvant chemo-radiotherapy. CRM was positive in 57.9%. A statistical trend was observed between MTW and CRM involvement in all patients (HR 0.68 (95% CI 0.44-1.04); $p = 0.07$). MTW was independently and significantly associated with CRM positivity in 60 patients treated with neo-adjuvant chemotherapy (HR 0.53, 95% CI 0.31-0.92, $p = 0.02$). There was a significant difference between the upper and lower quintiles in this group (mean MTW 0.97 vs 3.93cm, $p < 0.001$).
Conclusion: MTW of oesophageal tumours can predict CRM positivity. This knowledge further informs the MDT, suggesting neo-adjuvant chemo-radiotherapy should be given prior to surgery.
Disclosure of Interest: None declared

P1145 METFORMIN USE DURING TREATMENT OF RESECTABLE ESOPHAGEAL CANCER PATIENTS IS NOT ASSOCIATED WITH BETTER OUTCOMES

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Introduction: Metformin use has been associated with a dose-dependent increased response to neo-adjuvant chemo(radio)therapy in esophageal cancer patients. However, no association between metformin use and overall survival (OS) has been reported yet. The aim of our study is to investigate the effect of metformin use on pathological response as well as OS and disease-free survival (DFS) in patients with resectable esophageal cancer.
Aims & Methods: Between March 1994 and September 2013 all patients undergoing an esophagectomy for esophageal and gastro-esophageal junction cancer after neo-adjuvant chemo(radio)therapy with curative intent were included in a prospective database. A complete pathological response was defined as ypT0N0M0, Mandard 1. Kaplan-Meier curves with log rank testing were performed for OS and DFS.
Results: Four hundred and sixty-one patients were included with a median follow-up of 24 months (range 1-228); 43 patients were diagnosed with diabetes mellitus type II (9.3%) of whom 31 patients used metformin (6.7%). A total of 95 (20.4%) patients had a complete pathological response, which did not differ between metformin users (19.4%) and non-metformin users (20.5%, $p = 0.14$). We observed neither a statistically significant difference between metformin users and non-metformin users for median OS (20.8 vs 24.4 months, $p = 0.840$), nor for median DFS (20.5 vs 20.3 months, $p = 0.845$). A subgroup analysis in patients with diabetes mellitus type II showed a non-significant increase in median OS for metformin users (43.6 months) compared to non-metformin users (21.4 months, $p = 0.237$). For median DFS a similar non-significant increase was observed for metformin users (36.1 months) compared to non-metformin users (20.2 months, $p = 0.163$).
Conclusion: The use of metformin did neither result in in higher pathological response rates nor in an improved OS or DFS compared to non-metformin use in patients receiving neo-adjuvant chemo(radio)therapy for resectable esophageal cancer. In contrast to what has been postulated for other tumor types, metformin may not have a beneficial effect in esophageal cancer.
Disclosure of Interest: None declared

P1146 CLINICAL COMORBIDITIES FOR ESOPHAGEAL CANCER IN THE LAST THREE DECADES IN ITALIAN PATIENTS

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Introduction: The incidence of esophageal cancer (EC) has been increasing worldwide during the last few decades. The aim of this study was to investigate the variation in clinical comorbidities in a large cohort of Italian EC patients in the same period.
Aims & Methods: A retrospective cohort study was performed using a prospectively collected database. All patients presenting with a diagnosis of primary EC at the Center for Esophageal Diseases located in Padua between January 1, 1980, and December 31, 2011, were included in the study. Data on local comorbidities (reflux disease, Barrett esophagus, previous caustic ingestion, achalasia, peptic disease), previous regional neoplasms, radio-induced tumors, previous distant neoplasm and systemic comorbidities. Joinpoint regression analysis was performed to estimate annual percentage changes (APCs).
Results: A total of 4440 patients were included in the present study. Reflux rate increased until 1997 (APC 7.57%, $p < 0.01$) and then leveled (APC -3.18%, $p = 0.10$). The rate of patients presenting with Barrett esophagus increased from 1.4% in the first period to 6.3% in the last period (APC 6.95%, $p < 0.01$). Gastric ulcer rate started decreasing since 2004 (APC -18.93%). The rate of previous local neoplasm increased until 1995 (APC 8.47%) and then leveled (APC -3.11%). The rate of radio-induced tumors varied from 0% in the first period to 7.1% in the last period, without significant trend (APC 5.37%,). Few patients (less than 1% overall) had achalasia or previous caustic ingestion. The rate of patients presenting with a previous distant neoplasm increased from 3.0% in the first period to 7.8% in the last period (APC 2.97%, $p < 0.01$). Advanced liver disease and pulmonary disease decreased over time (APCs -2.94% and -1.94% , respectively; both $p < 0.01$), whereas hypertension, diabetes and cardiac disease increased (APCs 6.56% , 2.11% and 2.56%, respectively; $p < 0.01$).
Conclusion: In the last three decades patients with EC showed significant and clinically meaningful changes in their local and systemic comorbidities. These chages should be taken into account when dealing with such patients.
Disclosure of Interest: None declared

P1147 ENDOSCOPY VS. SURGERY FOR HIGH-RISK EARLY ESOPHAGEAL CANCER

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Introduction: Endoscopic treatment is a standard therapeutic option for patients with early esophageal cancer (EAC) with mucosal invasion (T1a). For patients with "high-risk" T1a cancer (e.g. advanced grading (G3/G4), invasion to lymphatic (L+) or blood vessels (A+), high degree of tumor cells dissociation (TCD 3) and for patients with T1b cancer (with any sm invasion)), surgery still remains a standard therapeutic approach.
Aims & Methods: To compare outcomes of endoscopic vs. surgical treatment in patients with high-risk EAC. High-risk cancer was defined as any cancer with submucosal (sm) invasion or mucosal cancer with at least one of the following: G3/G4 differentiation, invasion to blood (A+) and/or lymphatic (L+) vessels and high tumor cells dissociation (TCD3).
A single-center study. Patients with EAC underwent endoscopic resection (ER) or endoscopic submucosal dissection (ESD). Patients with high-risk EAC were referred for surgery if there were no contraindication such as advanced age, multiple co-morbidities, patient's refusal, etc. All other patients continued (if necessary) with endoscopic treatment which consisted of further sessions of ER (or ESD) and/or radiofrequency ablation (RFA). After treatment, all patients have been followed up for a median of 22 months (range 48-119).
Results: A total of 57 patients (50 men, 7 women, median age 63) underwent endoscopic treatment for EAC (47x adenocarcinoma, 9x squamous carcinoma, 1x duplicity (EAC + SCC)). Twenty-three patients (40%) had low-risk T1a cancer, and endoscopic treatment was considered curative. The remaining 34 patients (60%) had high-risk EAC (sm invasion: 56%; T1a cancers with "high-risk" features: 44%).
Eleven "high-risk" patients (32%) were referred for esophagectomy and 23 patients (68%) continued with endoscopic treatment. In one patient, the planned esophagectomy was finally not performed due to tumor generalization found during the operation. Among 10 patients who underwent esophagectomy, local residua of malignancy were present in only one (10%) patient and lymph node metastases have not been detected in any of these patients. During the follow-up, none of the patients who underwent esophagectomy has shown signs of generalization or a tumor relapse and no patient died.
In 23 "high risk" patients undergoing endoscopic treatment, local complete remission of neoplasia was achieved in all of them after a median of 2 treatment sessions. Neither local recurrence of neoplasia nor tumor generalisation have been observed so far, and there was no cancer related mortality.
Conclusion: Endoscopic therapy appears to be an effective alternative to esophagectomy in patients with "high-risk" early esophageal cancer.
Disclosure of Interest: None declared

P1148 INSTRUMENTAL PERFORATION IN ESOPHAGEAL CANCER : NONOPERATIVE TREATMENT WITH SELF-EXPANDABLE COVERED METAL STENTS

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Introduction: The standard approach to esophageal perforations consists of conservative treatment or surgery. Recent studies have suggested that stent-grafting may improve the treatment outcome of patiens with oesophageal perforation. However in neoplastic disease there still lack of evidence.
Aims & Methods: To assess the efficacy of endoscopic management of instrumental esophageal perforations in patients with neoplastic oesophagus using selfexpandable covered metal stents.
This is a prospective single-center study of 16 consecutive oesophageal cancer patients with acute therapeutic endoscopy perforation suffered during a dilatation of a neoplastic stenosis.
The mean age was 78 years, 8 patients (50%) were female, in 14 (87.5%) the tumor was located in the thoracic oesophagus and 2 (12.5%) in the cardioesophageal region. The histological type was squamous cell carcinoma in 14 (87.5%) and adenocarcinoma in the remaining 2 (12.5%). In 15 patients the diagnosis was made inmediately after the dilatacion by routine endoscopic and radiological post procedure review and in one case (6.3%), the perforation was diagnosed 22 hrs later. In the first 10 patients a fully covered self-expanding 18 mm in diameter metallic stent was inserted. In the remaining 6, in order to prevent migration, a 22 mm in diameter partially covered prosthesis was used. The outcome of patients and immediate complications (up to 24 hrs post procedure), early (30 days) and late (over 30 days) were studied. Patients were monitored up to 90 after the perforation.
Results: The prosthesis insertion was successful in all patients. In 6 (37.6%) immediate morbidity associated with the perforation was found: 3 (18.8%) subcutaneous emphysema and 3 (18.8%) transient fever. The presence of early complications was found in 3 cases (18.8%), 2 of them developed a pleural effusion and a slight mediastinitis and one pleural fistula secondary to esophageal stent migration (18 mm completely covered). The prosthesis remained in place until the end of follow up in the remaining 15 patients (93.5%).
Oral intake was restarted by a mean of 3.6 ± 1.2 days (range 1 – 7) and mean duration from the stent insertion to discharge was 8.3 ± 2.4 days (range : 2 – 21). At the end of follow up, the 15 patients who survived had recovered the hability of oral feeding.
One patient died 19 days post procedure, as a result of pleural fistula secondary to a fully covered 18 mm esophageal stent migration, giving 30 day a mortality rate for this series of 6.3%.
Conclusion: The use of self-expanding metal stent for the treatment of esophageal instrumental perforations in patients with esophageal cancer is a safe and effective method, with low morbidity, adequate recovery of oral intake and short hospital stay.
Disclosure of Interest: None declared

P1149 RELATION BETWEEN THE LOCATION OF SUPERFICIAL BARRETT'S ESOPHAGEAL ADENOCARCINOMA (S-BEA) AND THE DIRECTION OF DUODENOGASTRIC REFLUX

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Introduction: s-BEAs in Barrett's esophagus are frequently found in the right wall of the esophagus.[1)] Why are they located on the right wall? Tongue-like SSBE was more frequent in the right anterior wall (in the 12 to 2 o'clock position) than at other locations ($^*P < 0.05$).[2)] Okita et al reported using pH monitoring with 8 channel sensors and patients with non-erosive reflux esophagitis (NERD) and reflux esophagitis had radial asymmetric acid exposure that was predominanton the right wall of the distal esophagus.[3)]
Aims & Methods: This study revealed the relation between the location of s-BEA and the direction of duodenogastric reflux.
33 s-BEA patients were enrolled in this study. 28 patients (28/77; 74.8%) had long segment Barrett's esophagus (LSBE), the others (5/33; 15.2%) had SSBE. The invasion depth in 18 s-BEAs was mucosal cancer (18/33; 54.5%), the remaining was submucosal cancer (15/33; 45.5%). We performed 24-h pH monitoring study before s-BEA was treated by ESD or operation. All patients took PPI. This catheter has 8 pH sensors circumferentialy arrayed at the same level of the device (developed by Shimane Medical University and Star-medical). The catheter was inserted transnasally into the esophagus and positioned 2cm above the squamo-columnar junction (SCJ). All 33 s-BEA patients took the position for 24 hours every day as same as possible and they didn't take special position by themselves. This device didn't rotate in their every position. We measured the maximal total duration of acid ($pH < 4.0$) and alkaline ($pH > 8.0$) reflux in all 33 s-BEA patients. We evaluated the relation between the location of s-BEA and the direction of the maximal total duration of acid and alkaline reflux.
Results: Regarding as maximal total duration of acid reflux, in 28 SSBE patients except for 4 patients without acid reflux, the rate of coincidence was 19/24 (79.2%). On the other hand, in 5 LSBE patients, the rate of coincidence was 4/5 (80.0%). Regarding as maximal total duration of alkaline reflux, in 28 SSBE patients except for 3 patients without alkaline reflux, the rate of coincidence was 20/25 (80.0%). On the other hand, in 5 LSBE patients, the rate of coincidence was 3/5 (80.0%). In all 33 s-BEA patients, the rate of coincidence for maximal total acid or alkaline reflux was 29/33 (87.9%).

Conclusion: The location of the s-BEA mostly corresponds with the direction of maximal total duration of acid and alkaline reflux. Measuring the direction of duodenogastric reflux by using pH monitoring with 8-channnel might be useful for early detection of the s-BEA in LSBE.

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Disclosure of Interest: None declared

P1150 ENDOSCOPIC DIAGNOSIS FOR THE EARLY PRIMARY MALIGNANT MELANOMA OF ESOPHAGUS (PMME)

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Introduction: Primary malignant melanoma of the esophagus (PMME) is a rare disease, and most of the PMME had been found in advanced stage. Treatment for PMME is basically esophagectomy, but treatment effect is poor and it's prognosis is extremely poor. In contrast, the early esophageal squamous cell carcinoma and early gastric carcinoma can be cured by the local treatment such as the endoscopic resection (ER;ESD/EMR). The early diagnosis and treatment is the best strategy to improve the patients' survival. Based on this fact, we supposed that the early PMME have low possibility of lymph nodes metastases, and we can get a good prognosis by the ER. Early detection is important in early treatment. But early PMME is more rarethan advanced PMME and is very difficult to find because we do not know collect endoscopic findings. To clarify the endoscopic findings of the early PMME will help to find early PMME.

Aims & Methods: The purpose of this study is to clarify the endoscopic findings of the early PMME. From Jan 2006 to Apr 2015, we experienced 4 cases of early PMME. For those 4 cases, we investigated their clinical and pathological and endoscopic findings.

Results: We have 2 female cases (57y.o and 71y.o) and 2 male cases (69y.o and 61y.o). There ware no symptoms in all cases, and all cases were found by screening endoscopy. Lesions were located in all part of esophagus. The lesion size was 3-40mm. In most of the lesions, the shape of lesion was flat type (0-IIb). Slight irregularities appeared when the cancer becomes thicker, and in 1 case, clear polypoid elevation can be seen. In benign melanosis, color of lesion is a thin black from pale gray, but in PMME the color of lesion was a very clear black and the lesion was composed of irregular large and small black-spots. The demarcation line was irregular, ill-defined and faded in color. Case1: A 57y.o female with 6 lesions. All lesions were 0-IIb. After the CT examination showing no metastasis, ER was performed, as the patient chose ER rather than operation. Pathological diagnosis was PMME, T1a-LPM,ly0,v0. We followed up every 6 months by endoscopy, and 8 times ER had been done for new lesions. 8.5 years has passed from the first ER, the patient is alive and free from disease. Case 2: A 69-year male with 2 lesions. All lesions were 0-IIb. After the informed consent, 2 lesions were removed by ER. The pathological diagnosis were PMME, T1a-LPM,ly0,v0. Case 3: A 71y.o female with 1 lesions. Type of lesion was 0-Ip + IIa + IIb, lesion size was 40mm and clear black polypoid elevation can be seen. Total esophagectomy with LN dissection was done. Pathological diagnosis was PMME, T1a-LPM,ly0,v0,n0. Case4: A 61-year male with 2 lesions. All lesions were 0-IIb. After the informed consent, 2 lesions were removed by ER. The pathological diagnosis was PMME, T1a-LPM,ly0,v0 in both lesions.

Conclusion: Next 4 Features are typical endoscopic findings of early PMME 1. Shape of lesion: flat(0-IIb)∼slight irregularities on surface 2. Color of lesion: very clear black 3. Structure of lesion: irregular large and small black-spots 4. Demarcation line: irregular, ill-defined and faded in color. Our cases indicate the possibility to cure early PMME by ER.

Disclosure of Interest: None declared

P1151 CLINICAL OUTCOME ACCORDING TO ENDOSCOPIC EVALUATION OF NEOADJUVANT CHEMOTHERAPY AND PATHOLOGICAL TUMOR REGRESSION GRADE IN RESECTABLE ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Neoadjuvant chemotherapy (NAC) followed by surgery is one of the standard treatments for patients with resectable esophageal squamous cell carcinoma (ESCC). It was reported that surgery following NAC improved survival compared with surgery alone, especially in patients whose surgically resected specimens were assessed as pathological regression with chemotherapy. However, the clinical impact utilizing endoscopy for evaluating efficacy after NAC, especially for prediction of recurrence, is unknown.

Aims & Methods: The aim of this study was to clarify the correlation between recurrence-free survival (RFS) and the NAC therapeutic efficacy for primary tumors. The NAC therapeutic efficacy was evaluated with endoscopic evaluation and pathological tumor regression grade (TRG) of the superficial layer of the surgically resected tumor. We enrolled patients with clinical T2/3 ESCC who underwent NAC followed by definitive surgical resection in our institution between January 2008 and March 2013. We excluded any case that an endoscopic examination had not been performed after NAC. The NAC therapeutic effect was retrospectively estimated with each endoscopic image by 3 independent endoscopists, and patients were classified into 4 groups according to the degree of tumor regression (marked reduction [MR]: 90% or more reduction; half reduction [HR]: 50% or more reduction; insufficient reduction [IR]: less than 50% reduction; ineffective, resulting in growth [IG]: progression). In addition, we evaluated the therapeutic effect on the mucosal layer of resected specimens as grade 0–3 on the basis of TRG of the primary tumor. We evaluated RFS and clinicopathological factors, including endoscopic classification of the NAC therapeutic efficacy and superficial TRG. This study was approved by an institutional review board in our institution.

Results: We evaluated 129 patients (110 men, 19 women; median age 65 years, range 36-77) who were eligible. The numbers of patients with clinical stage IB/IIA/IIB/IIIA/IIIB/IIIC/IV were 9/28/6/50/25/2/9, respectively. The numbers of patients in group MR/HR/IR/IG were 44/35/44/6. In group MR, only 9 patients were regarded as complete remission. The numbers of patients with grade 0/1a/1b/2/3 superficial TRG score were 45/32/20/17/15. Most patients with grade 2-3 were evaluated as MR, and most patients with grade 0-1a were evaluated as IR or IG. The median follow-up period was 24 months, 56 patients had recurrence or death, and the median 3-year RFS was 56.3%. The median 3-year RFS of patients in group MR/HR/IR/IG was 85.3%/48.0%/39.3%/16.7%, respectively. A multivariate analysis demonstrated that cN factors and endoscopic classification for the NAC therapeutic efficacy were independent preoperative predictors of RFS, and ypT, ypN, ypR factors and superficial TRG were independent postoperative predictive factors.

Conclusion: In this study, there was a relationship between tumor recurrence and both of endoscopic evaluation for the NAC therapeutic efficacy and superficial TRG. These two factors could identify risk of recurrence.

Disclosure of Interest: None declared

P1152 OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL PHARYNGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Recently, the detection of superficial pharyngeal squamous cell carcinoma has been increasing in Japan. However, the outcome and prognosis for endoscopic submucosal dissection (ESD) are unknown.

Aims & Methods: The aim of this study is to clarify the outcome and prognosis of pharyngeal Squamous cell carcinoma (SCC) treated by ESD.

86 pharyngeal SCC in 65 patients were treated by ESD from Jan. 2006 to Jul. Dec. 2014 in Saku Central Hospital. All ESD were performed using a Hook knife under general anesthesia with tracheal intubation. Clip with line or forceps was used to make traction during ESD.

Male/Female was 64/1. Median age was 67 (40-92) years old. Median tumor size was 5 (1 - 50) mm. Median observation duration was 71(1-127) months.

Results: 1) En bloc and R0 resection rate was 100% (86/86) and 93% (80/86), respectively. R0 resection was defined as En block resection, lateral and vertical margin was negative.

2) Complication: Perforation wasn't shown. Delayed bleeding rate was 1% (1/86). Dysphasia was shown in 2% (2/86).

3) Invasion depth: Epithelial (EP) and subepithelial (SEP) lesion was 69% (59/86) and 31% (27/86) respectively.

96% (51/53) of small lesions less than 10mm were EP. On the other hand, 76% (25/33) of large lesions 10mm or bigger were SEP.

4) Lymph-duct involvement

0/59 of EP and 4/27 of SEP had lymph duct involvement.

5) Local recurrence

One case had local recurrence. The case was SEP with lymph duct involvement. The local recurrent lesion was treated by re-ESD.

6) lymph-node metastasis (LNM)

LNM rate of EP and SEP was 0% and 11% (3/27), respectively. Two of three patients had lymph duct involvement. All of 3 patients were treated by lymph node dissection.

7) Prognosis

Two patient died of pharyngeal SCC. Both patients had SEP with lymph duct involvement, and refused additional treatment such as chemo-radio therapy.

Conclusion: ESD is a useful treatment method for superficial pharyngeal SCC. Additional therapy should be recommended for the patient who had lymph duct involvement.

Disclosure of Interest: None declared

P1153 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR EARLY ESOPHAGEAL SQUAMOUS CELL CARCINOMA (EESCC): A LARGE STUDY OF 344 CONSECUTIVE CASES

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Introduction: To evaluate the long-term outcomes of Endoscopic submucosal dissection (ESD) for early esophageal squamous cell carcinoma (EESCC) on a large patient cohort in China.
Aims & Methods: From January 2007 to November 2013, a total of 344 EESCC patients with high-grade dysplasia (HGD) and superficial squamous cell carcinoma of esophagus were included in the present retrospective study and all of the patients were treated by ESD. Demographic, pathological, clinical parameters and follow-up data were collected and analyzed.
Results: In this study, the mean age of patients was 61.8 ± 8.2 years. The ratio of male and female patients was 250:94. Among these patients, there were 78 HGD and 226 superficial squamous cell 72 epithelial or lamina propria (EP/LPM), 109 muscularis mucosa (MM) and 45 submucosal (SM1) cancer carcinoma. The median follow-up period was 34 months.
1) The complication rate was 30.5% (102/334), including 1 perforation, 1 pneumonia, 8 delayed bleeding and 92 (26.7%) postoperative stricture (defined as complaints of dysphagia). Balloon dilation under endoscopy were performed for 34 (9.9%) severe stricture patients who were suffering from aphagia.
2) Recurrence rate was 16.0%. The median time to recurrence were 18 (range 1-67) months. Longitudinal length > =3cm ($p = 0.003$), Circumferential range > 3/4 ($p = 0.001$), lymph vascular involvement ($p = 0.004$), postoperative stricture ($p = 0.02$), and combined with other cancer ($p = 0.030$) were independent predictors of recurrence. The 5-year progression-free survival for high risk group and low risk group are 35% and 80%, respectively.
3) The 5-year progression-free survival rate was 72%, for HGD, EP/LPM, MM and SM1 were 82.5%, 67.1%, 74.6%, and 54.2%, respectively ($p = 0.003$). The median progression-free survival time was 72 months. Metastasis were observed in 10 (2.91%) patients, which were 7 lymph node, 3 lung, 2 laryngeal, 2 liver, and 1 stomach metastasis.
4) The 5-year overall survival rate was 95%, for HGD, EP/LPM, MM and SM1 were 97.40%, 87.30%, 92.62%, and 78.60%, respectively ($p = 0.008$). The median survival time was 84 months. There were 14 (4.1%) patients died. Death due to esophageal cancer occurred in 6 patients (1.74%), and 5 patients died owing to other cancer. The circumferential range > 3/4 ($p = 0.000$), combined with other cancer ($p = 0.000$), and infiltration depth of lesion ($p = 0.010$) were independent predictors of overall survivals.
Conclusion: ESD is efficient to treat EESCC. The risk of recurrence after ESD were mainly associated with longitudinal length > =3cm, lymph vascular involvement, circumferential lesion >3/4, combining with other cancer, and postoperative stricture. Overall survival appears to be affected by circumferential lesion >3/4, combining with other cancer, and infiltration depth of lesion. These risk should be taken into account when considering the indications for ESD.
Disclosure of Interest: None declared

P1155 RELATION BETWEEN THE PROGNOSTIC NUTRITIONAL INDEX AND MORBI-MORTALITY POST R0 RESECTION IN THE GASTRIC CANCER

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Introduction: A low prognostic nutritional index (PNI) has been related to a high complication rate after gastric cancer resection in Japanese reports, with no data in western countries.
Aims & Methods: To analyse in our media the relation between a pathologic PNI and the frequency and severity of post surgery gastric cancer complications.
This retrospective study included 124 cases of gastric carcinomas, consecutively operated in our centre, with R0 resection. The PNI was calculated with the form: [10 x serum albumin (g/dl) + 0.005 x total lymphocytes count/mm^2], being pathological a PNI < 40. Complication rates were compared between the group with normal and pathological PNI (Chi^2 test). A multivariate analysis of the complication rates according to PNI was performed [Cox model, stepwise, hazard ratio (HR) and 95% confidence interval (CI)] adjusting for: age >68 years, preoperative ASA (ASA 1-2 vs ASA 3-4) and pTNM stage (I, II and III + IV). We determined the relation between PNI ≥ 40 and < 40 and the severity of the complications according to Martin and cols. classification (J Am Coll Surg. 2002; 194: 565-77), grouped in: no complications, mild, severe and exitus.
Results: Complication rate was: no complication: 95 (76.6%), mild complications: 14 (11.3%), severe: 12 (9.7%) and exitus: 3 (2.4%). 11.5% of cases presented a PNI < 40. Patients with pathological PNI registered a high frequency of complications: 24.1% vs 7.5% [p 0.021; OR = 3.91; CI95% = (1.09-14.17)], which was confirmed in the multivariate analysis [p 0.042; HR = 3.61; CI95% = (1.05-12.43)]. Furthermore, we registered complications with a higher severity in the group with pathological PNI: mild = 14.3% versus 11.1%; severe = 21.4% versus 8.3% and exitus = 14.3% versus 0.9% ($p = 0.005$).
Conclusion: 1. Patients with a pathological Prognostic nutritional Index (<40) show a three times higher risk of suffering complications after R0 resection in the gastric cancer. 2. This higher risk is independent of age, preoperative ASA and pTNM tumor stage. 3. Besides, cases with a PNI < 40 were associated with a significant higher rate of severe complications and postoperative exitus.
Disclosure of Interest: None declared

P1157 CLINICOPATHOLOGIC FEATURES OF SYNCHRONOUS MULTIPLE EARLY GASTRIC CANCERS

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Introduction: The multifocality rate of early gastric cancer (EGC) ranges from 4 to 21%, but there are few data regarding both lymph node metastasis and characteristics of synchronous multiple gastric cancers of patients with EGC.
Aims & Methods: We investigated the characteristics of synchronous multiple gastric cancers of patients with EGC after endoscopic or surgical treatment. We retrospectively reviewed the clinicopathological features from patients who were diagnosed with EGC after endoscopic resection or surgical treatment between February 2008 and May 2013. Of 999 EGC patients treated with endoscopic or surgical resection, 987 were included in the analysis.
Results: Of 987 patients, 578 (58.6%) were initially treated with surgical resection and 37 (9.5%) were diagnosed with synchronous multifocal EGC. The mean age at treatment of patients with solitary and synchronous multifocal EGC was 61.5 ± 11.7 and 64.3 ± 9.6 years, respectively ($p > 0.05$). The rates of lymph node metastasis were 4.6% (44/950) in solitary EGC and 5.4% (2/37) synchronous multifocal EGC ($p > 0.05$). In the multivariate analysis, synchronous multifocal EGC was associated with male and depth of invasion in main lesion compared solitary EGC ($p < 0.05$). In the subgroup analysis, 70.3% and 64.9% of patients with multiple synchronous EGC were found to have tumors located in same thirds and same aspect of the stomach, respectively.
Conclusion: Synchronous multifocal EGC does not increase the risk of lymph node metastasis compared with solitary EGC, and tumor location is an important determinant of occurrence in synchronous lesion. Clinician should pay special attention to detect synchronous lesion near the main tumor.
Disclosure of Interest: None declared

P1158 ENDOSCOPIC CLUE OF EN BLOC RESECTION IN GASTRIC INDEFINITE NEOPLASIA

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Introduction: When gastric indefinite neoplasia (category 2 lesion) from endoscopic forceps biopsy is diagnosed, it is difficult to decide management. Especially, in some situations such as suspicious of early gastric cancer (EGC) macroscopically, it is hard to decide. The aim of this study was to discuss the results of final results of gastric indefinite neoplasia and associated clinical factors predictive of early gastric cancer.
Aims & Methods: This retrospective study enrolled 142 patients of gastric indefinite neoplasia on index forceps biopsy. We analyzed the initial endoscopic features of lesions and predictive factors of early gastric cancer (EGC).
Results:

Variable	Univariate analysis		Multivariate analysis		
P value	OR	P value	OR	95% CI	
Lesion size ≥ 10mm					
Nodular	**0.003**	12.500	0.021	11.401	1.432-90.759
Redness color	**0.002**	4.941	0.066	2.998	0.928-9.686
Pale color	**0.007**	4.048	0.014	3.777	1.306-10.923

After complete work-up, the final pathologic diagnoses were early gastric cancer (n = 34, 23.9 %), adenoma (n = 16, 11.3%), and non-neoplasm (n = 92, 64.8%). In the univariate analysis, lesion size more than 10 mm, surface nodularity and erythema were associated risk factors. In the multivariate analysis, lesions diameter (p = 0.019, OR 12.501, 95% CI 1.537-91.269) and surface redness (p = 0.015, OR 3.598, 95% CI 1.414-12.314) were significant risk factors.
Conclusion: Gastric indefinite neoplasia with larger size (≥ 10mm) and erythema might be need more definite diagnostic modalities rather than simple follow up endoscopy.
Disclosure of Interest: None declared

P1159 THE EFFICACY OF COLONOSCOPY IN PATIENTS WITH ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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Introduction: Our goal is to study the risk of colorectal cancer in patients who underwent endoscopic submucosal dissection(ESD) with EGC as compared to controls. And We assessed the need for surveillance colonoscopy in patients with early gastric cancer.
Aims & Methods: The study group included a total of 180 patients with EGC that underwent ESD. As a control group, 430 sex and age-matched patients without gastric neoplasm were included. All of the patients underwent screening colonoscopy before or after 6months from gastric ESD between January 2010 and December 2013.
Results: High-risk colorectal neoplasm was diagnosed in 52/170 patients (30.5%) in EGC group and 12/420(2.8%) in controls ($p < 0.01$). Colorectal cancer was diagnosed in 22/170 patients (12.9%) in EGC group and 3/220 (1.3%) in controls ($p < 0.01$). Univariate analysis demonstrated that high-risk colorectal neoplasm was associated with presence of EGC, age, DM, and colorectal cancer was associated with presence of EGC, colorectal cancer family history. Multivariate analysis demonstrated that age (OR 6.19, 95% CI 3.5-11.5), EGC (OR 7.50, 95% CI 4.41-18.10) were risk factors for high-risk colorectal neoplasm. And the presence of age (OR 3.58, 95% CI 1.57-10.92), EGC (OR 6.47, 95% CI 2.87-15.10), colorectal cancer family history (OR 3.07, 95% CI 1.92-9.34) were risk factors for colorectal cancer.
Conclusion: The incidence of colorectal cancer who underwent an ESD for EGC group was higher than the control group. Therefore, we believe that screening colonoscopy should be considered in patients with ESD because of early gastric cancer.
Disclosure of Interest: None declared

P1160 RISK FACTORS OF SUBMUCOSAL OR LYMPHOVASCULAR INVASION IN THE TREATMENT OF ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCER

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Introduction: Lymph node metastasis is important to evaluate the indication of the submucosal dissection (ESD). Submucosal invasion and lymphovascular invasion is considered to be an independent risk factor for lymph node metastasis in early gastric cancer. Accurate diagnosis of the invasion depth in the previous ESD remains a challenge and can only be confirmed by final pathologic report following ESD. The purpose of the study is to identify risk factors for SM/LV invasion in early gastric cancer.
Aims & Methods: We studied retrospectively pathological data of patients treated ESD from Jan 2010 to May 2014 and presenting EGC of differentiated-type adenocarcinoma, 2.0 cm or smaller in size and no ulceration.
Results: Among 390 lesions consecutively resected by ESD, 297 lesions in 277 patients were included in this study. Submucosal and lymphovascular invasions were detected in 32 lesions. Multivariate analysis revealed two independent risk factors for SM/LV invasions: Histology of moderate-differentiated (odds ratio (OR) 4.082; 95% CI 1.925-8.616; $P = 0.008$), location of upper and middle third (U/M) of stomach (OR 2.917, 95% CI 1.410-6.048;$P = 0.008$).
Conclusion: Histology of moderate-differentiated adenocarcinoma, and location of U/M were identified as independent risk factors of SM/LV invasion in EGC meeting absolute criteria for ESD.
Disclosure of Interest: None declared

P1161 CLINICOPATHOLOGICAL FEATURES OF ALPHA-FETOPROTEIN -PRODUCING GASTRIC CANCER WITH ENTEROBLASTIC DIFFERENTIATION

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Introduction: Gastric cancer with enteroblastic differentiation (GCED), which is a histologic type of alpha-fetoprotein (AFP)-producing gastric cancer, is very rare and its clinicopathological features have not been well investigated. Additionally, there is no report that focused on an early stage of GCED.
Aims & Methods: This study aimed to clarify the clinicopathological features of early stage of GCED by comparisons with conventional early gastric cancer (CGC: well to moderately differentiated carcinoma). We analysed 191 cases (143 males, 48 females; mean age 72.8 y; 214 lesions) of early gastric cancer that underwent endoscopic resection from September 2011 to February 2015 in our hospital. Five of 191 cases were GCED (2.6%). We evaluated the comparison between 5 cases (4 males, 1 female; mean age 75.8 y; 5 lesions) of early gastric cancer with a GCED component and 186 cases (139 males, 47 females; mean age 73.7 y; 209 lesions) of conventional early gastric cancer, clinicopathologically.
Results: No significant difference was observed in tumour locations (U/M/L = 1/2/2 and 23/91/95 in GCED and CGC, respectively), mean of tumour size (15.0 and 15.2 mm in GCED and CGC, respectively) and macroscopic types (flat or depressed type/ elevated type = 4/1 and 92/117 in GCED and CGC, respectively). Endoscopically, we could not find specific findings for GCED, and we did not anticipate deep submucosal invasion. No lesion was diagnosed as GCED by examination of biopsy specimens. Regarding depth of tumour invasion, total submucosal invasion rates were significantly higher in GCEDs than CGCs (60.0% vs. 11.4%, $P < 0.001$). Furthermore, positive rates of lymphatic and venous invasion were significantly higher in GCEDs than CGCs (40.0 vs. 2.3%; and 60.0 vs. 0.4%, $P < 0.001$). In 2 of 5 GCED cases, additional surgery was performed (A: T1N0M0, stage IA; B: T1N1M0, stage IIA). Histological examination demonstrated the presence of tubulopapillary carcinoma with clear cytoplasm at the deeper part of the mucosa. In all cases of GCED, the superficial mucosal layer was covered with a conventional tubular adenocarcinoma. Immunohistochemically, positive findings were as follows: AFP: 1/5(20%), PAS: 3/5(60%), glypican 3: 3/5(60%), SALL 4: 2/5(40%).
Conclusion: To our knowledge, this is the first report on multiple cases of early stage of GCED. Since GCED exists only in the deeper part of the mucosa in early stage cancer, preoperative diagnosis by biopsy is thought to be difficult. Additionally, ratio of lymphovascular invasion in GCED was significantly higher than CGC, which indicates that GCED has high malignant potential. Further investigations are needed to establish optimal treatment approaches for GCED.
Disclosure of Interest: None declared

P1162 DIFFERENCES IN MIRNA EXPRESSION PROFILES BETWEEN GIST AND LEIOMYOMA IN HUMAN SAMPLES ACQUIRED BY SUBMUCOSAL TUNNELING BIOPSY

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Introduction: A gastrointestinal stromal tumor (GIST) with malignant potential typically requires surgery. Differentiating GISTs from other submucosal tumors (SMTs), especially leiomyoma, is therefore important in daily practice. Although GISTs express specific proteins, such as c-kit and CD34, serum biomarkers for GISTs have not yet been established.
Aims & Methods: The aim of this study was to identify candidate microRNAs (miRNAs) for serum biomarkers of GIST through the investigation of miRNA expression patterns in human cases of GIST and leiomyoma. MiRNA expression was examined in 9 GIST samples and 6 leiomyoma samples that were diagnosed histopathologically and acquired by a novel sampling method, submucosal tunneling biopsy (STB). STB offers the advantage of sufficient tumor specimen acquisition without contamination under direct vision. Total RNA was extracted from these tissues and analyzed for miRNA expression patterns by microarray. Subsequently, reverse transcription and real-time qPCR were used to confirm specific miRNA overexpression in the microarray analysis, comparing GISTs with leiomyomas.
Results: Microarray analysis revealed the upregulation of 10 miRNAs and the downregulation of 22 miRNAs in GISTs compared to leiomyomas; in particular, the miR-140 families and miR-181a-5p were upregulated, whereas the miR-378 family was downregulated. MiRNAs extracted from tumor tissues clustered differentially between GISTs and leiomyomas. Real-time qPCR revealed that the expression level of miR-140-5p in GISTs was 28.5 times higher than that in leiomyomas, and the expression level of miR-140-3p was also 23.2 times higher in GISTs compared to leiomyomas.
Conclusion: The STB method provided suitable SMT samples for miRNA analysis. As shown by real-time qPCR, miR-140 family members may serve as serum biomarkers of GIST compared to leiomyoma, which could lead to the development of a non-invasive diagnostic tool.

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Disclosure of Interest: None declared

P1163 PREDICTIVE FACTORS FOR METACHRONOUS GASTRIC CANCER AFTER HP ERADICATION IN THE POST-ESD (ENDOSCOPIC SUBMUCOSAL DISSECTION) STATUS

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Introduction: Endoscopic submucosal dissection(ESD) is the standard therapy for early gastric cancer. Several studies reported successful *Helicobacter pylori*(HP) eradication reduced metachronous gastric cancer after ESD. In contrast, some other studies showed the HP eradication was not effective for reducing gastric cancer.

Aims & Methods: The aim of this study is to reveal the predictive factors for metachronous recurrence of gastric cancer after HP eradication in the post-ESD status.
370 patients with early gasric cancer received first ESD at our hospital between October 2004 and December 2012. Exclusion criteria were histories of gastric surgery, gastrectomy, and eradication, serologically HP negative, rejection of eradication, unsuccessful eradication, no recept of endoscopy after eradication. Of the 98 patients in the final analysis, we retrospectively evaluated endoscopic features associated with histopathological findings related to HP infection in the pre-ESD and post-eradication. A endoscopic examination in the post-eradication was carried out one year or more after eradication treatment. Outcome measures were the following endoscopic findings: fundic gland polyp, regular arrangement of collecting venules (RAC), flat erosion, severity of atrophy, intestinal metaplasia, rugal hyperplasia, nodularity, mucosal edema, spotty redness, xanthoma, and Map-like redness. These findings were analyzed to identify the predictive factor for recurrence.
Results: The subjects comprised 73 males and 25 females with a mean age (SD) of 68.0 (±8.9) years. There was no significant difference in age, gender, endoscopic findings except for map-like redness. Map-like redness after HP eradication was the only predictive factor showing a significant difference by univariate analyses. The cumulative recurrence-free survival was significantly lower in patients with map-like redness after HP eradication than in those without the finding since the time of successful HP eradication ($p = 0.003$, Log-rank test).
Conclusion: Map-like redness after HP eradication is a vital factor for metachronous gastric cancer after HP eradication in the post-ESD status.
Disclosure of Interest: None declared

P1164 ENDOSCOPIC TREATMENT OF MALIGNANT GASTRIC OR DUODENAL OBSTRUCTION USING SELF-EXPANDABLE METAL STENT PLACEMENT

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Introduction: Gastric outlet obstruction (GOO) is a clinical syndrome characterized by epigastric abdominal pain and postprandial vomiting due to mechanical obstruction. In past, treatment of malignant gastric outlet obstruction was palliative surgery including bypass through a gastro-jejunostomy. There have been significant technical advances in stent development and endoscopic technology over recent years. Self-expandable metal stents (SEMS) can be used to palliate patients with malignant gastric or duodenal obstruction and to restore the ability of oral feeding with the recent advances in endoscopic technology.
Aims & Methods: In this study, we tried to assess the feasibility and efficacy of SEMS which were inserted through the scope method for the palliation of malignant obstruction of gastric or duodenal obstruction. During January 2011 to April 2014, 220 patients with gastric or duodenal obstruction due to malignancy underwent endoscopic SEMS insertion at Asan Medical Center. We analyzed technical/clinical outcomes and complications according to the type of stent and the location of obstruction.
Results: Among 220 patients (median age was 63 years, men were 125), full covered SEMS was inserted in 16 patients, partial covered SEMS in 77 patients, and uncovered SEMS in 120 patients. %). The median width of stent was 20 mm (IQR, 20-20mm) and the median length of stent was 80 mm (IQR, 60-100mm). The location of obstruction was shown in gastric outlet including duodenal bulb ($n = 106$), in duodenal 2nd and 3rd portion ($n = 114$). Technical success was found in 213 of 220 cases (96.8%) and clinical success was in 184 of 213 (86.4%). According to the type of stent and site of obstruction, clinical success was shown in like these; full covered SEMS (15/16, 93.8%), partial covered SEMS (68/77, 88.3%), and uncovered SEMS (101/120, 84.2%) ($p = 0.476$); gastric outlet obstruction (95/104, 91.3%) and duodenal obstruction (89/109, 81.7%) ($p = 0.039$). Of total, migration was happened in 20 cases (9.1%) and obstruction was in 51 cases (23.2%). According to type and site, migration was shown in like these; full covered SEMS (6/16, 37.5%), partial covered SEMS (7/77, 9.1%), and uncovered SEMS (7/120, 5.8%) ($p < 0.001$); gastric outlet obstruction (16/104, 15.4%) and duodenal obstruction (4/109, 1.2%) ($p = 0.003$). According to type and site, obstruction was shown in like these; full covered SEMS (2/16, 12.5%), partial covered SEMS (17/77, 22.1%), and uncovered SEMS (32/120, 26.7%) ($p = 0.409$); gastric outlet obstruction (26/104, 25.0%) and duodenal obstruction (25/109, 22.9%) ($p = 0.724$). Early complications were observed in 10 patients and late complications were observed in 64 patients. The obstruction complication was occurred mainly (45 cases) in late complication patients. The median stent patency period was 84 days (IQR, 34.5-165.5 days) and median survival was 124 days (IQR 55.5-224.0 days).
Conclusion: In malignant GOO, We should carefully decide what type of stent to use according to the obstruction site. Especially, migration risk should be considered when fully covered stent is inserted at the peri-pyloric area.
Disclosure of Interest: None declared

P1165 EPSTEIN-BARR VIRUS ASSOCIATED GASTRIC CARCINOMA IN SOLID-ORGAN TRANSPLANT RECIPIENTS

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Introduction: Epstein-Barr virus (EBV), as well as *Helicobacter pylori*, has been accepted as an infective agent causing gastric cancer (GC). In conventional gastric adenocarcinoma of the diffuse and intestinal types, EBV is found in 7% > 14% of cases. Moreover, EBV associated GC (EBVaGC) occur more frequently in male and in young age group, in the proximal stomach. However, the incidence of EBV associated GC (EBVaGC) in patients that received solid organ transplantation (SOT) and immunosuppression therapy is still unknown.
Aims & Methods: The aims of this study were to evaluate the pathological characteristics and clinical outcomes of EBVaGC in patients who had performed SOT. Between January 1994 and December 2011, total 29 gastric carcinomas on 28 consecutive were confirmed and treated with endoscopic resection or operation in patients undergone SOT at Asan Medical Center, Seoul, Korea. Formalin-fixed paraffin-embedded tissue from these resection specimens were re-assessed for EBV by in situ hybridization and data from medical record were also reviewed retrospectively.
Results: Of the 6,491 patients who underwent SOT during the study periods, 30 patients (0.46%) with 31 lesions were diagnosed with gastric cancer. Among them, 28 patients with 29 lesions were treated by endoscopic resection or operation. The median age of patients was 59 years (IQR, 54-64 years) and men were 23. The median duration between transplantation and diagnosis of GC was 45 months (IQR, 34.5-80.5 months). Of total 29 GCs, 8 were found as EBVaGCs (27.5%) (6/23 males and 2/6 females). The location of tumor, histologic differentiation, initial stage[l1] and organ of transplantation showed no differences between EBVaGC and GC. The *Helicobacter pylori* was infected in 12.5% of EBVaGC and 23.8% in GC ($p = 0.615$).[l2] The survival rate was 62.5% (5/8) in EBVaGC and 81.0% (17/21) in GC ($p = 0.299$).
Conclusion: Although the incidence of EBVaGC was higher in SOT recipients than well-known incidence of EBVaGC in non-transplant patients, the pathological characteristics and clinical outcomes were not different according to the infection of EBV.
Disclosure of Interest: None declared

P1166 CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION OF GASTRIC GASTROINTESTINAL STROMAL TUMOR

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Introduction: Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal tract. Up to date, total surgical resection still constitutes the only standard treatment for non-metastatic GISTs and a wide surgical margin is not necessary for total resection as long as the premise of negative margins is respected in comparison with that of other GI malignant tumors. With the recent advances in endoscopic technology, endoscopic resection (ER) has been attempted for the curative treatment of gastric GIST.
Aims & Methods: Here we aim to investigate the feasibility and safety of ER of gastric GIST. Subjects who underwent ER for gastric GIST at the Asan Medical Center from May 2005 to April 2014 were eligible. Patient factors, tumor factors, procedure factors, and clinical outcomes were evaluated using medical record.
Results: A total of 25 patients underwent ER for GIST. The median age was 58 years (42-72 years), and the male to female ratio was 1.5:1. The location of tumors were upper third of the stomach in 11 patients (44%), middle third in 5(20%), and lower third in 9(36%). The median size of tumors was 24.1 mm (range: 10-40 mm). The median procedure time was 37.5 minutes (range:10-80minutes). All lesions were divided into three groups according to the size and mitotic index; very low risk (16/25, 64%), low risk (7/25, 28%, and intermediate risk (2/25, 8%). Complications occurred in 5 patients (20%) including microperforation ($n = 4$, 16%) and delayed bleeding ($n = 1$, 5%). Five patients underwent sequential wedge resection of stomach because of microperforation and noncurative resection, and the pathologic evaluation revealed residual tumors in 2 patients. There was no recurrence or metastasis occurred during the median follow-up period of 49.9 months(range: 2-108 months).
Conclusion: ER of gastric GIST may be a feasible and safe method, on the basis of favorable clinical outcomes.
Disclosure of Interest: None declared

P1168 CLINICOPATHOLOGICAL REVIEW OF PIT DYSPLASIA AFTER ENDOSCOPIC RESECTION OF GASTRIC EPITHELIAL NEOPLASMS : THE FEATURES AND IMPORTANCE OF PIT DYSPLASIA

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Introduction: Endoscopic resection (ER) is widely accepted as appropriate treatment modalities for gastric epithelial neoplasms. However, issues regarding discrepancy between forceps biopsy and ER specimens or negative pathologic diagnosis (NPD) after ER have been rising. Recently pit dysplasia (PD) is suggested as one of subtypes of gastric dysplasia.

Aims & Methods: We aimed to review clinicopathologic features of cases with NPD after ER for early gastric neoplasms, and to evaluate the role of PD in these cases. From January 2006 to September 2013, 29 NPD lesions after ER, which had 1) available pretreatment forceps biopsy specimen, 2) correct targeting during ER, 3) no cautery artifact on resection specimen, were included in this study. Pretreatment forceps biopsy and ER slides were reviewed by 2 expert pathologists in gastrointestinal pathology.

Results: Review of 29 NPD lesions after ER showed PD in 16 lesions and no neoplastic pathology in 13 lesions. Initial pretreatment forceps biopsy diagnoses of 29 NPD lesions were low-grade dysplasia (LGD) in 17 lesions, high-grade dysplasia (HGD) in 7 lesions, and adenocarcinoma in 5 lesions. Reviewed diagnoses of initial pretreatment forceps biopsy were PD in 19 lesions, LGD in 4 lesions, adenocarcinoma in 2 lesions and no neoplastic pathology in 4 lesions. Taken together, of 29 NPD lesions after ER, 9 lesions (31%) were removed by forceps biopsy due to small size of the lesion, 4 NPL lesions (14%) were initially misinterpretated as neoplastic lesions, and 16 PD lesions (55%) were misinterpretated as NPD lesions in ER slides.

Conclusion: In about half of lesions initially interpreted as NPD after ER, they were diagnosed as LGD or HGD on initial biopsy specimen, and their final diagnoses were changed into PD. Therefore, the use of PD as a subtype of gastric dysplasia could narrow diagnostic discrepancy between initial forceps biopsy and ER and could lessen the frequency of NPD.

Disclosure of Interest: None declared

P1169 CLINICAL FACTORS ASSOCIATED WITH DUODENAL TUMOR: DIFFERENCE BETWEEN THE 2ND PORTION AND THE BULB

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Introduction: Primary duodenal adenocarcinoma is a rare malignant neoplasm among all gastrointestinal malignancies which poor prognosis is likely to be associated with delayed diagnosis. Lee et al reported the characteristics and prognosis of 53 cases with duodenal adenocarcinoma [1]. According to this report, 14 of 60 cancers (23%) found in the 2nd portion and 8 of 12 cancers (67%) in the bulb were unresectable at diagnosis. This suggests that the duodenal tumors in the bulb would be rare but show poorer prognosis than those in the 2nd portion. The present case-control study was designed to evaluate the characteristics of patients with duodenal adenoma or adenocarcinoma. In addition, the characteristics between the tumor in the bulb and the 2nd portion were compared.

Aims & Methods: Patients who made a histological diagnosis of duodenal adenoma or duodenal adenocarcinoma at Keio University Hospital between January 2010 and June 2014 were enrolled as cases. On the other hand, two age- and gender- matched control subjects for each case were randomly extracted from individuals who underwent esophagogastroduodenoscopy for medical checkup in the same period and did not have duodenal tumors. Individuals with familial adenomatous polyposis or the Peutz-Jeghers syndrome were also excluded. Lifestyle characteristics, comorbidities, and endoscopic findings were compared between cases and controls.

Results: 157 cases (123 with duodenal adenoma and 34 with duodenal adenocarcinoma) and 314 age- and gender- matched healthy controls were investigated. Multivariable logistic regression analysis revealed that current smoking (odds ratio [OR], 2.5; 95% confidence interval [CI], 1.3 - 4.6]), the presence of Barrett's esophagus (OR, 4.7; 95% CI, 2.5 - 8.8), the presence of fundic gland polyps (OR, 2.5; 95% CI, 1.5 - 4.4) and a history of malignant diseases (OR, 3.0; 95% CI, 1.8 - 5.2) were independently associated with the presence of duodenal tumor. The presence of duodenal tumor in the 2nd portion ($n = 137$) was associated with current smoking (9% vs. 17%; $p = 0.03$), Barrett's esophagus (7% vs. 20%; $p < 0.01$), reflux esophagitis (7% vs. 13%; $p = 0.045$), fundic gland polyps (15% vs. 29%; $p = 0.002$) and a history of malignant diseases (13% vs. 24%; $p = 0.006$). On the other hand, the presence of duodenal tumor in the bulb ($n = 20$) was associated with the presence of Barrett's esophagus (3% vs. 25%; $p = 0.01$) and a history of malignant diseases (10% vs. 40%; $p = 0.01$). The presence of open-type atrophy was inversely correlated with the presence of duodenal tumor in the 2nd portion (25% vs. 15%; $p = 0.02$), whereas the presence of open-type atrophy was more frequently observed in individuals with duodenal tumor in the bulb (28% vs. 40%; $p = 0.38$).

Conclusion: Clinical characteristics were different between individuals with the duodenal tumors in the 2nd portion and those in the bulb. These results suggest the differences of the etiology of tumor development between the locations of primary duodenal tumor.

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P1170 CLINICAL OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER BEYOND THE EXPANDED CRITERIA

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Introduction: Endoscopic submucosal dissection (ESD) has been widely undertaken for the treatment of early gastric cancer. However, the long-term outcome of ESD beyond the expanded criteria remains uncertain.

Aims & Methods: From July 2006 to February 2015, ESD for early gastric cancer was performed in 302 patients in our hospital, and 53 patients met beyond the expanded criteria. We retrospectively studied their clinical course after ESD.

Results: En bloc resection rate and complete resection rate were 90.6 % and 60.4 %, respectively. Both rates of postoperative bleeding and perforation after ESD were 3.8 %. Among the 53 patients beyond the expanded criteria, 16 (30.2 %) underwent additional gastrectomy (surgical group) and 37 (69.8 %) did not (non-surgical group). Local recurrence rate was 0 % in the surgical group and 2.7 % in the non-surgical group. Lymph node metastasis was observed in 18.8 % and 0 %, respectively. Distant metastasis was not observed in both groups. Three-year overall survival rate was 93.8 % and 78.4 %, respectively. Death due to gastric cancer was observed only one patient in the non-surgical group.

Conclusion: Beyond the expanded criteria does not always lead to cancer recurrence or metastasis. Thus, if additional gastrectomy cannot be underwent because of patient's underlying condition or refusal, a close follow-up might be considered.

Disclosure of Interest: None declared

P1171 DETERMINANTS OF PATIENT'S AND DOCTOR'S DELAY IN DIAGNOSIS OF GASTRIC CANCER IN THE NETHERLANDS; A ROUTINE CARE DATA ANALYSIS

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Introduction: An efficient diagnostic process is important to reduce burden of disease for gastric cancer patients. Duration of this diagnostic process and determinants of relatively long duration are unknown for the Netherlands.

Aims & Methods: The aim of the present study was to determine the duration of the different phases of the diagnostic process of gastric cancer patients in the Netherlands and to identify determinants of relatively long duration ('delay'). A retrospective observational study was performed, using routine care data of 51 eligible gastric cancer patients diagnosed between 2008 and 2013, whose anonymized patient files were retracted from the Primary Care Network Utrecht (PCNU) database. Three phases in the diagnostic process were defined (T1 to T3): T1 – from onset of symptom(s) to first gastric cancer related consultation with general practitioner (GP); T2 – from first GP consultation to referral for diagnosis; T3 – from referral to final diagnosis. Based on manual exploration of free-text and coded data, the duration of these phases was determined. Median duration and interquartile ranges (IQR) were calculated in days. 'Delay' was defined as the longest quartile of phase duration. To find determinants of 'delay', the association between patient-, disease- and consultation related variables and 'delay' was assessed using univariate χ^2 and multivariate logistic regression analyses.

Results: The median time from onset of symptoms to final diagnosis was 128 days (IQR 61 - 213). Median duration of the different time periods was: T1: 17 days

(IQR 3 - 42); T2: 22 days (IQR 4 - 66); T3: 34 days (IQR 15 - 56). The only variable for which a suspicion of an association with 'delay' was found was psychiatric co-morbidity in T2 (OR 2.27, 95%CI 0.93 - 5.57).
Conclusion: Dutch gastric cancer patients face a modest 'delay' in the diagnostic process in primary and secondary care. No clear determinants of long duration could be identified. The variation in duration of each phase, particularly in time from first consultation to referral by the GP, is substantial. Since the time from referral by the GP to final diagnosis was relatively long, increasing efficiency of the secondary care diagnostic process is likely to be the most effective intervention to reduce 'delay'.
Disclosure of Interest: None declared

P1172 DEVELOPMENT OF AN E-LEARNING SYSTEM FOR THE ENDOSCOPIC DIAGNOSIS OF EARLY GASTRIC CANCER: AN INTERNATIONAL MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: Gastric cancer ranks the third highest cause of cancer deaths worldwide. Except Japan and Korea where screening program is implemented, most of the gastric cancers were diagnosed at advanced stage. We suspect one of the reason why gastric cancers around the world were detected late is because of limited knowledge and experience of endoscopists. Accordingly, the authors have developed an Internet-based e-learning system to teach medical practitioners how to detect early gastric cancer using standard white light endoscopy.
Aims & Methods: The aim of this study was to evaluate effectiveness of the e-learning system on teaching good practice for endoscopic screening of gastric cancer. The study was designed as a randomized controlled trial. Medical practitioners around the world participated in this study with a signed consent form. The participants first undertook a pre-test via Internet, and then they were randomly allocated into two groups (e-learning and non-e-learning groups). Pre-adjustment strata were the pre-test score, experience of endoscopy, a nurse endoscopist or a medical doctor, and medical institution and country. The participants only in the e-learning group were allowed to access to the e-learning system that consisted of video lectures to learn basic knowledge and self-exercise tests to accumulate experience. A post-test was conducted in the both groups two months after the pre-test. The pre-determined primary endpoint was the difference in improvement rate of the test result (post-test score/pre-test score) between the two groups. After completion of the post-test, the e-learning system was opened for all participants.
Results: Five-hundred fifteen medical practitioners from 35 countries were assessed eligibility for this study. Finally, 322 participants who met inclusion criteria completed the pre-test and enrolled in this study. One-hundred sixty-six were allocated to the e-learning group and 166 were allocated to the non-e-learning. Among them, 151 participants in the e-learning group and 144 in the non-e-learning group had completed the post-test, and were included into the analysis. The mean improvement rates (standard deviation) of the test result in the e-learning and the non-e-learning groups were 1.24 (0.26) vs. 1.00 (0.16), respectively ($P < 0.001$). Namely, our e-learning system yielded substantial improvement to medical practitioners in the e-learning group, while there was no improvement for those in the non-e-learning group.
Conclusion: This global study demonstrated efficacy of our e-learning system to improve ability for endoscopic detection of early gastric cancer among medical practitioners worldwide. The effectiveness will be evaluated on improvement of early gastric cancer detection rate of all participants in actual clinical practice. (UMIN: R000012039)
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Disclosure of Interest: None declared

P1173 ESD FOR GASTRIC TUMORS IN THE WESTERN WORLD: CHALLENGES TO FIT INTO STANDARD, EXPANDED INDICATIONS AND BEYOND

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Introduction: Compared to Asian countries, ESD is rarely performed for gastric lesions in the West. The aim of our study was to report our experience and results in absolute and expanded indications for endoscopic resection of early gastric cancer (EGC).
Aims & Methods: All patient files, included in a prospective register, treated for gastric lesions by endoscopic submucosal dissection between January 2005 and December 2014 were analysed focusing on pre-ER histology, curative resection rates, and clinical outcomes based on pathology specimen and follow-up. Patients were classified following the Japanese guidelines as standard (SC) and expanded criteria (EC). All patients not fulfilling these criteria were considered as "out of criteria" (OOC).
Results: The data for 118 consecutive gastric lesions resected by ESD in 106 patients were reviewed (mean follow-up 50 months), mean age 69 years, 71 (67%) men. Lesions were 70 EGCs, 23 HGD, 9 LGD adenomas, 4 neuroendocrine tumors, 10 benign various lesions. Mean lesion size was 25 mm (5-60). Perforation were observed in 2 pts (endoscopic management). R0 resection rate in EGC were 93% in SC (14/15 pts), 89% in EC (17/19 pts), and 42% (15/36 pts) in OOC. Significantly better resection rates were observed during the second period of ESD experience (2011-2014 vs 2005-2010: 100 vs. 86%, 90 vs 87% and 61% vs 22%, respectively. OOC classification was usually due to a combination of factors including lymphatic permeation (4), undifferentiated cancer foci (19), ulceration (12), and sm1 or 2 invasion (24). 13 pts with R1 resections and OOC underwent gastrectomy: 50% had no residual disease, all three intramucosal EGCs were staged pN0 whereas 2/10 of the ten EGCs reaching the submucosa were staged pN+ (20%).
Conclusion: In the Western world, a significant proportion of EGC treated by ESD are either expanded criteria indications or even out of criteria due to G3 foci, lymphatic permeation or a combination of factors. Most of these factors could not be detected before endoscopic resection. Excellent curative resection rates of more than 90% could be offered to patients with expanded indications. More than 2/3 of patients with R1 resection and OOC specimens were also effectively cured by ESD, as proven by subsequent gastrectomy. This treatment could therefore still be considered as a curative option in frail patients.
Disclosure of Interest: None declared

P1174 GERMLINE CDH1 MUTATIONS FOUND IN A SERIES OF SPORADIC GASTRIC CANCER PATIENTS

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Introduction: Loss of cadherin 1 (CDH1) expression, which is normally involved in cell adhesion and maintenance of tissue architecture, is a hallmark of Hereditary Diffuse Gastric Cancer (HDGC).
The frequency of CDH1 germline mutations in families with HDGC is 25-30% but the real frequency and characterization of germline variants for CDH1 in sporadic Gastric Cancer (GC) patients is not known. Moreover, recently CDH1 mutations have been demonstrated to have a prognostic role in overall GC. It is important to determine the prevalence of germline CDH1 mutations in overall patients with GC.
Aims & Methods: To this end, we tested CDH1 for germline mutations in a population of patients with non-Hereditary GC.
Peripheral blood from 142 patients with a histopathological confirmed GC diagnosis was investigated for CDH1 mutations. Patients attend from a single center (CRO, Centro di Riferimento Oncologico) at the Gastroenterology Unit. CDH1 mutations of all 16 exons and their flanking non coding regions were analyzed by using PCR followed by direct sequencing.
The frequency of CDH1 germline mutations in families with HDGC is 25-30% but the real frequency and characterization of germline variants for CDH1 in sporadic Gastric Cancer (GC) patients is not known. Moreover, recently CDH1 mutations have been demonstrated to have a prognostic role in overall GC. It is important to determine the prevalence of germline CDH1 mutations in overall patients with GC. To this end, we tested CDH1 for germline mutations in a population of patients with non-hereditary GC.
Results: Within the 142 samples screened a number of 20 mutations were found, including five which load to aminoacid replacement (non synonymous), nine synonymous variants, four intronic variants and two variant in the 5' untranslated region (UTR). More specifically, the five non synonymous variants were: G54R, G274S, A298T, T470I and A592T, with the last present in two patients. The G54R mutation is a new variant of exon 2 and studies are going to test the pathogenicity of the mutation.
Conclusion: The frequency of non synonymous CDH1 mutations in our series was 5 out of 142 cases (3.5 %). The pathogenesis and prognostic effect of these mutations in patients with GC are in course.). More specifically, the five non synonymous variants were: G54R, G274S, A298T, T470I and A592T, with the last present in two patients. The G54R mutation is a new variant of exon 2 and studies are going to test the pathogenicity of the mutation.
Disclosure of Interest: None declared

P1175 FACTORS OF CLINICAL SUCCESSFUL PLACEMENT OF SELF EXPENDABLE METAL STENT IN MALIGNANT GASTRIC OUTLET OBSTRUCTION

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Introduction: There are several reports of superiority of self expandable metal stent (SEMS) placement over surgery in symptom relief and shorter hospital stay in malignant gastric outlet obstruction (GOO). However, there is significant difference between technical and clinical success rate of placement of

SEMS placement. So, we investigated factors associated with clinical success on the placement of SEMS.
Aims & Methods: We analyzed retrospectively medical records of 124 patient who received endoscpoic placement of SEMS due to malignant GOO from February 2009 to June 2014 in Pusan national university Yangsan Hospital. The change of the Gastric Outlet Obstruction Scoring System (GOOSS) before and after the procedure was investigated. Then we analyzed some factors associated with the improvement of GOOS.
Results: The rate of techinical success of placement of SEMS was 98%(122/124). Clinical success of placement of SEMS was defined as improvement of GOOSS within 7 days after stent placement and it was 81.1% (99/122). Causes of stenosis were stomach cancer 39 (32%), pancreatic cacer 37 (30.3%), cholangiocarcinoma 20 (16.4%), ampulla of vater cancer 8(6.6%), gall bladder cancer 18 (14.7%). We reviewd variables related to improvement of GOOSS and identified some factors such as ECOG ≥ 3 (Adjusted OR 9.9, $p = 0.001$), gall bladder cancer (Adjusted OR 9.201, $p = 0.011$), carcinomatosis peritonei (Adjusted OR 33.11, $p < 0.001$) and impossibility of passing the endoscope through obstructive site (Adjusted OR 6.743, $p = 0.037$).
Conclusion: We realized some factors of clinical success in placement of self expandable metal stent in malignant GOO. Physician should take into account of these factor.
Disclosure of Interest: None declared

P1176 CLINICAL OUTCOME OF NONAMPULLARY DUODENAL NEUROENDOCRINE TUMORS DIAGNOSED AS G1 AND G2 CATEGORIES

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Introduction: The gastrointestinal tract is the most frequent site for neuroendocrine tumors (NETs). Duodenal NET is rare and occurs less frequently than gastric and rectal NETs. The surgical resection is a standard treatment for T2 duodenal NET invading into muscle layer or indicating more than 1cm in size. However, the endoscopic resection (ER) has the possibility to cure T1 duodenal NET invading within submucosal layer (SM) and 1cm or less in size because of a low frequency of lymph node and distant metastasis.
Aims & Methods: The aim of this study was to analyze the clinical outcomes of patients with duodenal NET and to assess the indication for ER as a curative procedure in selected cases. We included 47 consecutive patients with 49 lesions who were diagnosed to have nonampullary duodenal NETs as G1 and G2 categories of WHO classification between May 1997 and June 2014 in our hospital. Patients who underwent only chemotherapy were excluded from this study as well as patients diagnosed with ampullary NET. We analyzed patient characteristics, endoscopic findings, treatment methods, complications, pathological results and long-term outcomes.
Results: Male/female, 32/15; mean age, 65.2; 1st/2nd/3rd part, 42/6/1; single/multiple, 45/2; median tumor size in cases of ER/surgery, 5mm (range, 3-10)/10mm (1-40). 38 lesions were recognized as an elevation in the submucosal tumors and the finding of the delle was positive in 17 lesions endoscopically. Twenty-one patients with 22 lesions underwent ER including 7 endoscopic submucosal dissections and 15 endoscopic mucosal resections. The tumor depth was limited to SM in all lesions histopathologically. The proportions of positive lesions for vertical margin were 13% (5/7) for 5mm in size or less and 71% (2/15) for 6mm or more, and 2 patients received the additional surgery after ER. Twenty patients with 21 lesions, involving 2 cases with additional surgical resection, underwent surgery including local excision of the duodenum for 8 patients, distal gastrectomy for 8, total gastrectomy for 3, and pylorus preserving pancreaticoduodenectomy for 2. Eight lesions were incidentally detected in the surgical specimen. Eight patients were carefully followed up for various reasons. Lymph node metastasis (LNM) were positive histopathologically among 6 out of 20 surgical patients and all the lesions had the finding of the delle. Three lesions that invaded into muscle layer or deeper were 12-40mm in size and were diagnosed as G2 category with Ki-67 labeling index 3% or more. The remaining 3 limited into SM were 10mm or less in size and were diagnosed as G1 category with Ki-67 labeling index less than 3%. In the group of 39 patients treated endoscopically or surgically, there were no LMN (0/23) in T1 cases negative for the finding of the delle, 8.6% (3/35) in cases of G1 category and 9.7% (3/31) in T1 cases regardless of the finding of the delle. In 1 patient, second surgery was performed for the metachronous LNM 47 months after the initial operation. There were no death from duodenal NET and no recurrence of liver metastasis during 42 months of the median follow-up.
Conclusion: Surgical resection is basically recommended for nonampullary duodenal NET, however ER can be considered for T1 lesions without the finding of the delle and 5mm or less in size.
Disclosure of Interest: None declared

P1177 *HELICOBACTER PYLORI* INFECTION IN A POPULATION OF OBESE PATIENTS PROPOSED FOR BARIATRIC SURGERY

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Introduction: The estimated prevalence of *Helicobacter Pylori* (H.P.) in the Portuguese population is about 80%. Due to its ulcerogenic and carcinogenic potential, the screening and eradication of this bacteria before bariatric surgery has become common practice. Recently, the relation between H.P and multiple metabolic disorders has been deserving attention from the scientific community.
Aims & Methods: Our aim was to evaluate the prevalence of H.P. and its relation with metabolic comorbidities in obese patients. We did a retrospective study of patients who performed upper endoscopy before being submitted to bariatric surgery between January 2012 and December 2014.
Results: A total of 200 patients were included, 90% females with a mean age of 44.2 ± 11.2 years, weight 109.6 ± 18.2 Kg and Body Mass Index (BMI) 42.2 ± 4.9 Kg/m^2. As for metabolic comorbidities, Hypertension was present in 58% of patients, Hypercholesterolemia in 57.5%, Hypertriglyceridemia in 23.5% and type 2 Diabetes Mellitus in 28%. The prevalence of H.P in this population was 58%, with diagnosis made by endoscopic biopsy (histology or rapid urease test) in 109 patients (94%) and in the remaining through fecal antigen test. There was no significant correlation between the presence of dyspeptic symptoms, endoscopic or histologic findings, weight, BMI or age and testing positive for H.P. Concerning the metabolic comorbidities previously referred, there was a significant relation between altered cholesterol values and infection with H.P ($p < 0.05$). Twelve patients (6%) had postoperative complications, but there was no statistical association with H.P infection.
Conclusion: We have verified a lower prevalence of H.P. infection in obese patients when compared to the general population, as well as a statistical relation between hypercholesterolemia and the presance of infection. The eradication of this pathogen in obese patuients may therefore play a role in improving these patients' lipid profile.
Disclosure of Interest: None declared

P1178 INVERSE RELATIONSHIP BETWEEN *HELICOBACTER PYLORI* INFECTION AND ASTHMA

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Introduction: Recent studies suggested that *Helicobacter pylori* could prevent allergic disease, especially in the children. However, there are debates in the adults.
Aims & Methods: The aim of this study is to clarify the true association between *H. pylori* infection and asthma in a population with high prevalence of *H. pylori* in the age over 16 years. Medical records of subjects who received health surveillance checkup between January 2005 and December 2011 were reviewed. Their serum *H. pylori* IgG status, *H. pylori* eradication history, and history of asthma or other allergic conditions, such as allergic rhinitis, atopic dermatitis, chronic urticarial, food/drug allergy, and others were analyzed. Those who had *H. pylori* IgG or *H. pylori* eradication history were considered to have *H. pylori* infection. Information about patients' history of asthma or other allergic conditions was obtained from their questionnaire and medical records.
Results: Out of the total 15,999 patients, 9,662 had history of *H. pylori* infection, 376 had asthma, and 3,530 had other allergic conditions than asthma. *H. pylori* infection was positively related with age (OR 1.052, 95% CI: 1.049-1.055, $p < 0.001$). Among the total, *H. pylori* infection and asthma demonstrated no significant association (OR 1.031, 95% CI: 0.829-1.282, $p = 0.783$). However, among those under 50 years old, *H. pylori* was inversely associated with asthma with statistical significance (OR 0.649, 95% CI: 0.453-0.931, $p = 0.018$). Other allergic conditions than asthma also showed inverse relationship with *H. pylori* infection among the total (OR 0.923, 95% CI: 0.854-0.999, $p = 0.047$).
Conclusion: The inverse association between *H. pylori* infection with asthma or other allergic conditions in young population suggests underlying immune mechanism by *H. pylori* infection inhibits some allergic reaction in the adults.
Disclosure of Interest: None declared

P1179 GASTRIC JUICE POLYMERASE CHAIN REACTION (PCR) FOR THE DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION IN PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING: COMPARISON WITH OTHER CLASSICAL DIAGNOSTIC METHODS

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Introduction: The prevalence of *H. pylori* infection is approximately 70% in patients with peptic disease.[1] Many studies have demonstrated that rapid urease test and histology lack sensitivity for a bleeding peptic ulcer.[2,3] Gastric juice PCR has better accuracy for diagnosis of *H. pylori* infection than histology

in a non-bleeding peptic ulcer.[4] However, there is a lack of data for patients with UGIB.

Aims & Methods: To determine the diagnostic efficacy of gastric juice PCR for the detection of *H. pylori* infection compared to histology, rapid urease test and culture in patients with UGIB. Sixty-four patients who presented with UGIB and were undergoing upper GI endoscopy between 1 January, 2015 and 31 March, 2015 were enrolled consequetively. Gastric biopsy specimens from the corpus and antrum were taken for rapid urease test, histology (hematoxylin and eosin) and culture. Five milliliters of gastric juice was aspirated by a sterile ERCP catheter via the endoscope working channel. The sample was evaluated by agarose gel electrophoresis and Southern blot hybridization for the 23S rRNA gene of *H. pylori*. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, positive and negative likelihood ratio for gastric juice *H. pylori* PCR were compared to histology, rapid urease test and culture.

Results: Of 64 patients, 41 were male and 23 were female. The mean age was 59 years. There were 53.1% of patients who presented with melena, 26.6% with hematemesis, and 20.3% with both melena and hematemesis. The means of Rockall and Blatchford scores were 2.52 and 11.23, respectively. Endoscopic findings showed lesion at stomach in 51 patients, duodenum in 6 patients and in both stomach and duodenum in 7 patients. The most common cause was peptic ulcer (60%). The prevalence of *H. pylori* infection, either positive culture or positive rapid urease test plus histology, was 43.8%**.** The sensitivity of gastric juice PCR for *H. pylori* was significantly higher than histology (92.9% vs 25%, $P < 0.001$) but equal to rapid urease test (92.9%) and culture (96.4%). Further analysis showed a non-significant difference in the sensitivity of rapid urease test, culture and gastric juice PCR for *H. pylori* between patients with and without blood in the stomach (47% and 53%, respectively).

Conclusion: Gastric juice PCR for *H. pylori* is highly sensitive for diagnosing *H. pylori* infection in patients with upper gastrointestinal bleeding. It is non-invasive, non-biopsy-based test.

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Disclosure of Interest: None declared

P1180 REAL-WORLD *HELICOBACTER PYLORI* DIAGNOSIS IN PATIENTS REFERRED FOR ESOPHAGODUODENOSCOPY: THE GAP BETWEEN GUIDELINES AND CLINICAL PRACTICE

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Introduction: Among available tests to detect *H. pylori*, histopathology is the most accurate when performed correctly with unknown validity in daily practice clinic settings.

Aims & Methods: To determine the rate of potentially false negative *H. pylori* results that might be due to continued use of PPIs in routine endoscopy practice. We also aimed to establish whether gastroenterologists recommend routine cessation of PPIs before EGD and whether they regularly document that biopsies for *H. pylori* testing have been taken while the patients are on PPI treatment.

Detailed information about three known factors (PPIs, antibiotics or bismuth and prior *H. pylori* eradication treatment), which may cause histology or rapid urease test (RUT) to be unreliable, had been prospectively collected through interviews using a questionnaire before each test. The site and the number of the gastric biopsies that were obtained from each patient during esophagogastroduodenoscopy (EGD) were according to the local recommendations in each center. Gastric biopsies were stained with H&E for histological analysis.

Results: A total of 409 subjects at three academic Gastroenterology Institutions were tested 200 times with histology. Fifty six percent (68 of 122) of all negative tests fell in the category, of continuing PPI use, which had the potential to make the histology and RUT results unreliable.

Conclusion: These data demonstrate a clear and important gap between current guidelines and real-world practice with regards to the diagnosis of *H. pylori* during EGD. A negative histology or RUT should be considered false negative until potential protocol violations are excluded. In all patients documentation of PPI use during the EGD should be an integral part of the EGD report. The current practice of taking biopsies for *H. pylori* testing in patients under PPI, should be reevaluated.

Disclosure of Interest: None declared

P1181 USEFULNESS OF LINKED COLOR IMAGING (LCI) FOR DIAGNOSIS OF *HELICOBACTER PYLORI* (H. PYLORI) INFECTION

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Introduction: LCI is a novel image-enhanced endoscopy with a laser light source to enhance the slight difference in mucosal color. That is, LCI performs expansion and reduction of color information simultaneously so that a reddish color become redder, and a whitish color become whiter. Approximately half of the world's population is infected with *H. pylori*. It is now well known that *H. pylori* infection induce duodenal and gastric ulcer disease and gastric cancer. Diffuse redness of fundic mucosa was one of the most important endoscopic features of *H. pylori* infection. We expected LCI to enhance the diffuse redness in *H. pylori*-positive patient, and to facilitate the endoscopic diagnosis of *H. pylori* infection.

Aims & Methods: The aim of this study is to evaluate the usefulness of LCI for diagnosis of *H. pylori* infection compared to the conventional endoscopy with white-light image (WLI). We retrospectively analyzed 134 patients with *H. pylori* infection and 126 patients with negative *H. pylori* infection those were examined with WLI and LCI at Murakami Memorial Hospital Asahi University from July 2014 to April 2015. We performed the definitive diagnosis of *H. pylori* infection using several methods. Two endoscopists (A: an expert involved in the development of LCI, B: a senior resident) evaluating all of the endoscopic WLI and LCI images, divided patients into *H. pylori*-positive group and *H. pylori*-negative group. Additionally we divided patients in each groups into highly-suggestive (HS) and lower-suggestive (LS) sub-groups.

Results: The levels of accuracy / sensitivity / specificity of diagnosis of *H. pylori* infection by A using WLI, and LCI were 75.8% / 68.7% / 83.3%, and 83.8% / 83.6% / 84.1%, respectively. On the other hands, those of diagnosis by B using WLI, and LCI were 73.5% / 86.6% / 55.1%, and 81.5% / 95.5% / 77.7%, respectively. The accuracy and sensitivity of diagnosis with LCI was significantly higher than those of WLI by two endoscopists ($p < 0.05$). There were no difference between the specificity of diagnosis by WLI and LCI. The kappa value of variability between A and B for LCI (kappa value = 0.635) was higher than that for WLI (kappa value = 0.488). The ratio of HS group to LS group among patients correctly diagnosed using LCI is significantly greater than when it is diagnosed using WLI ($p < 0.01$).

Conclusion: LCI is valuable tool for diagnosis of *H. pylori* infection compared to WLI. LCI has the high accuracy and sensitivity of diagnosis of *H. pylori* infection. When it is suspected *H. pylori* infection using LCI, it needs to be carefully diagnosed using appropriate methods, because the consensus is that it should be eradicated as soon as possible and best before pre-cancerous lesions are present.

Disclosure of Interest: None declared

P1182 A SIGNIFICANT INCREASE OF PEPSINOGEN I/II RATIO IS A RELIABLE BIOMARKER FOR SUCCESSFUL *HELICOBACTER PYLORI* ERADICATION; A SINGLE INSTITUTE EXPERIENCE IN JAPAN

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Introduction: Heretofore, there were many reports about the evaluation criteria of eradication therapy for *Helicobacter pylori (H.pylori)* using pepsinogen. Almost all reports were based on the percentage changes in serum PG before and after eradication therapy. In addition, the evaluation criteria using multi cut-off level was higher accuracy than the evaluation criteria using mono cut-off revel. If we could evaluate *H.pylori* eradication using serum PG, it is convenient and cost-effective compared to ^{13}C-urea breath test.

Aims & Methods: The aim of this study was to evaluated usefulness as the evaluation criteria using the percentage changes in serum PGI/II ratios of eradication therapy for *H.pylori*. A total of 650 patients received eradication therapy from October 2008 to March 2013 and we could measure serum pepsinogen I (PGI) and pepsinogen II (PGII) levels in 562 cases with *H.pylori* infection before and after eradication therapy. We also determined percentage changes in serum PGI: PGII ratios before and 3 months after the treatment by CLEIA (FUJIREBIO Inc, Tokyo, Japan) and established cut-off values for them to distinguish success from failure of *H.pylori* eradication. Cut-off values for percentage changes in serum PGI: PGII ratios were set as +40%, +25%, and + 10% when the serum PGI:PGII ratios before treatment were less than 3.0, not les than 3.0 but less than 5.0 and not less than 5.0, respectively. The percentage change in values were calculated as follows: percentage change = {(value 3 months after end of the treatment) –(value before treatment)}/(value before treatment)$\times 100^{2)}$. Gold standard of *H. pylori* eradication was defined as a negative by the use of a ^{13}C-urea breath test performed 3 months after completion of the eradication treatment. The statistical significance of serum levels of PGI, PGIIand PGI:PGIIratios as function of the eradication status was determined by Student's *t* test. Findings of $p < 0.05$ were taken to indicate statistical significance.

Results: Patients characteristics were as follows: 562 patients (226 males 40.3%, 336 females 59.7%) with a mean age of 62 ± 10 yr. The ratios of first, second, third line eradication treatment were 77.9% (438/562), 19.9% (112/562), 2.2% (12/562), respectively. Eradication of *H. Pylori* was achieved in 433 cases (77.0%). There were no significant differences serum level of PGI, PGII, and

PGI:PGIIratios before eradication treatment between the eradication success group and failure group. (PGI:55.0 ± 30.6 vs 57.9 ± 30.2, PGII: 24.7 ± 12.1 vs 24.9 ± 12.8, PGI/II: 2.3 ± 1.0 vs 2.4 ± 0.9, p = n.s) On the other hand, there was were significant differences of each factors after eradication treatment.(PGI: 33.6 ± 19.6 vs 54.2 ± 26.7, PGII: 7.5 ± 3.5 vs 23.3 ± 12.2, PGI/II: 4.5 ± 1.6 vs 2.5 ± 1.1, $p < 0.05$) Increasing percentage in serum levels of PGI:PGIIratios after treatment compared with the values before treatment clearly distinguished success from failure of eradication. (108.2 ± 57.2 vs 6.8 ± 30.7, $p < 0.05$) Using above cut-off values, the sensitivity (non-eradication: *H.pylori*+), specificity (eradication: *H.pylori* -), and validity for determination of *H.pylori* were 93.1, 93.8 and 93.2%, respectively.

Conclusion: In conclusion, our findings suggested that the percentage changes in serum PGI/II ratios are useful as the evaluation criteria of eradication therapy for *H. pylori*.

Disclosure of Interest: None declared

P1183 THE HELICOBACTER ERADICATION ASPIRIN TRIAL (HEAT): A LARGE SIMPLE RANDOMISED CONTROLLED TRIAL USING NOVEL METHODOLOGY IN PRIMARY CARE

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Introduction: Clinical trials measuring the effect of an intervention on clinical outcomes are more influential than those investigating surrogate measures but are costly. We developed methods to reduce costs substantially by using existing data in primary and secondary care systems, to ask whether *Helicobacter pylori* eradication would reduce the incidence of hospitalisation for ulcer bleeding in aspirin users.

Aims & Methods: The Helicobacter Eradication Aspirin Trial (HEAT) is a HTA-funded, CRN-supported, double-blind placebo controlled randomised trial of the effects of *H. pylori* eradication on subsequent ulcer bleeding in infected individuals taking aspirin daily, conducted in practices across the whole of England, Wales and Northern Ireland. A bespoke web-based trial management system developed for the trial (and housed within the secure NHS N3 Data Network) communicates directly with the HEAT Toolkit software downloaded at participating practices, which issues MIQUEST queries searching entry criteria (≥60 years, on chronic aspirin ≤325mg daily, not on anti-ulcer therapy or non-steroidal anti-inflammatory drugs) for GP review of eligibility. Trial participation is invited using a highly secure automated on-line mail management system that ensures patients receive an invitation within 48 hours. Interested patients are seen once for consent and breath testing. Those with a positive test are randomised to eradication treatment (lansoprazole, clarithromycin, metronidazole) or placebo with drug sent by post. Events are tracked by upload of accumulating information in the GP database, patient contact, review of national Hospital Episode Statistics and ONS data.

Results: HEAT is the largest CRN CTIMP trial, with 105,276 invitation letters sent from 772 practices, 20,509 volunteers, and 2,847 H. pylori positive patients randomised to active or placebo treatment after 2.5 years of recruitment. 178 practices have performed their first follow-up MIQUEST search to identify 21 potential endpoints to date.

Conclusion: HEAT is important medically, because aspirin is so widely used, and methodologically, as a successful trial would show that large-scale studies of important clinical outcomes can be conducted at a fraction of the cost of those conducted by industry, which in turn will help to ensure that trials of primarily medical rather than commercial interest can be conducted successfully in the UK.

Disclosure of Interest: None declared

P1184 COMPARISON OF NON-INVASIVE TESTS; STOOL HPSA ELISA AND C13UREA BREATH TEST IN THE DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION IN A LOW PREVALENCE COHORT

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Introduction: Non-invasive testing for *H. pylori* infection has allowed for cost effective and safer ways to diagnose infection in both primary care and hospital settings. The reduced prevalence of *H. pylori* infection in the Irish population in keeping with other developed nations, can negatively impact on the diagnostic accuracy of a given test. Frequent evaluation and comparison of commercially available tests has been recommended and should be performed to ensure that the most sensitive and specific are used in clinical practice.

Aims & Methods: To evaluate and compare two non-invasive *H. pylori* tests; premier platinum HpSA and C^{13}UBT in an Irish cohort**.** Adult patients referred for a C^{13}UBT at the Adelaide and Meath Hospital were prospectively recruited. Patients on recent antibiotics, regular PPI or who had previously received a course of eradication therapy were excluded. Following informed consent patients were asked to collect and bring in a stool sample on the day of their C^{13}UBT testing. HpSA ELISA testing was carried out in accordance with manufacturer's instructions (Meridian Biosciences, Germany). An absorbance cut off of ≥0.140 (at 450nm) was considered positive. C^{13} UBT was considered as the gold standard and a delta value of ≥4% was deemed positive.

Results: To date 124 patients mean age 41 years, male gender 87(30%) have been recruited. In all 45(36%) percent where *H. pylori* positive on C^{13}UBT. Overall the performance of HpSA was disappointing with only 29(23%) positive tests. In all there were 17 false negative and 1 false positive HpSA test. As such the sensitivity, specificity, positive and negative predictive values for HpSA compared with C^{13}UBT were 62%, 99%, 97% and 82% respectively. Overall correlation between these two non-invasive tests was poor 0.13, 95% CI 0.016 – 0.242. The low sensitivity may reflect specific collection and storage requirements which are a common problem for many faecal tests.

Conclusion: HpSA performance in this study does not meet international guidelines for a diagnostic test for *H. pylori* infection and cannot be recommended for regular clinical use. The accuracy of UBT appears to be less affected by the relatively low prevalence of *H. pylori* infection in our community, however formal comparison with invasive modalities should be undertaken to assess its accuracy. C^{13}UBT testing continues to remain the first line non-invasive diagnostic tool in detection of *H.pylori* infection.

Disclosure of Interest: None declared

P1185 DISAPPEARANCE OF DIFFUSE REDNESS AND APPEARANCE OF MAP-LIKE REDNESS ARE THE MOST IMPORTANT FINDINGS FOR DIAGNOSIS OF *H. PYLORI* ERADICATED STATUS

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	Hp positive	Hp eradicated	Total	Sensitivity	Specificity	PPV	NPV	ROC/AUC
	446	297	743					95% CI
RAC +	34	21	55	92.9%	6.6%	60.0%	38.2%	75.4%
RAC-	412	276	688					0.707-0.800
Atrophic change +	405	270	675	90.8%	9.1%	60.0%	39.7%	49.8%
Atrophic change -	41	27	68					0.456-0.540
Diffuse redness +	440	1	441	98.7%	99.7%	99.8%	98.0%	99.0%
Diffuse redness -	6	296	302					0.983-0.998
Spotty redness +	226	42	268	50.7%	85.9%	84.3%	53.7%	68.3%
Spotty redness -	220	255	475					0.645-7.721
Rugal hyperplasia +	204	217	421	45.7%	26.9%	48.5%	24.8%	35.9%
Rugal hyperplasia -	242	80	322					0.319-0.399
Mucosal swelling +	56	24	80	12.6%	91.9%	70.0%	41.2%	51.7%
Mucosal swelling -	390	273	663					0.475-0.559
Exudation +	229	3	232	51.3%	99.0%	98.7%	57.5%	75.1%
Exudation -	217	294	511					0.717-0.785
	Hp eradicated	Hp positive						
Map-like redness +	207	8	215	69.7%	98.2%	96.3%	83.0%	84.0%
Map-like redness -	90	438	528					0.806-0.873

Diffuse redness, which had been generally observed in patients with *Hp* positive cases, was almost totally disappeared after *Hp* eradication. In contrast, map-like redness appeared in approximately 70% of patients with *Hp* eradicated status.

Introduction: Little has been reported on endoscopic findings related to *Helicobacter pylori* (*Hp*) eradicated case while several findings have been revealed to be useful in diagnosing *Hp* positive status.
Aims & Methods: To clarify the characteristic endoscopic appearance of *Hp* eradicated status upper GI endoscopy was performed in 446 patients with *Hp* positive and 297 patients proved to be negative 12 months after its treatment (women, 380; mean age, 62.4 years). Serum *Hp* IgG antibody level or rapid urease test were adopted to confirm *Hp* infection in all the cases and at least 2-site biopsy specimens were examined for histology and ^{13}C UBT was performed in all the *Hp* treated cases. The presence or absence of the following 8 endoscopic findings were evaluated: regular arrangement of collecting venules (RAC), atrophic change, diffuse redness, spotty redness, rugal hyperplasia, mucosal swelling, exudation, map- like redness. Five well-trained endoscopists who were blinded to clinical information assessed the findings.
Results: See table.
Conclusion: Disappearance of diffuse redness is the most important and decisive finding and map-like redness appearance is also beneficial to diagnose *Hp* eradicated status.
Disclosure of Interest: None declared

P1186 RELATIONSHIP BETWEEN SERUM PEPSINOGENS AND GASTRITIS SCORES BASED ON KYOTO-CLASSIFICATION OF GASTRITIS

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Introduction: Serum pepsinogens (PGs) reflect the atrophy and inflammation of gastritis induced by *H. pylori* infection. Recently, Kyoto-classification of gastritis has been developed and used widely.
Aims & Methods: The aim of the study was to investigate the relationship between Kyoto-classification of gastritis and serum PGs.
A total of 283 patients who underwent gastroscopy were enrolled. Serum levels of PG I and PG II were measured. Of the parameters of Kyoto-classification of gastritis, atrophy (C0-CII:A0, CII-C-III:A1, and OI-OIII:A2), intestinal metaplasia (None:I0, within antrum:I1 and up to corpus:I2), hypertrophy of gastric fold (-:H0, +: H1), nodular gastritis (-:N0, +:N1) and diffuse redness (-:DR0, mild: DR1, severe:DR2) were scored based on endoscopic findings.
Results: Mean PGI levels of A1, A2 and A3 groups were 67.7, 68.9 and 50.0 (ng/ml), respectively ($P < 0.001$). Those of PG II were 15.2, 26.1 and 23.8 (ng/ml), respectively ($P < 0.001$). Therefore, the expansion of gastric atrophy can be estimated by PGI and PG II. The PG I/PG II ratios in I0 and I1 gorups were 3.0 and 2.2, respectively ($P < 0.001$). Therefore, presence of intestinal metaplasia can be estimated by measurements of PG I/PG II ratios. In H0 and H1 groups, mean PG I levels were 56.8 and 65.2 (ng/ml), respectively, those of PG II were 21.1 and 32.1 (ng/ml), respectively and those for PG I/PG II were 3.0 and 2.2, respectively ($P < 0.001$), suggestion that hypertrophy of gastric folds are related to severe inflammation of gastric mucosa. Nodular gastritis were observed more often in females. Means of PG I, PG II and PG I/PG II in patients with nodular gastritis were 66.2 (ng/ml), 24.4 (ng/ml) and 2.9, respectively, suggesting that nodular gastritis is tempted to be induced in female patients with severe gastric inflammation but mild atrophy. The total score was significantly correlated with PG I/PG II. After eradication of *H. pylori*, the mean of PG I decreased from 61.1 to 37.2 ($P < 0.001$), that of PG II decreased from 25.0 to 9.0 ($P < 0.001$) and PG I/PG II ratios increased from 2.7 to 4.5 ($P < 0.001$). The mean of total gastritis score also decreased from 4.6 to 2.5 ($P < 0.001$).
Conclusion: We confirmed that serum PGs reflects the gastric atrophy as well as inflammation. Kyoto classification of gastritis is implicated with not only atrophy but also inflammation and is well correlated with serum PGs.
Disclosure of Interest: None declared

P1187 THE EFFECTS OF *HELICOBACTER PYLORI* ERADICATION THERAPY FOR CHRONIC IDIOPATHIC THROMBOCYTOPENIC PURPURA

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Introduction: The aim of this study was to evaluate the ability of *Helicobacter pylori* eradication treatment for increasing platelet counts in patients in Korea with chronic idiopathic thrombocytopenic purpura (ITP).
Aims & Methods: The medical records of patients diagnosed with chronic ITP were retrospectively reviewed between January 2003 and December 2013. All patients were assessed for *H. pylori* infection using a 13C-urea breath test, and those with a positive result received standard triple therapy. A total of 102 patients were evaluated against two criteria. First, those diagnosed with *H. pylori* infection in whom eradication was successful were assigned to the *H. pylori*-positive and -eradicated group (n = 39), while those diagnosed with *H. pylori* infection in whom eradication failed were assigned to the *H. pylori*-positive and -non-eradicated group (n = 3) and those without *H. pylori* infection were assigned to the *H. pylori*–negative group (n = 60). Second, those with complete remission in whom the platelet recovery effect was maintained over the average follow-up period of 6 months after eradication therapy were defined as the responder group (n = 58), while those with partial or no response were defined as the non-responder group (n = 44).
Results: Platelet counts of the *H. pylori-positive* and -eradicated group increased significantly 6 months after eradication therapy compared to those of the *H. pylori-positive* and -non-eradicated group and *H. pylori-negative* group (43.2 ± 29.1 to $155.3 \pm 68.7 \times 103/\mu L$ vs. 42.5 ± 28.1 to $79.8 \pm 59.7 \times 103/\mu L$ vs. 43.1 ± 28.9 to $81.2 \pm 62.2 \times 103/\mu L$, $p = 0.041$). The eradication therapy success rate in the responder group was 100.0% (39/39) versus that of the non-responder group (0.0%; 0/3) ($p < 0.001$).
Conclusion: Platelet counts of the *H. pylori-positive* and -eradicated group increased significantly 6 months after eradication therapy compared to those of the *H. pylori-positive* and -non-eradicated group and *H. pylori-negative* group. *H. pylori* eradication therapy was related to increasing platelet count, and successful eradication affected the increased platelet count in patients in Korea with chronic ITP.
Disclosure of Interest: None declared

P1188 COMPARISON OF EFFICACY OF MOXIFLOXACIN-BASED SEQUENTIAL THERAPY AND HYBRID THERAPY AS FIRST-LINE ERADICATION REGIMEN FOR *HELICOBACTER PYLORI* INFECTION

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Introduction: The aim of this study was to evaluate the efficacy of 14-day moxifloxacin-based sequential therapy compared with 14-day hybrid therapy as a first-line eradication treatment of *Helicobacter pylori* infection.
Aims & Methods: From August 2014 to January 2015, 284 patients with confirmed *H. pylori* infection randomly received 14days of moxifloxacin-based sequential (MSQT group, n = 140) or hybrid (Hybrid group, n = 144) therapy. Successful eradication therapy for H. pylori infection was defined as a negative 13C-urea breath test 4 weeks after the end of eradication treatment.
Results: The eradication rates by intention-to-treat (ITT) analysis were 91.4% (128/140; 95% confidence interval [CI]: 90.2-92.9%) and 79.2% (114/144; 95% CI: 77.3-80.7%) in the MSQT and Hybrid groups, respectively ($p = 0.013$). The eradication rates by per-protocol (PP) analysis were 94.1% (128/136; 95% CI: 92.9-95.6%) and 82.6% (114/138; 95% CI: 80.6-84.1%) in the MSQT and Hybrid groups, respectively ($p = 0.003$). Compliance was good in both groups (MSQT/ Hybrid group: 100%/100%). The adverse event rates were 11.8% (16/136) and 19.6% (27/138) in the MSQT and Hybrid group, respectively. ($p = 0.019$).
Conclusion: The eradication rates were 91.4% and 79.2% in the MSQT and Hybrid groups by intention-to-treat (ITT) analysis. The eradication rates by per-protocol (PP) analysis were 94.1% and 82.6% in the MSQT and Hybrid groups. The 14-day moxifloxacin-based sequential therapy is effective and, moreover, shows excellent compliance and safety compared with the 14-day hybrid therapy.
Disclosure of Interest: None declared

P1189 1-WEEK AND 2-WEEK MOXIFLOXACIN-CONTAINING TRIPLE THERAPIES FOR SECOND-LINE ERADICATION OF *HELICOBACTER PYLORI* INFECTION AFTER NON BISMUTH QUADRUPLE SEQUENTIAL AND CONCOMITANT TREATMENT FAILURE

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Introduction: PPI-based standard triple therapy for *Helicobacter pylori* infection has fallen considerably. To increase the eradication rate, non-bismuth quadruple sequential and concomitant therapies were introduced recently. Nevertheless, not inconsiderable patients fail to achieve eradication and need second-line treatment.
Aims & Methods: We tried to know the efficacy of moxifloxacin-containing triple therapy after non-bismuth quadruple therapy failure. A total of 98 patients who were not eradicated with non-bismuth quadruple therapy received 1-week or 2-week moxifloxacin-containing triple therapy (400 mg of moxifloxacin once daily, and 20 mg of rabeprazole and 1 g of amoxicillin twice daily). *H. pylori* status was evaluated 4 weeks later, after completion of treatment by ^{13}C-urea breath test.
Results: 60 patients and 38 patients received 1-week and 2-week moxifloxacin-containing triple therapy, respectively. The intention-to-treat and per-protocol eradication rates were 56.7% (95% CI, 45.0-70.0) and 59.6% (95% CI, 46.6-71.7) in 1-week group, and 76.3% (95% CI, 63.2-89.5) and 80.6% (95% CI, 66.7-91.9) in 2-week group ($p = 0.048$, 0.036). There were no significant between-group differences, in regard to the compliance and side effects.
Conclusion: 2-week moxifloxacin-containing triple therapy showed a better efficacy than 1-week regimen after non-bismuth quadruple therapy failure. More large sample sized prospective study will be needed.

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Disclosure of Interest: None declared

P1190 THE USE OF REBAMIPIDE IN COMBINATION WITH A PROTON PUMP INHIBITOR AND ANTIBIOTIC IN THE TREATMENT OF *H. PYLORI*-ASSOCIATED PEPTIC ULCER DISEASE: A META-ANALYSIS

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Introduction: *Helicobacter pylori (H. pylori)* resistant strains to amoxicillin, clarithromycin or metronidazole have been increasing rapidly owing to widespread use of antibiotics with proton pump inhibitors (PPI) for eradication. The standard therapy includes the use of an antibiotic with a PPI. Rebamipide, one of the gastro-protective agents in common use, has been shown to exhibit preventive or healing effects in gastric mucosa or mucosal lesion by increasing endogenous prostaglandin or by suppressing oxygen-free radicals.
Aims & Methods: A meta-analysis of randomized control trials (RCTs) was conducted to determine if the use of Rebamipide in combination with a PPI and antibiotic can augment the eradication rate of *H. pylori*-associated gastric inflammation in adult patients diagnosed to have peptic ulcer disease.
A literature search was performed on the PubMed database and resulted in six articles, of which four were selected. Allocation concealment, intention-to-treat analysis, completeness of follow-up and blinding of investigators, participants and outcome assessors were independently analyzed by three authors and was critically appraised with regards to methods of minimizing selection bias, performance bias, exclusion bias and detection bias. Trial results were combined under a random-effects model. Dichotomous data were analyzed by calculating the risk ratio with 95% confidence interval (CI) and a significant p value of 0.05. Subgroup analyses were performed to statistically compare subgroups. Cochrane Review Manager Software version 5.0 statistical software was used for all analyses.
Results: The primary outcome of the meta-analysis was the eradication rate of *H. pylori*-positive peptic ulcer disease. Across all four trials, 209 of 293 patients (71.3%) had successful eradication of *H. pylori*-associated peptic ulcer disease using Rebamide in combination with an antibiotic and PPI compared with 179 of 271 control group patients (66.0%). The risk ratio for the eradication rate of *H. pylori*-associated peptic ulcer disease in all four trials were highly consistent ranging narrowly from 0.98 – 1.31. The pooled risk ratio was 1.07 with 95% CI of 0.98-1.17.
Conclusion: There is no significant difference in the eradication of *H. pylori* associated peptic ulcer disease with the use of Rebamipide in addition to antibiotic and PPI compared to the standard therapy alone. However, due to the rise in resistant strains of *H. pylori*, there may be an increasing need to add Rebamipide to the standard therapy as it has protective effects shown to augment ulcer healing. As such, Rebamipide may still be used in peptic ulcer disease as per the discretion of the clinician.

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Disclosure of Interest: None declared

P1191 DIPHENYLENEIODONIUM CHLORIDE AND PARTHENOLIDE: POTENTIAL SUBSTANCE FOR NOVEL ANTI-HELICOBACTER PYLORI AGENTS

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Introduction: Increased resistance of *Helicobacter pylori* (*H. pylori*) to antibiotics has increased the need to develop new treatments for *H. pylori*. Thus, there is clearly an urgent need to develop new drugs that are effective against resistant strains.
Aims & Methods: The aim of our study is to develop new substance that have an anti-*H. pylori* activity by using high-throughput screening assay. Chemical library composed of 1200 chemical compounds were obtained from high-throughput screening core laboratory. Antimicrobial susceptibility test was performed using the broth microdilution technique. A 96-well microtiter plates were prepared for 82 chemical compounds which showed anti-*H. pylori* activity in high-throughput screening assay. Among chemical compounds which showed growth inhibitory potential, potent chemical compounds for practical application were selected.
Results: Diphenyleneiodonium chloride (DPI) and parthenolide (PTL) were selected and measured minimal inhibitory concentrations (MICs) against reference and resistant strains of *H. pylori*. Furthermore, DPI and PTL was further evaluated to validate susceptibility against resistant *H. pylori* strains. The MIC value of parthenolide (PTL) and diphenyleneiodonium chloride (DPI) showed MIC value of 2.0-8.0 μg/ml and lower than 0.03 μg/ml. DPI also show antibacterial activity against common aerobic bacteria showing MICs ranges from 0.5 to 2 μg/ml.
Conclusion: This study shows that DPI could be a powerful new class of drugs against *H. pylori*. Further in vivo study is needed to develop this substance as anti-*H. pylori* drug.
Disclosure of Interest: None declared

P1192 MODIFIED SEQUENTIAL THERAPY CONTAINING LEVOFLOXACIN VERSUS LEVOFLOXACIN TRIPLE THERAPY IN THE SECOND LINE TREATMENT OF *HELICOBACTER PYLORI*: A RANDOMIZED TRIAL

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Introduction: Levofloxacin triple therapy (LT) has been recommended as one of the second line eradication regimen for *Helicobacter pylori (H. pylori)* according to the Maastricht Consensus Report. However, recent studies showed unsatisfactory efficacy (<80%) of this regimen. Our previous pilot study showed that the eradication rate of modified sequential therapy containing levofloxacin (MS) was higher than 90%.
Aims & Methods: Therefore, we further conducted this randomized trial to compare the efficacy and tolerability of the two regimens. This open-label, randomized, multicenter trial was conducted in 9 hospitals and one community in Taiwan between 2012 and 2015. *H. pylori* infected subjects who failed from clarithromycin-based regimens (N ± 600) were randomized (1:1) to receive MS ((lansoprazole and amoxicillin for the first 5 days, followed by lansoprazole, levofloxacin, and metronidazole for another 5 days) or LT (lansoprazole, amoxicillin, and levofloxacin for 10 days). Successful eradication was defined as negative ^{13}C-urea breath test at least 6 weeks after treatment. Our primary outcome was the eradication rate by intention-to-treat (ITT) and per-protocol (PP) analyses. Antibiotic resistance was determined by agar dilution test. (ClinicalTrials.gov NCT01537055)
Results: The prevalence of clarithromycin, levofloxacin, and metronidazole resistance in this study population were 60%, 17.6%, and 36.9%, respectively. The eradication rates of MS and LT were 84.4% (249/295) and 76.3% (225/295) in the ITT analysis ($p = 0.013$), respectively, and 86.5% (249/288) and 79.2% (225/284) in the PP analysis ($p = 0.022$), respectively. There were no differences in the compliance. The efficacies in strains susceptible and resistant to levofloxacin were 92.7% (76/82) and 47.2% (9/19) for MS ($p < 0.001$), respectively, and were 76.4% (55/72) and 19.2% (5/26) for LT, respectively ($p < 0.001$). The efficacies in strains susceptible and resistant to metronidazole were 92.3% (55/59) and 83.3% (30/36) for MS, respectively.
Conclusion: Modified sequential therapy containing levofloxacin was more effective than levofloxacin triple therapy in the second line treatment for *H. pylori* in populations with high clarithromycin resistance.

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Disclosure of Interest: None declared

P1193 RANDOMIZED TRIAL FOR HELICOBACTER PYLORI ERADICATION IN A NAIVE PORTUGUESE POPULATION - IS SEQUENTIAL TREATMENT SUPERIOR TO TRIPLE THERAPY IN REAL WORLD CLINICAL SETTING

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Introduction: *Helicobacter pylori* (HP) is the most prevalent infectious agent in the world adult population, and its eradication has become increasingly difficult as resistances to several commonly used antibiotics develop. The most adequate first-line eradication regimen for HP in Portugal has not yet been determined.
Aims & Methods: We aimed to compare HP eradication rates between triple therapy (TT) and sequential therapy (ST) in a naive Portuguese population.
Prospective randomized trial including consecutive patients with HP infection referred for first-line eradication treatment. Exclusion criteria for enrollment included previous gastric surgery or neoplasia, pregnancy or lactancy, allergy

to any of the drugs. The compared eradication regimens were TT (pantoprazol 40 mg, amoxicillin 1000 mg and clarithromycin 500 mg 12/12h for 14 days) and ST (pantoprazol 40 mg 12/12h for 10 days, amoxicillin 1000 mg 12/12h during days 1-5 and clarithromycin 500 mg 12/12h, metronidazol 500 mg 12/12h during days 6-10). Eradication success was confirmed with urea breath test, and side-effects as well as the need to stop treatment were registered. Statistical analysis was performed with SPSS v21.0 and a p value < 0.05 was considered statistically significant.

Results: Of the 63 randomized patients, 3 were lost to follow-up, resulting in the inclusion of 60 patients, 39 (65%) female with mean age 52 years (SD± 14.3). Chief indications for HP eradication were functional dyspepsia (42%), premalignant gastric lesions (23%) and peptic ulcer disease (13%). TT (n = 31) and ST (n = 29) groups were homogeneous for gender, age and indication for treatment.

No statistical differences were encountered between ST and TT eradication rates (86.2% versus 77.4%, p = 0.379), global eradication rate was 82%.

Side-effects were reported in 10 (16.7%) patients (5 in each treatment arm), most commonly dyspepsia, diarrhea and dysgeusia. In only 2 patients, both in the ST group, treatment adhesion was irregular because of moderate dyspepsia, but in both cases, HP eradication was proven successful.

Conclusion: In this randomized controlled trial in a naive Portuguese population, we found a satisfactory global *Helicobacter pylori* eradication rate of 82%, with no statistical differences observed in the efficacy of the treatment between triple and sequential regiments. These results support the use of either therapy for the first-line eradication of *Helicobacter pylori*.

Disclosure of Interest: None declared

P1194 HIGH PREVALENCE OF SINGLE, DUAL AND MULTIDRUG RESISTANT *HELICOBACTER PYLORI* INFECTION AND MECHANISM OF CLARITHROMYCIN RESISTANCE IN INDIA

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Introduction: Antibiotic resistance to commonly used antibiotics against *H. pylori* is increasing very rapidly. Resistance of *Helicobacter pylori* to clarithromycin is associated with single base substitution in the 23S rRNA gene.

Aims & Methods: To determine antimicrobial susceptibility pattern of *H. pylori* strains against commonly used antibiotics in *H. pylori* treatment and to analyze the mechanism of clarithromycin resistanc in India.

H. pylori were cultured from 68 patients suffering from different gastro-duodenal diseases. Minimum Inhibitory concentration to different antibiotics was determined by agar dilution method. The point mutation in clarithromycin resistant strains were recognized by PCR- Restriction Fragment Length Polymorphism (RFLP) and DNA sequencing.

Results: The clinical diagnosis of 68 patients who were *H. pylori* culture positive were Gastro Esophageal Reflux Disease (GERD) (n = 23), Nonerosive reflux Disease (NERD) (n = 22), Non Ulcer Dyspepsia (NUD) (n = 13), Antral Gastritis (n = 3), Duodenal ulcer (n = 2) and others (n = 5). Of the 68 *H. pylori* isolates, 29.4 % (20/68) had no resistance, the prevalence of total drug resistance was 70.6% (48/68) which includes the resistance against Metronidazole (48.5%), Furazolidone (22.1%), Amoxicillin (17.6%), Tetracycline (16.2%) and Clarithromycin (11.8%). Dual and multiple drug resistance were found in 26.5 % (18/68) and 8.9% (6/68) of cases.

In our study, A2143G point mutation in 23S rRNA gene was found in 87.5% (7/8) clarithromycin resistant strains. Another most common mutation A2142G and T2182C was found in 12.5% (1/8) clarithromycin resistant strain.

Conclusion: We conclude that more than two- third of the isolated *H. pylori* strains showed resistance to at least one of the antibiotics for *H. pylori* treatment. Metronidazole showed the maximum resistance. Emergence of dual and multi-drug resistance is of great concern and there is an urgent need for regular antibiotic resistance surveillance studies. Amoxicillin and clarithromycin based anti- *H. pylori* regimens commonly prescribed for triple therapy in India shows least resistance and hence appropriate for anti *H. pylori* management in India. To our knowledge this is the first study in India to report that the point mutation at position A2143G, A2142G and T2182C is associated with clarithromycin resistance which confirms the reports available from other parts of the world.

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Disclosure of Interest: None declared

P1195 A COMPARISON OF SEQUENTIAL THERAPY WITH STANDARD TRIPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION IN AN IRISH COHORT

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Introduction: Eradication rates for the standard first line triple therapy for *H. pylori* infection have fallen to an unacceptably low level. Sequential therapy has been suggested as a treatment option to replace standard triple therapy. The efficacy of sequential therapy has not been assessed to date in an Irish population.

Aims & Methods: To compare the efficacy of standard triple therapy with sequential therapy for *H. pylori* eradication. A prospective, multicentre, randomised controlled study was conducted after ethical approval in all participating hospitals. Treatment-naïve *H. pylori*-infected patients (>18 years), as assessed by a positive urea breath test (UBT), were invited to participate and informed consent was obtained. Patients were randomised to receive either standard triple therapy (20 mg omeprazole, 1 g amoxicillin and 500 mg clarithromycin twice daily for 7 days) or sequential therapy (20 mg omeprazole and 1 g amoxicillin twice daily for 5 days, followed by 20 mg omeprazole, 500 mg clarithromycin and 500 mg metronidazole twice daily for 5 days). A follow-up UBT was performed 6-8 weeks post-treatment to assess treatment success.

Results: To date, 86 eligible patients (mean age: 41.7 ± 11.8 years; 64% female) who tested positive for *H. pylori* infection by the UBT have been recruited to the study. 90% (N ± 77) were referred for dyspepsia. A smoking habit was reported by 22% (N ± 19) of the patients. 51% (N ± 44) patients (mean age: 43.2 ± 12.6 years; 75% female) received standard triple therapy and 49% (N ± 42) patients (40.1 ± 11 years; 52% female) received sequential therapy. The eradication efficacy by intention-to-treat analysis was 56.8% (95% CI: 42.2-71.4%) for standard triple therapy and 69% (95% CI: 55.0-83.0%) for sequential therapy. In the standard triple therapy group, 2 patients did not attend for follow-up and one patient did not complete their medication due to side effects. All patients in the sequential therapy group attended for follow-up and were compliant. The eradication rates by per-protocol analysis for standard triple therapy and sequential therapy were 61% (95% CI: 46.1-76.0%) and 69% (95% CI: 95% CI 55.0-83.0%) respectively. The differences in eradication rates by either intention-to-treat or per-protocol analysis were not statistically significant. The most common adverse event reported was mild nausea at 15% (95% CI: 7.5-22.6%). Incidence in adverse events was not significantly different between the study groups.

Conclusion: Sequential therapy has a non-statistically significant advantage over standard triple therapy in our patient cohort. However, eradication rates for both standard triple therapy and sequential therapy fall considerably short of the 80% intention-to treat-rate. Further studies are required to identify potential alternatives to standard first line triple therapy.

Disclosure of Interest: None declared

P1196 CUMULATIVE HELICOBACTER PYLORI ERADICATION THERAPY IN OBESE PATIENTS UNDERGOING GASTRIC BY-PASS SURGERY

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Introduction: The Maastricht IV Consensus Report has recently updated guidelines for the management of *Helicobacter Pylori* (HP) infection with special emphasis in high clarithromycin (CLT) resistance geographical areas. However, in Portugal, there are some limitations with HP eradication treatments as bismuth is not available. In line with the recommendations of the European Guidelines on surgery of severe obesity (1) and with the recommendations of the American Society of Gastrointestinal Endoscopy on endoscopy of the bariatric patient (2) we perform HP eradication in obese patients undergoing Roux-en Y gastric by-pass (RYGB) surgery.

Aims & Methods: Over a 4-year period (2011-2014), our aim was, in obese patients undergoing RY GB surgery to assess the cumulative HP eradication rates by adopting a 14 days quadruple concomitant therapy in first line treatment as proposed by the Maastricht IV consensus – proton pump inhibitor (PPI) bid, CLT 500mg bid, metronidazole (MTX) 500 bid and amoxicillin (AMX) 1000mg bid – and a 14 days second line levofloxacin based regimen – PPI bid, AMX 1000 mg bid and levofloxacin 500mg od. HP infection status was determined by histology or urea breath test and post treatment HP status was assessed by urea breath test 4-6 weeks after the end of therapy.

Results: Six hundred twenty consecutive HP-positive patients completed concomitant first-line treatment: 511 (82.4%) female, age 40.8 (±10.3) years, median age of 41 years, age range of 18-64 years. HP was eradicated in 458 patients – 73.9% (95%CI: 70.3-77.2%). In the remaining 162 patients, second-line levofloxacin based regimen eradicated HP in 95 patients – 58.6% (95%CI: 50.9 - 65.9%). These results give 89.2% (95% CI: 86.5-91.4%) cumulative eradication rates. Eradication rates were not significantly different by gender, age and smoking habits.

Conclusion: By adopting IV Maastricht guideline quadruple concomitant first-line treatment and second-line levofloxacin-based therapy high cumulative HP eradication rates are achieved but still leaves around 11% of obese patients undergoing RYGB in need of the culture and susceptibility testing prior to third-line treatment.

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Disclosure of Interest: None declared

P1197 TREATMENT TRIAL RESULTS FROM COMMUNITY H. PYLORI PROJECTS IN THE CANADIAN ARCTIC

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Introduction: The Canadian North *Helicobacter pylori* (CAN*Help*) Working Group links northern community leaders and health officials with scientists to conduct research focused on community concerns about health risks from *H.pylori* infection. To date, we have initiated four community *H.pylori* projects: in 2007 in Aklavik, Northwest Territories (NT) (population~600); in 2010 in Old Crow, Yukon, YT (population~250); in 2011 in Tuktoyaktuk, NT (population~850); and in 2012 in Fort McPherson, NT (population~800).

Aims & Methods: The design of each community project was guided by a local planning committee. Projects components include: surveys of health and socio-environmental factors, urea breath test (UBT) screening for *H. pylori* infection, upper gastrointestinal endoscopy, treatment, knowledge exchange, and policy development.

We invited all *H.pylori*–positive participants ≥15 years to enrol in a treatment trial that randomly assigned alternate 10-day *H.pylori* therapies: 1) PPI-CA - the Canadian standard 3-drug therapy with a proton pump inhibitor (PPI), amoxicillin, and clarithromycin; 2) ST - sequential therapy with a PPI and amoxicillin for days 1-5, followed by a PPI, clarithromycin and metronidazole for days 6-10; 3) QT - quadruple therapy with a PPI, bismuth, metronidazole, and tetracycline. Only treatment naive participants not known to have clarithromycin-resistant *H.pylori* could be assigned PPI-CA, which was discontinued after initial results showed poor effectiveness. To assess infection status after treatment, we offered UBT at > = 10 weeks post treatment. Each participant's treatment outcome was classified as successful or failed according to a negative or positive UBT result, respectively.

Results: Of 921 community *H.pylori* project participants to date, 832 had results from *H.pylori* screening by UBT (positivity = 60%), 323 had endoscopy with gastric biopsy, 267 enrolled in the treatment trial, and 179 had a post-treatment UBT.

Of trial participants with a follow-up UBT, treatment was successful in: 62% (29/47; 95%CI 46-75%) of those randomized to PPI-CA; 73% (65/89; 95%CI 63-82%) of those randomized to ST; 95% (39/41; 95%CI 83-99%) of those randomized to QT. If non randomized patients are also included (PPI-CA 11, ST 10 and QT 12) the cumulative success rates are: PPI-CA 62%, ST 71 % and QT 92%.

Of 205 *H.pylori* isolates tested for antibiotic susceptibility, 43% (88) were resistant to > = 1 antibiotic: 35% (71) to metronidazole, 16% (33) to clarithromycin, 4% (8) to ciprofloxacin, 1% (2) to nitrofurantoin, 1.5% (3) to rifampicin; 0 to tetracycline or amoxicillin.

Conclusion: Treatment success estimates from this Canadian Arctic community treatment trial are imprecise due to small group sizes; however preliminary results show that QT is superior to ST and PPI-CA across communities.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00–17:00
SMALL INTESTINAL II – HALL 7

P1198 LINKAGE OF SMALL INTESTINAL BACTERIAL OVERGROWTH WITH IRRITABLE BOWEL SYNDROME: IS THIS AN EPIPHENOMENON OF PROTON PUMP INHIBITORS?

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Introduction: Current knowledge suggests that small intestinal bacterial overgrowth (SIBO) participates in the pathogenesis of irritable bowel syndrome (IBS). It is questionable is this association is modulated by intake of proton pump inhibitors (PPIs). We aimed to provide a clear-cut answer analyzing a big prospective cohort of patients undergoing small intestinal quantitative aerobe culture.

Aims & Methods: Duodenal aspirates were collected from 897 outpatients subjected to upper GI endoscopy and quantitatively cultured under aerobic conditions. SIBO was diagnosed as the isolation of at least one coliform $\geq 10^3$ cfu/ml. Results were correlated with history of IBS, PPI intake, type of PPI and duration of treatment, age, body mass index (BMI) and endoscopic findings. Odds ratios (OR) and 95% confidence intervals (CIs) were measured according to Mantel and Haenzel. Comparison between OR were done by the Tarone's test. Factors independently linked with SIBO were found after forward logistic regression analysis providing ORs. Definition of a cut-off for a continuous variable to enter regression analysis was done after Receiver Operator Characteristics curve analysis with specificity greater than 90%.

Results: 158 had SIBO and 739 did not have SIBO; 20.2% and 22.2% respectively had a history of PPI intake (p: 0.558). Among patients without history of PPI intake, 123 had SIBO and 590 did not have SIBO; 56.9% and 19.0% respectively had IBS (OR: 5.63, 95%CIs: 3.76-8.5, $p < 0.0001$). Among patients with history of PPI intake, 35 had SIBO and 149 did not have SIBO; 65.7% and 31.5% respectively had IBS (OR: 4.16, 95%CIs: 1.91-9.06, $p < 0.0001$; p: 0.498 between ORs). Factors independently linked with SIBO were age ≥60 years (OR: 2.36, p: 0.001), body mass index ≥22 kg/m^2 (OR: 0.60, p: 0.049), presence of IBS (OR: 6.29, $p < 0.0001$), type 2 diabetes mellitus (OR: 1.59, p: 0.032) and endoscopic gastritis (OR: 0.47, $p < 0.0001$). Among patients with IBS predominant-diarrhea (IBS-D), 22.1% had history of PPI intake of more than 9 months; this was 10.1% among patients without IBS (p: 0.004). This effect was pronounced among patients reporting esomeprazole consumption (OR: 3.59, $p < 0.0001$).

Conclusion: The association between IBS and SIBO was completely independent from PPI intake. Long-term treatment with PPI of more than 9 months was associated with IBS-D; this was mainly an effect of esomeprazole. Although gastritis was protective against SIBO, results show that modulation of gastric pH with PPI cannot prime SIBO.

Disclosure of Interest: E. Pyleris: None declared, E. Giamarellos-Bourboulis Financial support for research: Alfa-Wassermann SpA, Italy, C. Barbatzas: None declared, A. Pistiki: None declared, M. Pimentel Financial support for research: Beatrice and Samuel A. Seaver Foundation, Consultancy: Salix Pharmaceuticals

P1199 FECAL MICROBIOTA TRANSPLANTATION FOR TREATMENT OF SLOW TRANSIT CONSTIPATION: A PROSPECTIVE OPEN-LABEL STUDY

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Introduction: Fecal microbiota transplantation (FMT) has been proposed as a therapeutic approach for functional gastrointestinal disease (FGID). Previous studies suggested dysbiosis is frequently complicated in constipation and gut microbiota can affect gastrointestinal transit.

Aims & Methods: We launched a clinical study (NCT02301221) to examine the safety and efficacy of FMT for slow-transit constipation (STC). Twenty patients with STC, aged 20 to 74, were enrolled in this prospective open-label study. Patients received FMT on three consecutive days via nasojejunal tube with follow-up at 1, 2, 4 and 8 weeks after treatment. Bowel movements per week, Wexner Constipation Scores, Patient Assessment of Constipation Quality of Life (PAC-QOL) and adverse events were evaluated at each study visit.

Results: The rate of clinical improvement and remission based on clinical symptoms at 8 weeks postoperatively was 60% (12/20) and 35% (7/20) respectively. The patients' spontaneous complete bowel movements (SCBMs) increased from a mean of 1.75 ± 1.27 per week pre-FMT to 4.54 ± 1.36 at 8 weeks without laxative-use ($p < 0.01$). Over 8 weeks, Wexner constipation scores, scored 9.75 ± 4.88 at 1 week, 7.50 ± 2.57 at 2 weeks, 7.43 ± 3.65 at 4 weeks and 7.48 ± 1.57 at 8 weeks, showed a significant reduction as compared with 14.1 ± 3.29 at pre-FMT ($p < 0.01$ for all comparisons). Compared with baseline, significant overall improvements were also seen in PAC-QOL scores at 1, 2, 4 and 8 weeks of follow-up ($p < 0.01$). Meanwhile, there were no severe treatment-related adverse events during the whole FMT procedure follow-up except for venting, abdominal pain, bloating and diarrhea.

Conclusion: This is the first study to demonstrate that FMT has the potential to be somehow of help in managing patients with slow-transit constipation, but considerable further efforts are necessary to maintain a long-term effect.

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Disclosure of Interest: None declared

P1200 PERINATAL ANTIBIOTIC TREATMENT ALTERS OFFSPRING'S GUT MICROBIAL PROFILE PREDISPOSING THEM TO EXPERIMENTAL COLITIS

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Introduction: The use of antibiotics in the perinatal period is associated with delayed microbial colonization. Postnatal maturation of the immune system is largely driven by exposure to microbes, and thus the nature of the intestinal colonization may be associated with the development of childhood diseases that may persist into adulthood, including inflammatory bowel diseases.

Aims & Methods: Therefore, we have explored whether prenatal antibiotic therapy can increase offspring susceptibility of experimental colitis through an alteration of the gut microbiota.

Pregnant C57Bl/6 mice were treated with cefazolin at 160 mg/kg body weight (bw) or with saline starting six days before the due date. At 7 weeks, male offspring from the two groups received 4% dextran sulfate sodium (DSS) in the drinking water for 5 days. Disease activity index (DAI), histology, colonic interleukin (IL)-6, IL-1β and serum C-reactive protein (CRP) were determined. From colon and fecal samples, the V3-V4 region of bacterial 16S rRNA was amplified

and subjected to Illumina sequencing. Alpha-diversity was calculated using Chao 1 and beta-diversity was determined using QIIME. Differences at the genus level were determined using partial least squares discriminant analysis (PLS-DA), and phylogenetic investigation of communities by reconstruction of unobserved states (PICRUSt) was used for bacterial functional predictions.
Results: Prenatal ATB increased the onset of clinical disease as assessed by stool consistency, weight loss and rectal bleeding. On day 5, macroscopic and histologic scores were significantly increased. Colonic IL-6 was increased, but IL-1β levels were not changed. Conversely, in the ATB-DSS group, the CRP level was significantly decreased. In colitic mice compared to the control group, ATB significantly decreased the richness of the bacterial species in fecal samples but not in the colon, and bacterial community composition differed between the groups in both sample types, although this was further influenced by the mother. PLS-DA analysis revealed an association of specific taxa with ATB-DSS or control-DSS at lower taxonomic levels. Also, there were differences in microbial functional pathways in both fecal and colonic samples.
Conclusion: These results support the hypothesis that prenatal antibiotics modulates offspring intestinal bacterial colonization and susceptibility to develop colonic inflammation in a murine model of colitis. Furthering our understanding of the impact of prenatal antibiotics on gut bacterial colonization and susceptibility to colitis may guide future interventions to restore physiologic intestinal colonization in offspring born to antibiotic-exposed mothers.
Disclosure of Interest: None declared

P1201 SMALL INTESTINAL BACTERIAL OVERGROWTH AS A CAUSE OF SECONDARY LACTASE DEFICIENCY

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Introduction: Human microflora is a stable genetically determined system. Most bacteria are in the colon with their concentration reaching up to 10^{10}–10^{11} CFU/ml and more. The concentration of microorganisms in the small intestine fluctuates from 10^1 to10^4 CFU/ml of the intestinal content.
Secondary lactase deficiency (SLD) is inability to digest lactose, the predominant sugar of milk. This inability results from decrease of lactase enzyme activity, which is produced in the small intestine. **Purpose:** to define the influence of SIBO in patients with SLD in adult patients.
Aims & Methods: : In this study, 386 patients (the mean age – 33.9 ± 9.09; F/M - 249/137) with postinfectious irritable bowel syndrome (IBS) were analyzed concerning lactase deficiency. All patients underwent intestinal endoscopy with biopsies from the mucosa of the descending duodenum in order to determine lactase deficiency. The biopsies were taken in order to determine lactase deficiency (normal, mild and severe) by means of lactose quick test (LQT). To diagnose small intestinal bacterial overgrowth (SIBO) all patients underwent lactulose breath test during 2 hours.
Results: SLD was detected in 36.5% of patients with postinfectious IBS. Mild SLD was determined in 25.6% of patients, and severe SLD – in 10.9% of patients. The specific clinical symptoms of mild SLD were moderate flatulence with abdominal pain (80.7%); the majority of patients (73.7 %) had normal stool consistency, one time a day; the other patients had semi-liquid faeces, 2-3 times a day (26.3%). The clinical symptoms of severe SLD were diarrhea (stool $>$ 4 times a day) in 85.7% of patients, abdominal pain and flatulence (90.5%). SLD in all cases was accompanied by SIBO (the average level of lactulose breath test was 80.3 ± 28.3ppm, N $<$ 20ppm). It turned out that the degree of lactase deficiency depends on the severity of SIBO in the lumen of the small intestine. Thus, when mild SLD average value SIBO was 72.4 ± 25.1ppm, whereas severe SLD average indicators of SIBO achieved higher values, 99.3 ± 26.9ppm (N $<$ 20ppm). To establish the degree of dependence of SIBO in the small intestine and the degree of deficiency of lactase in the small intestine biopsies performed a statistical analysis of the results by calculating the Spearman rank correlation coefficient in order to study a statistically significant link between the various phenomena. In this study, an inverse correlation between the degree of lactase deficiency in patients with the SLD and the severity of SIBO in the small intestine, i.e. the higher the hydrogen concentration in the exhaled air, the less activity of the enzyme lactase in the small intestine biopsy specimens ($r = -0.49$, $p < 0.001$).
Conclusion: SIBO in all cases was accompanied by SLD. Thus, the high frequency of the SLD associated with SIBO in the small intestine in patients postinfectious IBS can be explained by the growth of pathogenic microflora in the small intestine.
Disclosure of Interest: None declared

P1202 SMALL INTESTINAL BACTERIA OVERGROWTH AND USE OF PPI AS A PREDISPOSING FACTORS FOR NSAID-ENTEROPATHY

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Introduction: There is good evidence from animal studies that gut bacteria play an important role in the pathogenesis of NSAID-induced small bowel damage. Other studies demonstrated alterations in the composition of small bowel bacteria in human, often with increases in gram-negative bacteria, after the administration of NSAIDs. In a prospective study of chronic NSAID users, 50-60% were found to have severe small bowel damage by video capsule endoscopy, associated with small intestinal bacteria overgrowth (SIBO). There is ample evidence that proton pump inhibitors (PPIs) can induce alteration of intestinal flora and SIBO too.
Aims & Methods: Our aim was to evaluate the frequency of SIBO by using a hydrogen glucose breath test (H_2-GBT) and frequency of small bowel lesions in chronic PPIs (standard doses of omeprasole) and NSAIDs (diclofenac) users. We investigated 34 pts with NSAIDs-gastropathy (20 male, mean age – 45 years) with H_2-GBT (EC60 Gastrolyzer 2, Bedfont Scientific Ltd, Rochester, UK). All patients with positive results of H_2-GBT were examined with video capsule endoscopy (Given, Israel) and were treated with rifaximine (1200 mg/day during 10 days). The efficacy of treatment was controlled with repeated H_2-GBT.
Results: Overall, 20 pts (58.8%) had demonstrated positive results of H_2-GBT and presence of SIBO. Among this patients the small bowel lesions were found in 16 pts (80%) by using a video capsule endoscopy. After use of rifaximine (1200 mg/day during 10 days) negative H_2-GBT was found only in 2 (10%) patients with initially diagnosed SIBO.
Conclusion: High prevalence of SIBO in patients with NSAID- induced gastric damage treated with PPIs may confirm its important role in pathogenesis of NSAID-enteropathy. PPIs may exacerbate small bowel damage induced by NSAIDs through alteration of gut microbiota. Rifaximine is highly effective for treatment of SIBO.
Disclosure of Interest: None declared

P1203 SACCHAROMYCES BOULARDII STRAIN CNCM I-745 SHOWS PROTECTIVE EFFECTS AGAINST B. ANTHRACIS LT TOXIN

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Introduction: Anthrax disease is a severe bacterial infection often characterized by both septicemia and toxemia. Toxemia depends on a tripartite toxin secretion. LT toxin, composed of the PA binding sub-units and LF catalytic unit, has been directly implicated in epithelia and endothelia barrier dysfunction observed in the gastrointestinal form of the disease. Massive reorganization of the actin cytoskeleton promoted by LT through MEK inhibition is a great system to study inhibitors of the intoxication process. The probiotic yeast *Saccharomyces boulardii* CNCM I-745 (*S.b*) is prescribed worldwide for prophylaxis and treatment of diarrheal diseases caused by bacteria, virus or antibiotics. Several studies have shown that *S. b*. exerts a proteolytic effect on several bacterial toxins while maintaining the barrier function of intestinal epithelium.
Aims & Methods
Aim: In this study we tested whether *S.b* might confer protective effect on cell intoxication by *B. anthracis* LT-toxin.
Material and Methods: The study was performed on filter grown polarized T84 cells or non-polarized HUVEC cells. Permeability was measured by trans-epithelial resistance (TER). The modifications in the distribution of the tight junctions associated protein ZO-1, and reorganization of actin cytoskeleton were monitored by confocal microscopy. MEK-2 cleavage, PA and LF degradation were detected by western-blot.
Results: After 15 and 24 hours incubation, LT toxin affected epithelial integrity which was visualized by a significant drop of TER in polarized T84 cells. In parallel we observed that LT toxin caused modification of tight junctions morphology with a diffuse staining of ZO-1. It induced as well formation of actin stress fibers in both cell lines. LT toxin is known to target mitogen-activated protein kinase kinases (MEK); kinetics studies on MEK-2 cleavage reveals in our study that it occurs at 2 hours of incubation in HUVEC cells and is delayed to 6 hours of incubation in T84 cells.
An overnight treatment with *S. b* before LT toxin incubation maintained the integrity of the monolayers, prevented morphological modification of tight junctions, restricted LT effects on actin remodeling and delayed LT-induced MEK -2 cleavage. Finally, to unravel the molecular mechanism by which *S.b* protects cells, the yeast was incubated with the LT subunits (PA and LF) for 2, 6, and 24 hours. After centrifugation, we determined that cleaved forms of PA were detected in the supernatant after 24 hours of incubation. A small quantity of PA and LF were also founded in the pellet containing *S.b* corresponding probably to yeast-bound toxins fraction. These results could explain the anti-toxin activity of *S. b*.
Conclusion: Our study highlights the therapeutic potential of *S.b* strain CNCM I-745 to be used as prophylactic agent against the gastrointestinal form of *B. anthracis* infection.
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P1204 EFFECT OF SACCHAROMYCES BOULARDII STRAIN CNCM I-745 ON DENDRITIC CELLS POPULATIONS IN THE LAMINA PROPRIA OF MICE FOLLOWING SALMONELLA TYPHIMURIUM INFECTION

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Introduction: Recent studies characterized, in the lamina propria, two DCs populations that include: $MHCII^+CD11c^{hi}CD103^+CD11b^+$(referred as $CD103^+CD11b^+$DCs) and MHC^{hi} $CD11C^{hi}CD103^-CD11b^+$(referred as $CD103^-CD11b^+$DCs). Buganovic M et al. (*Immunity* 2009) have previously

established a difference of involvement of both populations of DC during infection of streptomycin-pretreated mice with *Salmonella typhimurium* (ST). The transport of pathogenic *Salmonella* from the intestinal tract to the mesenteric lymph nodes involves $CD103^+CD11b^+$DCs, whereas intracellular bacteria in the lamina propria reside in $CD103^-CD11b^+$ DCs. The probiotic yeast *Saccharomyces boulardii* CNCM I-745 (*S.b*) is prescribed worldwide for prophylaxis and treatment of diarrheal diseases caused by bacteria, virus or antibiotics. In the streptomycin-pretreated model, we demonstrated that *S.b* modifies ST propagation along the intestinal tract and ST translocation (Plos One 9 e103069).

Aims & Methods

Aim: Investigate the effect of *S. b* on the different DCs populations in the intestine of mice after *Salmonella* infection.

Material and Method: Bioluminescent imaging (BLI) was used to evaluate the effect of *S.b* on the progression of luminescent ST (ST-lux) in the GIT of mice pretreated with streptomycin. The intestine was sampled in three parts and the photon emission reflecting ST-*lux* progression was recorded in i) the site of maximum photon emission (''I°''), ii) the ileum, which showed no photon emission (''I^-''), and iii) the duodenum, which had already been in contact with the bacteria (''I^+''). The different DCs populations extracted from the Inflammatory cells were characterized by FACS. *In vitro* studies were performed on RAW264.7 cells exposed or not to *S.b* before infection. GM-CSF was detected in the supernatant by array.

Results: FACS analysis of DCs extracted from ST-*lux* alone infected mice revealed that the ''I°'' sample presented a population expressing $CD103^+CD11b^+$DCs and $CD103^-CD11b^+$DCs that was absent in the other part of the intestine: ''I^-'' and ''I^+''. The ''I°'' sample obtained from *S.b* pretreated mice before infection presented a significantly reduced population expressing $CD103^+CD11^+$DCs and $CD103^-CD11b^+$ DCs when compared to ''I°'' portion of ST alone infected mice. Interestingly the ''I^-'' portion of *S.b* treated mice (portion of intestine that has not been in contact with ST but has been in contact with yeast) contained a population expressing $CD103^-CD11b^+$ DCs. GM-CSF was required for the development of CD103 + CD11b + DCs. *S.b* abolished secretion of GM-CSF in RAW 264.7 infected by ST.

Conclusion: Altogether these data demonstrate that *in vivo,* shortly after ST administration, *S.boulardii* CNCM I-745 modulates the DCs composition of lamina propria by inducing the $CD103^-$DCs and reducing the $CD103^+$ DCs populations.

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P1205 WHEN GASTRIC INHIBITION IMPLIES INTESTINAL BACTERIAL ALTERATION. A CONFIRMATION FROM A FOLLOW-UP STUDY

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Introduction: The causative role of PPIs on small intestinal bacterial overgrowth (SIBO) is still controversial. However, the incidence of SIBO is increasing, probably because of the increase of pharmacological risk factors (1). Although SIBO can satisfactorily be eradicated by Rifaximin (2), its recurrence and retreatment are so far poorly investigated and may pose clinical challenges. Here we investigated the effect of PPIs, on a follow-up study, after the first successful eradication of SIBO by Rifaximin.

Aims & Methods: One hundred and forty four patients (pts) treated with long-term PPIs for gastro-esophageal reflux disease (GERD), successfully eradicated from SIBO with high dose Rifaximin were followed-up for 1 year for relapse investigation. A group of pts continued full dosage PPIs therapy (A group) while another stopped it (B group). An additional group of pts with IBS, eradicated from SIBO, not taking PPIs, was also followed-up, as control (C group). At the end of follow-up, or before if symptoms suggested it, glucose hydrogen breath test (GHBT) (Quintron, Milwaukee, WI, USA) was performed to each patient and symptoms were recorded. All relapsed pts were retreated with Rifaximin 1200 mg/die for 2 weeks, as in the first course. The outcome of therapy was assessed both clinically and by means of GHBT, 2 months after the completion of Rifaximin course.

Results: Out of a cohort of 144 pts (M 84; mean age 46 ± 14) successfully eradicated from SIBO with Rifaximin, 97 pts continued treatment with PPIs (M 52, mean age 45 ± 13) and 47 (M 31, mean age 44± 14) discontinued it. An additional series of 20 pts with IBS (M11, mean age 43 ± 17), eradicated from SIBO, PPIs-free, were followed-up for 1 year. Forty-nine out of 97 pts of A group (50%), 3 out of forty-seven of B group (6%) and 1 out of 20 of C group (5%) had a SIBO relapse , with a statistically significant difference between the first group and the others ($p < 0.001$). Forty-seven out of 52 pts retreated with Rifaximin showed negative GHBT along-side symptoms remission (90%), indicating a successful eradication from SIBO. No relevant side effect was registered.

Conclusion: 1) Relapse rate of SIBO within 1 year is high if treatment with PPIs is not discontinued (90%). 2) Retreatment with Rifaximin 1200 mg/die for 2 weeks results to be effective and safe.

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P1206 ABNORMAL DUODENAL PATHOLOGY IN SMALL INTESTINAL BACTERIAL OVERGROWTH AND FUNCTIONAL DYSPEPSIA

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Introduction: Small intestinal bacterial overgrowth (SIBO) is characterized by a variety of clinical features thought to result from alteration of the microbiota within the upper gastrointestinal (GI) tract and commonly defined as the presence of $> 10^5$ colony forming units/ml of bacteria in an aspirate of fluid collected from the upper small intestine[1]. SIBO can be diagnosed with the lactulose H2 breath test, which is a non-invasive, low cost, simple test[2]. Symptoms related to SIBO are heterogeneous and may mimic functional GI disorders, including functional dyspepsia (FD).

Aims & Methods: This study aimed to define whether abnormal duodenal pathology previously related to dyspeptic symptoms (increased duodenal eosinophilia) occurs in patients with dyspepsia and SIBO.

This was a prospective case-control study, 9 patients with normal upper endoscopy, upper abdominal ultrasonography, and symptoms of functional dyspepsia (FD; 8 females, mean age 37 years, range 19-63,) were compared to 9 patients with SIBO (defined by lactulose H2 breath test) and functional dyspepsia (7 females, mean age 46 years, range 31-72). Biopsies were taken from the gastric antrum and duodenum, and examined for routine pathologies by haematoxylin and eosin staining, plus additionally eosinophil counts/ mm^2 and mast cells by immunocytochemistry (CD117). Symptoms of FD and the presence of postprandial distress syndrome (PDS), and epigastric pain syndrome (EPS) were recorded. Effect sizes are reported as Cohen's d (> 0.5 moderate, > 0.8 is large effect size) and comparisons between SIBO and non-SIBO FD was undertaken using the Mann-Whitney test for immune cell counts and Chi-Square for categorical measures.

Results: All patients were non-smokers, with no allergies and no parasitic ova on stool microscopy. SIBO patients were more likely to have postprandial distress symptoms (PDS) (77% v 44%, $p = 0.1$) or PDS alone (33% v 11%, $p = 0.3$). SIBO patients showed evidence of reduced duodenal eosinophils ($d = -0.76$, $p = 0.08$), elevated duodenal intraepithelial lymphocytes ($d = +0.50$, $p = 0.3$) and reduced duodenal mast cells ($d = -0.57$, $p = 0.5$) compared to those with FD alone. Failure to reach statistical significance despite moderate to large effect sizes is likely due to low sample size with statistical power 0.3 or less for all comparisons. In contrast there was minimal evidence of difference between SIBO and non-SIBO FD patients with respect to gastric eosinophils ($d = -0.14$, $p > 0.9$) or gastric intraepithelial lymphocytes ($d = -0.37$, $p = 0.7$).

Conclusion: SIBO in patients with functional dyspepsia appears to be associated with alteration in duodenal but not gastric innate immune response and may be associated with the PDS rather than EPS FD subtype. Larger studies are required to improve the statistical certainty of these findings.

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P1207 SMALL INTESTINAL BACTERIAL OVERGROWTH MAY INCREASE THE LIKELIHOOD OF LACTOSE, FRUCTOSE AND SORBITOL INTOLERANCE FALSE POSITIVE DIAGNOSIS

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Introduction: Small intestinal bacterial overgrowth (SIBO) is defined by the presence of an excessive concentration of bacteria in the small intestine. Lactose intolerance (LI), fructose intolerance (FI) and sorbitol intolerance (SI) and SIBO share many gastro-intestinal (GI) symptoms usually attributed to patients diagnosed with irritable bowel syndrome (IBS).

Aims & Methods: To evaluate the role and effect of SIBO in the formation of LI, FI and SI symptoms in affected patients. A total of 348 patients with suspected IBS underwent SIBO and LI, FI and SI diagnosis by hydrogen breath test (HBT). 15 gr of lactulose dissolved in 50 ml of water and 50 gr of lactose, 25 grams of fructose and 15 grams of sorbitol dissolved in 250 ml of water were used for SIBO and LI, FI and SI HBT respectively. The test results were considered positive when hydrogen concentration acceded 10 PPM for SIBO and 20 PPM for LI, FI or SI above baseline.

Results: Out of the 348 patients tested for SIBO and LI, 101 (29%) were positive for both tests. Out of the 197 patients tested for SIBO and FI, 17 were positive for both tests. And finally, out of the 196 patients tested for SIBO and SI, 45 were positive for both tests. Out of the 101 SIBO and LI, 17 SIBO and FI and 45 SIBO and SI positive patients, 82 (81%), 14 (82%) and 23 (53%) respectively had an increase of hydrogen measurement above threshold between 30-90 minutes during their LI/FI/SI-HBT, implying SIBO.

Conclusion: The fermentation of lactose, fructose or sorbitol in the small bowel due to SIBO may increase the likelihood of LI, FI and SI incorrect diagnosis. We suggest that all symptomatic patients will undergo SIBO testing and eradication if diagnosed positive, prior to LI, FI or SI HBT evaluation.

Disclosure of Interest: None declared

P1208 A PROSPECTIVE APPLICATION OF THE ESPGHAN GUIDELINES IN A SYMPTOMATIC ADULT POPULATION

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Introduction: Current adult guidelines require histological confirmation of celiac disease (CD)[1]. However, recent pediatric guidelines have proposed algorithms to reduce the need for biopsy in genetically susceptible symptomatic children[2].

Aims & Methods: To explore the applicability of the current ESPGHAN criteria and assess the accuracy of serology in detecting mucosal abnormalities in a prospective cohort of symptomatic adults. We recruited 234 consecutive symptomatic adults (mean age = 33.9ys) referred to our tertiary center, showing EMA positivity and genetic susceptibility. All patients underwent upper endoscopy with multiple biopsy sampling in the duodenum. Histological lesions were graded according to the Corazza-Villanacci classification and considered diagnostic for grades $\geq$ B. Anti-tTG titers were assessed with 12 different assays; one ELISA kit (specified Upper Limit of Normal = 3.5U/ml) was used in 141 subjects (60.3%), while a second one in 59 (25.2%, ULN $\pm$ 9.9U/ml). Accuracy of anti-tTG testing and optimal cut-off levels were determined by means of a ROC curve. Performance was also calculated for a cut-off 10 times ULN.

Results: Mean anti-tTG levels at inclusion were 71.1 $\pm$ 4.4U/ml, while mean adjusted levels (anti-tTG/ULN) were 14.8 $\pm$ 0.9 times ULN (mean $\pm$ SE). Among the 234 patients, 21 (9%) showed no atrophy; partial and total atrophy were present in 85 (36.3%) and 128 (54.7%) respectively. Anti-tTG levels significantly correlated to the degree of villous atrophy (ANOVA $p < 0.001$; $\rho_s = 0.397$, $p < 0.001$). AUC proved a fair diagnostic accuracy both for the unadjusted and adjusted anti-tTG levels (respectively 0.803, 0.807; $p < 0.01$). For the ESPGHAN criterion of anti-tTG $\geq$ 10 times ULN, a positive predictive value (PPV) of 97.7% was calculated (sensitivity = 59.2%, specificity = 86.9%). The optimal cut-off for adjusted anti-tTG levels was $\geq$16 times ULN, with a PPV of 98.9% (sensitivity = 41.2%, specificity = 95.7%). Considering different assays, results were puzzling; although in the first one PPV(= 97.14%) seemed to peak at around 50U/ml (14.3 times ULN), the second assay proved considerably more predictive: for a cut-off = 37.3U/ml (3.7 times ULN) it showed a superior PPV = 100% (sensitivity 53.1%, specificity 100%). Age and sex did not correlate with histology or serology.

Conclusion: In an adult population of symptomatic patients showing EMA positivity and genetic susceptibility, anti-tTG titers correlate with the degree of villous atrophy. The ESPGHAN criteria showed a PPV similar to that of symptomatic children[3]. However, PPV was higher for a cut-off 16 times ULN and peaked when considering a single ELISA assay, indicating a possible kit-specific variability. Further studies are required to determine if optimal cut-off levels are dependent on patient or assay characteristics. The findings of this study could prove useful when assessing equivocal histological cases of CD, and could help in guiding patient follow-up.

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P1209 THE DIAGNOSTIC DELAY IN CELIAC DISEASE IS SIGNIFICANTLY INCREASED IN WOMEN DUE TO DOCTOR'S BUT NOT PATIENT'S DELAY

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Introduction: The majority of celiac disease (CD) cases are associated with a considerable diagnostic delay or even remain undiagnosed due to a variety of reasons, such as silent disease, unspecific symptoms with overlap to other diseases and insufficient awareness in both patients as well as physicians. The total diagnostic delay can be subdivided into patient's (gap between beginning of symptoms and first medical consultation) and doctor's (gap between first medical consultation and definitive diagnosis of CD) delay. There is insufficient data on diagnostic delay, its comprising two components and associated factors in CD. In addition, it remains to be clarified, whether its extent has an impact on the course of the disease.

Aims & Methods: We performed a large systematic, nation-wide patient survey study among unselected CD patients in Switzerland.

Results: A total of 1689 patients (76% female; mean age 41.3 y, range 0-92y, mean age at diagnosis 31.1y, range 0-83y) were analysed. We found a mean total diagnostic delay of 72.3 months (median 18, IQR 4-72), with an enormous range from 0 up to 780 months and roughly equal fractions of patient's and doctor's delay with a mean/median of 39.9/4 (IQR 0-28) and 39.4/3 (IQR 0-24) months, respectively. While the mean age of diagnosis was not different in female vs. male patients (31.2 vs. 31 years), both, mean/median total (76.2/21 vs. 56.9/12, $p = 0.008$) and doctor's (43.8/5 vs. 25.6/2, $p < 0.001$) diagnostic delay was significantly higher in female vs. male patients, whereas patient's delay was similar (39.4/3 vs. 37.8/2, not significant).

A total of 15.3% of patients reported that IBS was diagnosed or suspected by their treating physician(s), prior to establishing the diagnosis of, significantly more women than men (16.7 vs. 10.5%, $p = 0.004$). Notably, a significantly higher doctor's delay in women was equally observed if patients with antecedent IBS diagnoses were excluded (mean/median total, patient's and doctor's delay of 67.1/16 vs. 45.5/11, $p = 0.015$; 37.8/3 vs. 33/2, n.s.; 36/4 vs. 22.5/2, $p = 0.004$ in non-IBS women vs. men).

Treatment of any nutritional deficiencies states was significantly more often required in patients with a delay $\geq$24 vs. $<$24 months (74.6 vs. 58.4%, $p < 0.001$). The same was observed for need of steroids and/or immunosuppressants to treat CD with 4.4 vs. 2.0%, corresponding to a relative risk of 0.48 (CI 0.26-0.87, $p = 0.016$).

In addition, total, patient's and doctor's diagnostic delay was significantly higher in patients diagnosed after vs. up to the age of 30 (mean/median 106.3/32, 59.5/4 and 58.5/6 vs. 35.7/12, 18.9/2 and 19.3/3 months, respectively, for all $p < 0.001$).

Conclusion: There is a substantial diagnostic delay in CD, which is significantly longer in patients with older age at diagnosis and in female patients. The increased diagnostic delay in women is due to doctor's but not patient's delay. This increase in doctor's delay cannot be explained by antecedent symptoms or diagnosis of IBS prior to establishing the diagnosis of CD. Our findings point to an insufficient awareness for CD in physicians especially in women and older patients. In addition, a longer diagnostic delay is associated with more frequent need of immonusuppressants to treat CD and a lower chance of clinical remission after diagnosis.

Disclosure of Interest: None declared

P1210 THE SELECTED PARAMETERS OF OXIDATIVE STRESS, ANTIOXIDANT CAPACITY AND INFLAMMATORY MEDIATORS IN TREATED AND UNTREATED ADULT PATIENTS WITH COELIAC DISEASE - A PRELIMINARY REPORT

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Introduction: It has been assumed that oxidative stress is one of the mechanism that can play a role in gluten toxicity although its role in patients with celiac disease (CD) is not fully elucidated.

Aims & Methods: To evaluate the cytotoxic effect of gluten by determining the selected parameters of oxidative stress, antioxidant capacity and inflammatory mediators in treated and untreated adult patients with CD The study has enrolled 98 patients, including 72 patients with CD. The subjects were divided into 3 groups: 1) patients with untreated CD (N = 35), including patients with newly diagnosed CD (N = 10) and patients not adhering to a gluten-free diet (GFD) (N = 25), 2) patients with CD on GFD for at least two years (n = 37), 3) healthy control group (N = 26). A standard blood test, the level of anti-tissue transglutaminase antibodies and /or endomysial antibodies and

histopathological study of duodenal biopsy were evaluated. The serum concentration of nitric oxide (NOx), IL-15, FRAP (Ferric Reducing Antioxidant Power), reduced glutathione (GSH) and glutathione peroxidase (GPx) were detected.
Results: There were no differences between the groups in serum concentrations of Il-15. The concentration of GSH in untreated patients was lower than in patients on GFD and control group. GPx activity was lower in treated and untreated CD group than in controls. FRAP level was reduced in patients with CD compared to the controls. The serum level of nitrate in patients with CD without GFD were significantly higher than those of controls ($p < 0.001$). Patients who were on a gluten-containing diet had also significantly lower values of RBC, HGB and HCT in comparison to control group. Patients who did not obey GFD had significantly higher serum level of nitrate and the level of coeliac antibodies ($p < 0.001$) and lower level of MCV in comparison to the patients who used recommended diet. It was observed that ferritin concentration was positively correlated with iron concentration (CW = 0.402), AST (CW = 0.542), bilirubin (CW = 0.501), and with GGTP (CW = 0.824). The latter parameter was also correlated with AST (CW = 0.551), bilirubin (CW = 0.493) and with total cholesterol level (0.417). Two parameters, nitrate level and ALT were also highly positively correlated (CW = 0.503).
Conclusion: Oxidative/antioxidative balance is shifted toward oxidative side by gluten-containing diet in patients with CD. GFD, especially enriched in antioxidants may decrease oxidative stress in this group. Results of study suggested the role of serum NO as an indicator of diet compliance. Strong correlation between NO level and ALT may suggest the role of NO in the pathogenesis of gluten-induced hepatitis. Further research are needed.
Disclosure of Interest: None declared

P1211 GLUTEN-FREE DIET DOES NOT INFLUENCE THE OCCURRENCE AND THE TH1/TH2 NATURE OF IMMUNE-MEDIATED DISORDERS ASSOCIATED WITH COELIAC DISEASE

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Introduction: Even though coeliac disease (CD) is considered to be the most common lymphocyte T helper-1 (Th-1) mediated enteropathy in Western countries, it seems that Th1- and lymphocyte T helper-2 (Th-2)-mediated diseases could co-exist in CD patients.
Aims & Methods: The aims of the study were: 1) to establish the prevalence of immune-mediated disorders at time and after CD diagnosis; 2) to evaluate a possible change in immune response after starting gluten-free diet (GFD); 3) to investigate the potential role of GFD in reducing and/or preventing immune-mediated disorders in adult CD patients.
Methods: We carried out a database-driven study including all consecutive adult CD patients followed-up at our Gastrointestinal Unit. CD diagnosis was made in accordance with the Oslo classification. The main demographic, clinical, serological, endoscopic and histological features were recorded for all CD patients. All patients were investigated for the presence of Th1 and/or Th2-mediated disorders at time of CD diagnosis. The search for Th1 and/or Th2 diseases were reassessed after a 5-years follow-up period. Statistical analysis included chi-square (χ^2) test, Mann-Whitney U test, ANOVA and odds ratio (OR) when indicated. All results were considered significant with a $p < 0.05$.
Results: Finally, 1255 CD were enrolled (M/F 258/997). 257 patients out of 1255 (20.5%) suffered from immune-mediated diseases at time of CD diagnosis, with 150 of them (58.4%) presenting a Th1-predominant disease vs 107 (41.6%) with Th2-mediated diseases ($p = 0.7$). After a 5-years follow-up period, 682 out of 1255 patients (54.3%) showed an immune-mediated disease even if following a restrict GFD; among them, 391 subjects (57.3%) presented a Th1-related condition vs 291 (42.7%) with a Th2-mediated disease ($p = 0.8$). When comparing the prevalence of immune-mediated diseases before and after CD diagnosis, no significant ''switch'' from Th1- to Th2-response or vice versa was seen (58.4% and 41.6% before CD vs 57.3% and 42.7% after CD diagnosis, respectively; p = ns). The number of patients with a Th1- and/or a Th2-merdiated disease increased during the GFD period (20.5% vs 54.3%; $p < 0.01$; OR 1.9). The most frequent CD-related immune-mediated diseases were: Hashimoto's thyroiditis (8.2% before vs 24% after CD diagnosis; $p < 0.01$; OR 1.6); psoriasis (0.7% before and 2.7% after CD diagnosis; $p < 0.01$; OR 1.5), type 1 diabetes mellitus (1.8% before vs 0.2% after CD diagnosis; $p < 0.01$; OR 0.08). No correlation was found between the developed immune-mediated diseases and age at the time of CD diagnosis, clinical symptoms, a-tTG serum levels and Marsh grade.
Conclusion: The prevalence of immune-mediated diseases at time of CD diagnosis, particularly as regards with Hashimoto's thyroiditis, psoriasis and type 1 diabetes mellitus, is high and it seems to increase in the follow-up period despite GFD. GFD does not influence and/or reduce the prevalence, the occurrence and the Th1/Th2 nature of immune-mediated diseases in CD.
Disclosure of Interest: None declared

P1212 THE PREVALENCE OF COELIAC DISEASE AT THE INTERSECTION OF EUROPE AND ASIA: A POPULATION-BASED CROSS-SECTIONAL STUDY FROM MERSIN, TURKEY

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Introduction: Coeliac Disease (CD) has emerged as a public health problem, and the disease prevalence varies among different races and nations. In Turkey, which stands at an important transition point at the junction of Europe and Asia where the races mix, an adult community-based prevalence study has not been conducted as yet. Thus, the present study was designed to investigate the prevalence of undiagnosed CD in Turkish adult population in Mersin and to detect the characteristics of these pts.
Aims & Methods: This study was undertaken during the June 2011–January 2013. Mersin is a cosmopolitan city in the South of Turkey, which has 10 different districts. Adults aged 18 and older living within the Mersin formed the target population of the study. According to 2009 population census results, there are 1133935 people in this age group living in Mersin. The minimum sample size has been calculated as 1519. It was planned to include 1600 people in the study group. The study group was sorted based on age, gender and district via stratified sampling method. Family physicians were selected district-wide through random sampling method. Respondents to be sampled were chosen from those registered to each family physician by using stratified sampling method. Participants were evaluated for demographic features, and gastrointestinal symptoms, and were tested for anti-tissue transglutaminase (tTG) and anti-Deaminated Gliadin Peptid (DGP) immunoglobulin (Ig) A and IgG using an ELISA assay. Small intestinal biopsies were obtained from the seropositive pts, and they were examined according to the Marsh classification. HLA-DQ2 and DQ8 genotyping and blood tests were done.
Results: 1554 people participated in this study and the participation rate was 97.1%. The mean age was 42 years and 50.4% were female. 12 of the participants showed anti-tTG/DGP IgA or IgG positivity. Thus, the total seropositivity was 0.77%. The mean age of seropositive participants was 41 years, and 83% of them were female. All seropositive participants were either HLA-DQ2 or DQ8 positive. 5 pts had Marsh type 3 pathology, 1 had Marsh type 2. The other 6 pts had Marsh type 0. Endoscopic findings concordant with celiac disease observed in only 5 pts with Marsh type 3 pathology. All pts were asymptomatic; but 5 pts had iron deficiency anemia, 1 had deficiency of vitamin B12 and premenopausal osteoporosis and her daughter was diagnosed with CD earlier. One had the IgA deficiency. 1 pt had been diagnosed Hashimato tiroiditis before. The niece of 1 pt was diagnosed with CD. The son of a male pt, who had diagnosis of irritabl bowel syndrome earlier, was diagnosed with CD after reevaluation.
Conclusion: This study is the first population-based prevalence study of CD in Turkish adults. We found that seroprevalence of CD is 0.77%. All pts were asymptomatic. Iron deficiency anemia was the most common finding and positive family history stood out. The importance of serology for diagnosis should not be disregarded and it should be kept in mind that histologic and endoscopic findings were negative in half of the cases.
Disclosure of Interest: None declared

P1213 INNATE AND ADAPTIVE CYTOKINES AND CHEMOKINES IN THE DUODENAL MUCOSA OF SUBJECTS WITH NONCELIAC GLUTEN SENSITIVITY VERSUS CELIAC DISEASE

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Introduction: Immune mechanisms have been implicated in the pathogenesis of nonceliac gluten sensitivity (NCGS), a condition characterized by intestinal and/or extraintestinal symptoms caused by the ingestion of gluten in nonceliac/non-wheat allergic individuals.
Aims & Methods: We here investigated both innate and adaptive cytokines and chemokines in the duodenal mucosa of subjects with NCGS. Duodenal biopsies from 14 NCGS subjects, nine patients with untreated celiac disease (CD) and 12 control individuals were cultured ex vivo for 24h, and in the culture supernatants we detected by ELISA interleukin (IL)-15, and by cytokine array a number of innate cytokines, including tumor necrosis factor-a, IL-1b, IL-6, IL-12p70, IL-23, IL-27 and IL-32a, adaptive cytokines, including interferon (IFN)-g, IL-17A, IL-4, IL-5, IL-10 and IL-13, chemokines, including CCL1, CCL2, CCL3, CCL4, CCL5 and CXCL1, and growth factors, including granulocyte colony stimulating factor (G-CSF) and granulocyte-macrophage colony stimulating factor (GM-CSF). Eleven out of 14 NCGS subjects underwent a double-blind, placebo-controlled crossover trial, over which their intestinal and extraintestinal symptoms were scored.
Results: Both innate and adaptive cytokines, chemokines and growth factors did not differ between NCGS subjects and control individuals. On the contrary, mucosal levels of IL-6, IL-15, IL-27, IFN-g, IL-17A, IL-23, G-CSF, GM-CSF, CCL1 and CCL4 were significantly higher in patients with untreated CD in comparison to NCGS subjects and control individuals. No statistical significant correlation was found between innate/adaptive cytokines, chemokines or growth factors and clinical response to gluten or placebo.
Conclusion: Abnormalities of the mucosal immune response in terms of either innate/adaptive cytokines or chemokines do not seem to be implicated in the pathogenesis of NCGS.
Disclosure of Interest: None declared

P1214 A CROSS-SECTIONAL STUDY OF THE CLINICAL PHENOTYPE IN COELIAC DISEASE IN A LARGE COHORT OF IRISH PATIENTS

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Introduction: Coeliac disease (CD) occurs both in adults and children at a rate of approximately 1% in most populations [(1)]. There has been a considerable increase in CD positive serology over time. CD has a wide spectrum in its clinical presentation [(1-4)]. The co-existence of CD with other disorders has been well reported [(5, 6)]. Few studies have addressed the clinical phenotype of CD in Ireland, and those available consist of small samples with little information on associated disorders [(7-9)].
Aims & Methods: The aim of this study is to explore the clinical phenotype of a large cohort (n = 443) of Irish CD patients (310 females, median age 57 years, range 16-87 years) through the retrospective analysis of medical charts.
Results: The median age of diagnosis was 45 years (range 0.5-86 years). Onset of CD was symptomatic in 383 patients (93%), while 29 presented with a subclinical phenotype (7%). 305 (68.8%) patients reported having ever suffered from common disorders associated with CD (i.e. osteoporosis, iron deficiency, depression). These patients were diagnosed later in life (Median = 48 years) than those who did not report having had any of these conditions (Median = 39 years) (p = 0.001). 145 patients (32.7%) had a coexistent autoimmune disorder, the most prevalent being thyroid disease (19.6%).
Conclusion: CD patients commonly present with other autoimmune and non-autoimmune conditions. Diagnosis later in life appears to be associated to the development of co-existent non-autoimmune disorders.

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Disclosure of Interest: None declared

P1215 PREDICTING HISTOLOGICAL REMISSION IN PATIENTS WITH CELIAC DISEASE ON A GLUTEN-FREE DIET

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Introduction: Up to 30% of patients with celiac disease (CD) will have persistent symptoms despite the introduction of a gluten-free diet (GFD). Assessment of adherence in celiac disease can involve any combination of patient self-reporting adherence, dietetic assessment, serology and biopsy with histology. Histology is considered to be the 'gold standard' but this requires a repeat endoscopic examination with its associated risks and problems with tolerance. As a result surrogate markers of persistent gluten exposure and histological changes such as serology are frequently used but the relationship between serology and persistent histological changes is not linear. A structured interview with a dietician has been shown to be the most accurate method of assessing GFD adherence however this is time consuming and requires extra clinic visits. The aim of this study was to assess the usefulness of two novel options. Firstly a previously internally validated scoring system for assessing GFD adherence[1] (which has never been externally validated) and secondly a rapid deamidated gliadin peptide based point of care test (POCT, Simtomax) for the prediction of persistent villous atrophy (VA).
Aims & Methods: All patients with known CD and persistent symptoms coming to a specialist CD endoscopy list for the re-assessment of histology were invited to take part. All patients were tested for Endomysial Antibody (EMA), tissue transglutaminase (tTG), immunoglobulins and the POCT. They were also asked to complete a questionnaire to calculate a 5 point score (0 – 4) with a high score representative of improved adherence to a gluten-free diet. All patients underwent gastroscopy with at least 4 biopsies from the second part of the duodenum and 1 to 2 biopsies from the bulb.
Results: 94 patients (77% female, mean age 52.6) were recruited between April 2013 and December 2014. Median duration of GFD was 84 months (range 6-768). 36 (38.3%) patients had persistent VA on duodenal biopsy. The POCT was the most sensitive marker with 63.4% of patients with VA having a positive test. EMA was the most specific surrogate marker at 82.8% although it was highly insensitive with only 33.0% of patients with VA having a positive EMA. The adherence score could not be reliably used to predict VA with a sensitivity of only 30.6%.

Measure	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Adherence Score	30.6	79.3	47.8	64.8
tTG	50.0	75.9	56.3	37.9
EMA	33.0	82.8	54.5	66.7
POCT	63.4	60.3	50.0	72.9

Conclusion: An accurate surrogate marker for VA could reduce the number of endoscopies required. In this cohort the POCT had the best sensitivity, detecting 23/36 (63.4%) cases of villous atrophy, however this is pilot data and further work is required. It may be that additive methods for assessing adherence could achieve 100% sensitivity.

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P1216 HEART RATE VARIABILITY (HRV) – PREDICTOR OF MESENTERIC ISCHEMIA IN CARDIAC PATIENTS

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Introduction: Reduced HRV is proved to be a predictor of mortality after myocardial infarction and other medical conditions, including congestive heart failure, diabetic neuropathy, depression or post-cardiac transplant status. Mesenteric ischemia (MI) is a medical condition in which inflammation and injury of the small intestine result from inadequate blood supply.
Aims & Methods: We aimed to identify if the decrease-frequency component of HRV may be used as a predictor for the mesenteric ischemia (MI) occurrence in cardiac patients before the onset of digestive symptoms. Using ECG recordings, we measured the HRV in 170 patients admitted in Cardiac Care Unit (CCU) of St. Apostle Andrew Emergency Hospital of Constanta County. The study was done in collaboration with Gastroenterology Department of the same medical institute. We created a model of prediction for occurrence of MI in patients with cardiac diseases using correlations between the type of HRV and MI.
Results: From the total of 170 patients hospitalized in CCU in 3 months (January - March' 15), 24 (14.11%) patients developed MI. From the total of 36 patients with decreased high-frequency HRV, 18 patients (50%) developed the MI. In contrast, only 6 patients (4%) of those with high-frequency value of HRV get the disease. Our results fixed a positive correlation between reduced high-frequency of HRV and MI occurrence (r = 0.98).
Conclusion: Identifying the HRV in cardiac patients and making interventions to improve the parasympathetic nervous system activity we can simply avoid the occurrence of a high risk mortality disease that can worsen the prognosis of cardiac patients.
Disclosure of Interest: None declared

P1217 SUPERIOR MESENTERIC ARTERY SYNDROME: CLINICAL, ENDOSCOPIC AND RADIOLOGICAL FINDINGS

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Introduction: The superior mesenteric artery (SMA) syndrome is a rare entity presenting with upper gastrointestinal tract obstruction and weight loss, due to the compression of the third part of duodenum between the aorta and the SMA. Studies to determine the optimal methods of diagnosis and treatment are essential.

Aims & Methods: This study aims to analyze the clinical presentation, the diagnosis and the management of SMA syndrome. Over a 2-year period (2013-2014), 10 cases of SMA syndrome (out of 2074 esophagogastroduodenoscopies (EGDS)) were initially suspected through EGDS. Therefore, these patients performed computed tomography (CT) scan to confirm the diagnosis. Once the diagnosis was confirmed, the patients were referred to a gastroenterologist and to a nutritionist to discuss a personalized approach of therapy; furthermore, for each patient a surgical consultation was proposed.
Results: In our series we evaluated retrospectively 10 cases of SMA (8 females), with a prevalence of 0.005%. Median age was 23.5 years (range 14-40), and the median body mass index was 21.5 kilos/m2. Symptoms developed between 6 to 24 months (median 18). Premorbid conditions were present in four patients (Anorexia nervosa in two patients, and Spina bifida and Crohn's disease in two patients). Only 2 of 10 patients were hospitalized, due to severe malnutrition. Median aorto-mesenteric angle was 22°, and median aorta-SMA distance was 6 mm. Interestingly, all the patients improved on conservative treatment.
Conclusion: o date, SMA syndrome represents a diagnostic and therapeutic challenge. With regard to previous series published, our results show: the importance of the endoscopic suspicion of SMA syndrome, confirmed by CT scan; the preponderance of a longstanding and chronic onset; a female preponderance; the importance of the nutritional counseling in the therapeutic approach; the absence of need for surgical intervention; the better diagnostic accuracy of the narrowing of the aorta-SMA distance, rather than the narrowing of the aortomesenteric angle. Further prospective studies, with a larger number of patients, are needed to clarify the best way to diagnose and manage the SMA syndrome.
Disclosure of Interest: None declared

P1218 HIGH VARIATION IN TREATMENT STRATEGIES FOR GASTROINTESTINAL ANGIODYSPLASIAS: A NATIONWIDE SURVEY IN THE NETHERLANDS

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Introduction: Gastrointestinal angiodysplasias are the second leading cause of gastrointestinal bleeding in the elderly. On the other hand, angiodysplasias can be a coincidental finding on endoscopy and asymptomatic. Guidelines assisting in a treatment strategy in patients with symptomatic angiodysplasias are lacking.
Aims & Methods: Our aim was to assess current practice of the treatment of gastrointestinal angiodysplasias and attitudes concerning these practices among Dutch gastroenterologists.
To achieve this aim, a 19-item web-based survey covering current practices in the treatment of gastrointestinal angiodysplasias was administered between February and April of 2015 to gastroenterologists in the Netherlands.
Results: Of the 395 e-mailed questionnaires, a total of 111 (28%) gastroenterologists completed the survey (mean age = 47 years; 24% women), and the sample is representative for the profession in the Netherlands. Respondents correctly identified Von Willebrand disease (17%), chronic kidney disease (21%) and aortic stenosis (86%) as risk factors for the development of angiodysplasias. Colonoscopy (54%) and esophagogastroduodenoscopy (43%) were the preferred first tools to screen for angiodysplasias. The favoured (77%) first treatment option is endoscopic argon plasma coagulation, while 20% starts iron supplementation or blood transfusions. This decision on treatment strategy is mostly (65%) based on the location of the angiodysplasia. Thirteen percent of the gastroenterologists would treat angiodysplasias as a coincident finding during endoscopy for another indication than anaemia. Of the pharmacological therapies, thalidomide (40%) is preferred over octreotide (19%). In case octreotide is prescribed, 20 mg monthly is mostly (52%) given after a test period with short-acting octreotide (86%).
Conclusion: Identification of risk factors, the diagnostic tools used and treatment strategies varies widely between gastroenterologists in the Netherlands. Moreover, a considerable proportion of gastroenterologists would treat angiodysplasias found by coincidence, which is not according to endoscopic guidelines. A guideline for the treatment of angiodysplasias might be helpful to create a more uniform and evidence-based practice.
Disclosure of Interest: None declared

P1219 PROSPECTIVE, QUANTITATIVE ASSESSMENT OF PAIN REDUCTION AND QUALITY OF LIFE IMPROVEMENT FOLLOWING VASCULAR INTERVENTION IN CHRONIC MESENTERIC ISCHEMIA; A PILOT STUDY

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Introduction: There is a lack of knowledge of the quantitative effects of treatment of chronic mesenteric ischemia (CMI) on pain and health-related quality of life (HRQOL). This prospective pilot-study was designed to determine the mid-term change of pain intensity and HRQOL in CMI treatment.
Aims & Methods: Patients with mesenteric ischemia, treated with endovascular intervention for luminal stenosis or endoscopic release of the diaphragm crux in celiac artery compression syndrome between August and December 2013 were enrolled. For pain we used the visual analogue scale for pain intensity (VAS-PI, graded 0-100 mm). For HRQOL we used the 36-item Short Form Health Survey (SF-36). All parameters were obtained before and three months after the intervention.
Results: We included 29 patients; mean age 55.9 years (SD 20.0), 79.3 % female. Single-vessel (n = 7), multi-vessel (n = 15) atherosclerosis and celiac artery compression syndrome (n = 7). The VAS for pain improved following treatment: for the average pain from median 60 (IQR: 48 – 72) to 2 (IQR: 0 – 40, $p < .001$), for postprandial pain from median 74 (IQR: 63–84) to 2 (IQR: 0–40, $p < .001$), and for post-exercise pain from median 63 (IQR: 50–80) to 4 (IQR: 0–30, $p < .001$). The number of painful days per week decreased from median 7 days (IQR: 5–7) to 1 day (IQR 0–6.8 days, $p < .001$). The HRQOL measured with SF-36 improved for five of eight dimensions (role physical (p.005), bodily pain (p.001), vitality (p.004), social functioning (p.001) and mental health (p.001)) and the both component summary scores (physical (p.008) and mental (p.009)).
Conclusion: This pilot study showed that three months after vascular intervention for CMI the pain is significantly reduced and quality of life for patients improved. The magnitude of effects exceeded our expectations, but larger studies with longer follow-up are needed to confirm this observation.
Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015 09:00–17:00
NUTRITION II – HALL 7

P1220 EFFECTS OF GUT MICROBIOTA MANIPULATION BY ANTIBIOTICS ON PLASMA AMINO ACID LEVELS IN OBESE HUMANS

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Introduction: Gut bacteria can alter the bioavailability of amino acids and have been implicated in the pathogenesis of metabolic disease. Obesity and type 2 diabetes are associated with elevated systemic concentrations of aromatic and branched-chain amino acids (BCAA).
Aims & Methods: We aimed to investigate the effects of gut microbiota knockdown on arterial amino acid levels in humans. For this, 38 obese male subjects (BMI $31.2 \pm 2.6 kg/m^2$, age $59 \pm 7y$, HOMA-IR 4.5 ± 0.2) with impaired fasting glucose and/or impaired glucose tolerance participated in a randomized double-blind placebo-controlled trial. Subjects were orally treated with 1500mg/day amoxicillin (AMOX; broad-spectrum antibiotic), vancomycin (VANCO; aimed at Gram-positive bacteria), or placebo (PLA; microcrystalline cellulose) for 7 days. Before and after treatment, arterial concentrations of 21 amino acids were measured using liquid chromatography.
Results: Baseline BCAA concentrations were high but did not differ between groups: 445.0 ± 35.9µmol/L (VANCO), 423.3 ± 42.7µmol/L (AMOX), and 440.6 ± 44.7µmol/L (PLA), $P = 0.406$. AMOX treatment specifically increased BCAA levels in comparison to PLA (464.3 ± 60.7µmol/L vs. 434.6 ± 66.5µmol/L; $P = 0.042$), whilst VANCO treatment did not (441.9 ± 30.3µmol/L; $P = 0.867$). Within treatment groups, isoleucine (one of the BCAA) concentrations increased significantly upon both AMOX (from 68.4 ± 8.1µmol/L to 79.3 ± 10.9µmol/L; $P = 0.003$) and VANCO treatment (from 70.3 ± 7.7µmol/L to 78.3 ± 9.6µmol/L; $P = 0.001$), but not in the PLA group (from 75.6 ± 10.5µmol/L to 78.1 ± 12.3µmol/L; $P = 0.305$). Besides, arginine concentrations increased significantly only upon AMOX treatment (from 89.9 ± 20.1µmol/L to 101.5 ± 21.2µmol/L; $P = 0.025$). Other amino acids were not affected by any treatment.
Conclusion: The broad-spectrum antibiotic AMOX increases plasma BCAA concentrations. Current ongoing analyses will shed light on the nature of the gut microbiota alterations provoked by AMOX in relation to specific amino acid aberrations, parameters of insulin sensitivity, and substrate metabolism in obese subjects with impaired glucose tolerance.
Disclosure of Interest: None declared

P1221 ADIPOCYTE HYPERTROPHY AND INFLAMMATION COULD AFFECT LIVER INJURY IN NAFLD BY ALTERNATIVE MECHANISMS

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Introduction: Lifestyle changes and obesity have spread over the world, leading to an obesity epidemic. Metabolic syndrome (MS) induced by obesity is similarly common in industrialized countries and accordingly non-alcoholic fatty liver disease (NAFLD) and the more severe form non-alcoholic steatohepatitis (NASH) are the most common liver diseases in industrialized countries.
Aims & Methods: Aim of the present study was to investigate if changes in adipose tissue affect development or severity of NAFLD and NASH in MS. To this end visceral adipose tissue, liver tissue samples and blood were obtained from 145 morbidly obese patients (age median = $49 \pm 10y$; 114w/30m; mean BMI: $53 \pm 8.7 kg/m^2$) undergoing bariatric surgery. Biopsies were scored with NAFLD activity score (NAS; median 3/range 1-7) and patients were grouped as NAFL ($NAS \leq 4$) or NASH ($NAS > 4$). Blood samples taken before surgery were analyzed for parameters of liver injury M30 (Apoptosis) and M65 (Overall cell death) and adiponectin. Visceral adipose tissue and hepatic mRNA levels of genes for inflammasome activity and fatty acid metabolism were assessed by qRT PCR.

Results: NASH patients showed significantly higher concentration of markers for cell death (M65), HbA1c, classic liver parameters (ALT, AST), and CRP in serum. Adiponectin serum concentration was significantly lower in NASH. Expressions of analyzed genes did not differ between the groups. Though, NAS was significantly correlated to visceral adipocyte cell size, classic liver parameters, fasting blood glucose and HbA1c, M65, and to liver mRNA expression of MCP1 and NLRP. Cell size of visceral adipocytes was correlated to serum leptin and liver mRNA expression of ATG12 and was inversely correlated to mRNA expression of FASN and CGI-58 in the liver. Moreover MCP1 mRNA expression in adipose tissue correlated with mRNA expression of MCP1, autophagy genes (ATG5, ATG12, LC3), and PPARγ2 in the liver. Expression of the FAS-Receptor in adipose tissue correlated with mRNA expressions of CGI-58 and PPARγ2 in liver tissue.
Conclusion: These results suggest that visceral adipocyte hypertrophy affects hepatic regulation of fatty acid metabolism by downregulation of genes involved in triglyceride breakdown. This may lead to accumulation of lipotoxic compounds and increased liver injury. In contrast high HbA1c might be associated to increased inflammation in the adipose tissue which seems connected to inflammatory gene expression and autophagy in the liver, affecting liver metabolism by other mechanisms.
Disclosure of Interest: None declared

P1222 ACTIVATORS OF THE TRANSCRIPTION FACTOR NRF-2 AS NEW REGULATORS OF HEPCIDIN EXPRESSION

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Introduction: Hepcidin, an acute phase protein, is regarded as central mediator of the cytokine-induced anaemia of chronic inflammation (ACI), one of the most common causes of iron deficiency anaemia in patients with inflammatory bowel disease and obesity. Identified as primary trigger is the STAT-3 mediated induction of hepcidin synthesis in the liver and macrophages by cytokines of the IL-6 family (IL-6, oncostatin M).
Aims & Methods: The current study aimed to determine additional signal transduction paths of cytokine-induced hepcidine synthesis, with particular focus on a possible role of the transcription factor NF-E2-related factor 2 (Nrf2). HepG2 and Huh7 cells were cultivated in standard conditions and treated for 6 or 16 h with either IL-6 (10 ng/ml) or OSM (10 ng/ml) alone, or in combination with STAT-3 inhibitor (50 μM), sulforaphane (SFN) (10 μM), dimethylfumarat (DMF) (100 μM), 15-Deoxy-Delta-12-14-prostaglandin J2 (15d-PGJ2) (10 μM). For the reporter gene assay, the cells were transfected by lipofectamine with hepcidin promoter plasmid, and the luciferase activity was measured luminometrically. Quantitative real time PCR was performed for quantitative determination of mRNA. Proteins were analysed using western blot.
Results: Both IL-6 (10 ng/ml) and OSM (10 ng/ml) trigger significant hepcidin promotor activation (***$p < 0.001$), which could be significantly reduced (***$p < 0.001$) by coincubation with the STAT3 inhibitor (VI, S3I-201). Coincubation of OSM and IL-6 with the Nrf-2 activators SFN (***$p < 0.001$), DMF (**$p < 0.01$) and 15d-PGJ2 (*$p < 0.05$) led not only to significant inhibition of hepcidin promotor activity, but also to a significant reduction of intracellular hepcidin mRNA levels (mind. *$p < 0.05$). No reduction of the pSTAT/STAT ratio was observed after 8 and 16h incubation with SFN.
Conclusion: The results indicate the transcription factor Nrf-2 to play a role in the expression of the iron regulator hepcidin, with possible involvement of STAT-3 independent signal transduction pathways.

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Disclosure of Interest: None declared

P1223 IRREGULAR BOWEL HABIT INCREASES THE RISK OF OBESITY

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Introduction: Bowel habit in accordance with chronobiology is one of the fundamental circadian rhythms with the regular frequency of at least 7 times a week. The slowing of the rhythm in the form of constipation is a risk factor for colorectal cancer [1,2], the risk of which is increased in obesity [3,4]. However, the impact of the slowdown of the rhythm on the risk of obesity remains poorly studied.
Aims & Methods: The aim of this study was to elucidate the relation between irregular bowel habit and the risk of obesity.
Methods: Validated questionnaires were used for weekly monitoring of circadian rhythm of defecation at 2501 persons, who consider themselves healthy. Regular bowel habit was detected in 1399. Irregular bowel habit was diagnosed in 1102. To diagnose the risk of obesity we randomized two groups of 200 persons with regular and irregular rhythm of defecation. The first group of 100 people (86 women) 23-85 years demonstrated regular bowel habit (daily morning bowel movement with a frequency of 7 times per week). The second group of 100 persons (90 women) 25-79 years demonstrated irregular bowel habit (not daily defecation, frequency 1-6 times per week). The analyzed groups did not significantly differ by gender and age. We calculated the body mass Index (BMI), according to which each group was divided into three subgroups: I – BMI 20-25 kg/ml — normal, II — BMI 25-30 kg/ml— overweight, III — BMI above 30 kg/ml is obesity.
Results: There were identified 53 persons with normal BMI, 37 persons with overweight and 10 subjects with obesity among 100 individuals of the first group with regular bowel habit (RBH). Consequently, in a group of persons with regular bowel habit the risk of obesity was 10%. There were 36 persons with normal BMI, another 36 persons - with overweight, and 28 subjects with obesity among 100 persons of the second group with the irregular bowel habit (IBH). Consequently, in the group of persons with a broken, irregular bowel habit the risk of obesity was 28%. Thus, the risk of obesity among patients with IBH was almost three times (2.8 times) higher than among persons with RBH.
Conclusion: Among individuals with regular bowel habit the probability of normal body mass index (53%) was almost 1,5 times higher than in patients with irregular bowel habit (36%). Among those with irregular bowel habit the risk of obesity (28%) was almost 3 times higher than in those with regular bowel habit (10%). The lack of regular bowel habit predominantly in women of different age significantly (almost 3 times) increases the risk of obesity.

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Disclosure of Interest: None declared

P1224 PRELIMINARY RESULTS OF AN ONGOING MULTI-CENTER, PROSPECTIVE, CONTROLLED TRIAL OF THE DUODENAL-JEJUNAL BYPASS LINER FOR THE TREATMENT OF TYPE 2 DIABETES MELLITUS IN OBESE PATIENTS: EFFICACY AND FACTORS PREDICTING A SUB-OPTIMAL EFFECT

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Introduction: The global increase in obesity incidence results in an increase of type 2 diabetes mellitus (T2DM) incidence. Surgical treatment has proven to be effective, however it carries a high risk of complications. The duodenal-jejunal bypass liner (EndoBarrier®, GI Dynamics, DJBL) is an endoscopic implant that mimics the intestinal bypass portion of the Roux-en-Y Bystric Bypass. It results in weight loss and improvements in glucose control in obese patients with T2 diabetes mellitus (T2DM).
Aims & Methods: This is an interim report of an ongoing three years study. The aim of this prospective, controlled, multicentre study is to determine the effectiveness of DJBL and to identify clinical factors associated with a sub-optimal outcome of DJBL.
Results: Fifty seven subjects (32 with an implant, 25 controls) were included in the study. The groups were comparable with respect to age, gender, BMI (mean 40.7 vs. 38.5 kg/m2), T2DM duration (7.3 vs. 8.1 years), HbA1c level (89 vs 83 mmol/mol) and T2DM treatment. In the DJBL group, all devices were successfully implanted. Only four devices had to be explanted prior to the end of the 10 months study period (bleeding, dislocation and need for ERCP because of choledocholithiasis). The mean procedure time was 19.2 minutes for an implantation and 18.5 minutes for an explantation. At 10 months there was significantly greater weight loss and %EWL (21% vs. 8% and 44 vs. 14) and significantly improved long term compensation of T2DM marker HbA1c (decreased by 25 vs. 11 mmol/mol) in the DJBL group. T2DM medicinal treatment could be reduced in more device subjects than controls. There was no serious adverse event. Mild abdominal pain and nausea after implantation were experienced by 72% of patients during first 14 days after implantation, 33% of patients during the first month and 10% of patiens after one month. Lower initial BMI, distal position of the anchor and lower body height were identified as negative prognostic factors for pain.
Conclusion: The DJBL is safe when implanted for 10 months, and results in significant weight loss and HbA1c reduction. This suggests that this novel device is a candidate for the primary therapy of morbid obesity and T2DM. Lower initial BMI, distal position of the anchor and lower body height could be negative prognostic factor for pain.
Disclosure of Interest: None declared

P1225 CD24 POLYMORPHISMS ARE ASSOCIATED WITH OBESITY RISK

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Introduction: Background: Obesity is a global epidemic and major risk factor for various health conditions. It is a multifactorial condition and has genetic and environmental etiology. Several studies have suggested candidate genes that may predispose to obesity. CD24 is a small, mucin-like glycoprotein that is expressed in almost all tumors. We have recently found that *CD24* knockout male (but not female) mice are overweight and display greater insulin sensitivity than their wild-type (WT) littermates. Several single nucleotide polymorphisms (SNPs) in the *CD24* gene are known to be associated with various cancers and autoimmune diseases.
Aims & Methods
Aim: Evaluate whether *CD24* SNPs are associated with risk of obesity.
Methods: Genomic DNA was obtained from peripheral blood leukocytes of 63 obese Israeli patients (BMI ≥ 35; 27 males, 36 females) and 53 age- and gender-matched healthy controls (BMI ≤ 27; 30 males, 23 females). Samples were genotyped for the *CD24* SNPs: C170T (rs8734), TG1527del (rs3838646), A1626G (rs1058881) and A1056G (rs1058818) by real-time PCR using Custom TaqMan® SNP allelic discrimination assays. χ^2 test was used to examine whether the *CD24* gene polymorphisms are associated with obesity. An association was considered statistically significant if $p < 0.05$. Odds ratio (OR) and 95% confidence interval (CI) were estimated by logistic regression models.
Results: A1056G and A1626G SNPs were found to be more prevalent in obese patients than in normal weight subjects (OR = 2.973, 95% CI: 1.155-7.6527, p = 0.0234 and OR = 4.7212, 95% CI: 2.1408-10.412, p = 0.0001, respectively). Moreover, all four CD24 SNPs carriers were more predominant in the obese group, although the correlations were not statistically significant. In addition, gender adjustment revealed a significant association between A1626G and obese male patients. The prevalence of the WT variant was 0% in the obese males and 76.7% control males (p = 0.0001). A similar trend was found for A1056G, although the correlation was not statistically significant (OR = 4, 95% CI:0.9667 -16.551, p = 0.0613).
Conclusion: CD24 may play a role in male obesity
Carriers of A1056G and A1626G *CD24* SNPs may be more prone to develop obesity, and in particular male A1626G carriers.
No correlation was found between age-dependency and genetic variant distribution in obese patients.
Disclosure of Interest: None declared

P1226 CERIUM DIOXIDE NANOPARTICLES IN THE NOVEL ANTIOBESITY TREATMENT STRATEGY

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Introduction: Childhood obesity is a predisposing factor for poor health in adolescence and also in adulthood. The number of overweight has more than doubled in children and quadrupled in adolescents in the past 30 years. Today the correction of lifestyle and diet remain the most effective way of obesity treatment. Despite of this a lot of obese people do not improve their health and the search of nontoxic antiobesity drugs is still urgent.
Aims & Methods: So, the aim of the study was to investigate the influence of cerium dioxide nanoparticles ($nCeO_2$) intermittent administration on the obesity in rats induced with neonatal injection of monosodium glutamate (MSG).
The study was carried out on 3 groups of rats: control, MSG- and MSG + $nCeO_2$, 10 animals in each. Just after the born they were injected with saline (control) or MSG (4 mg/g, 3M) at 2nd–10th day of life subcutaneously. A month after born MSG-rats had been treated with water in a volume of 2.9 ml/kg, MSG + CeO_2 groups – with 1 mM solution of CeO_2 (1 mg/kg) intragastrically (i.g.). Introduction had been performed intermittently (two-week courses alternated with two-week breaks) for 3 months. In 4-month rats visceral adipose tissue (VAT) mass was measured, content of lipid peroxidation products in serum and enzymatic activity of superoxide dismutase (SOD) and catalase was estimated by standard biochemical methods. The content of proinflammatory cytokines (interleukin (IL)-1β, IL-12Bp40, interferon-γ (INF-γ)) and anti-inflammatory cytokines (IL-4, IL-10, tumor growth factor-β (TGF-β)) were measured by ELISA kits.
Results: In 4-month MSG-rats it was observed the development of visceral obesity in rats that was confirmed by the increase of the VAT mass, alteration of body mass index, index Lee, malfunction of cytokine system and shift to prooxidative processes. In MSG + $nCeO_2$ we established the decrease of visceral obesity (the VAT mass in MSG-group *vs.* MSG + $nCeO_2$ group 19.0 ± 2.0 g *vs.* 8.3 ± 1.4 g., $p < 0.05$). $nCeO_2$ significantly reduced the conjugated dienes content by 27% ($p < 0.05$), TBA-products – by 43% ($p < 0.05$) and Schiff bases – by 21% ($p < 0.05$) compared to MSG-group. Nanoparticles reduce the content of proinflammatory cytokines (IL-1β, IL-12Bp40, INF-γ) in rat serum. We have also performed the preclinical study of $nCeO_2$ on rat and showed its very low toxicity ($LD_{50} > 2000$ mg/kg i.g., V toxicity class).
Conclusion: Thus, it was revealed the antiobesity properties of intermittent administration of $nCeO_2$. The reduction of visceral adiposity in rats by $nCeO_2$ was associated with its antioxidant and anti-inflammatory properties. Discovered properties and low toxicity of $nCeO_2$ allow to recommend it for clinical investigation.
Disclosure of Interest: None declared

P1227 COLONIC BIOMASS: EFFECT OF DIET, MEALS AND DEFECATION

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Introduction: The metabolic activity of colonic microbiota is influenced by diet and meals, but their effect on colonic biomass is not known. Our aim was to determine whether and to what extent meals and diet influence colonic content.
Aims & Methods: In 10 healthy subjects 2 abdominal MRI scans were acquired during fasting one week apart after 3 days on low- and high-residue diets, respectively. On each diet, daily fecal output and the number of the daytime anal gas evacuations were measured. On the first study day, a second scan was acquired 4 h after a test meal (n = 6) or after 4 h without ingesting anything (n = 4). On the second study day, a scan after a spontaneous bowel movement was also acquired.
Results: On the low-residue diet, daily fecal output averaged 145 ± 17 mL, subjects passed 11 ± 2 anal gas evacuations during daytime and by the third day colonic content was 622 ± 44 mL. The high-residue diet increased the 3 parameters up to 223 ± 19 mL fecal output, 17 ± 3 anal gas evacuations and 821 ± 59 mL colonic content ($p < 0.05$ vs low-residue diet for all). On the low-residue diet, 4 hours after the test meal colonic content increased up to 732 ± 51 mL ($p < 0.05$ vs first fasting scan), whereas no significant change was observed after 4 hours fast. Defecation significantly reduced colonic content in distal colonic segments (by $29 \pm 5\%$; p = 0.002).
Conclusion: Meals and diet influence microbiota metabolic activity and colonic biomass as well.
Disclosure of Interest: A. Bendezú: None declared, M. Mego: None declared, X. Merino: None declared, A. Accarino: None declared, E. Monclus: None declared, M. Izquierdo: None declared, I. Navazo: None declared, F. Azpiroz Financial support for research: Danone, Given, Beneo, Shire, Clasado, Consultancy: Danone, Almirall

P1228 THE INTERACTIONS BETWEEN DIET, MUCOSAL PROLIFERATION AND GI CANCER RISK IN RURAL AFRICANS AND AFRICAN AMERICANS

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Introduction: Based on the analysis of worldwide epidemiological studies, it has been estimated that >90% of GI cancers are diet-related. African Americans have an extremely high risk of colon cancer (~65:100,000) while rural Africans rarely get the disease. On the other hand, rural Africans have an extremely high risk of squamous cell carcinomas of the esophagus (125/100,000 in men) while African Americans have a low risk.
Aims & Methods: We investigated the usual diets and performed upper and lower endoscopies to obtain mucosal biopsies for the measurement of mucosal biomarkers of cancer risk form the esophagus, stomach, and colon (Ki67 staining of proliferative epithelial cells) in matched groups (n = 20, age 50-65, BMI 18.5-35 kg/m2) from each population.
Results: Dietary analyses based on 3-day recalls have shown that there are major differences in the diets of rural Africans when compared to African Americans. Our measurements show that the Ki67 staining of esophageal epithelial proliferative cells was higher in rural Africans than African Americans. The glandular gastric ki67 cell staining was also higher in the rural Africans compared to African Americans. On the other hand, African Americans had higher proportions of Ki 67 staining cells in the colonic mucosal crypts.
Conclusion: Based on our measurements of epithelial proliferation rates by Ki67 immunohistochemistry as a biomarker of cancer risk, our results support the view that the high fiber, low meat and fat African diet suppresses colon cancer risk, but that its lower vitamin and antioxidant content may increase the risk of upper GI cancers as compared to African Americans. The high prevalence of *H pylori* infections in Africans (i.e. 80%) was associated with higher antral proliferative rates, but not with cancer rates in the population as a whole.

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P1229 INTAKE OF NATURALLY-OCCURRING OLIGOSACCHARIDES WITH POTENTIAL PREBIOTIC ACTIONS: VALUABLE DATA FOR FUTURE PREBIOTIC RESEARCH

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Introduction: Reducing intake of indigestible, fermentable, short chain carbohydrates (low FODMAP diet) has recently been shown to reduce absolute and relative abundance of 'beneficial' bacterial in the faeces. Furthermore, mildly increasing FODMAP intake over that in the habitual diet had prebiotic effects [1]. These variations are likely to be due to alteration in dietary fructo-oligosaccharides (fructans) and galacto-oligosaccharides (GOS), which, when given as pure supplements at doses of 5-10 g/d can be prebiotic. However, the impact in clinical trials of such prebiotics on clinical outcomes has been in general disappointing. Dietary prebiotic intake has never been taken into account in such studies.

Aims & Methods: The aim of this study is to define the potential influence of normal dietary intake of oligosaccharides by quantifying dietary fructan and GOS intake and examining variance across individuals.

Data obtained during the validation of a food frequency questionnaire in 72 healthy Australians [2] was reanalysed using an updated FODMAP database that included recent publications [3] and unpublished addition. Intakes of fructans and GOS were calculated and expressed as g/d, presented as mean, range and quartiles.

Results: Mean (SD) of fructan and GOS intake was 3.8 (1.1) and 1.2 (0.9) g/d, respectively. Combined prebiotic fructan and GOS intake ranged from 1.4 – 10.3 g/d. Common foods contributing to the higher fructan intake were wheat and rye breads, pasta, onion, garlic and shallots and the most common sources of GOS were legumes and nuts.

Table 1: Prebiotic Fructan and GOS consumption data from the CNAQ validation study

FODMAP type	Mean (SD) g	Range (g)	1st Quartile (g)	2nd Quartile (g)	3rd Quartile (g)	4th Quartile (g)
Fructan	3.8 (1.1)	1.1-7.3	<2.9	2.9-3.7	3.8-4.6	>4.6
GOS	1.2 (0.9)	0.2-4.3	<0.6	0.6-0.9	1.0-1.4	>1.4
Fructan + GOS	5.0 (1.6)	1.4-10.3	<3.7	3.7-4.8	4.9-6.2	>6.2

Conclusion: Dietary intake of potentially-prebiotic oligosaccharides varies widely from minimal (where effects of supplemented prebiotics may be high) to high (where additional prebiotic effects of supplements are less likely). These findings imply that the highly variable inter-individual effect of supplemental prebiotics in clinical trials might reflect habitual dietary intake, which should be assessed in any prebiotic trial. Such an approach might assist in defining the value or otherwise of prebiotic supplementation.

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P1230 THE ROLE OF FODMAPS IN GASTRIC ACCOMMODATION AND UPPER GASTROINTESTINAL MOTOR ACTIVITY

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Introduction: There is accumulating evidence for the benefit of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) for the management of irritable bowel syndrome (IBS) symptoms. Whether FODMAPs alter the upper GI response to nutrients, including gastric accommodation (GA), remains to be assessed.

Aims & Methods: The objectives were to assess the role of different FODMAPs in the intragastric pressure (IGP) response to nutrient ingestion (which reflects GA), upper GI motility, meal-induced satiation and symptom generation. A high resolution manometry and infusion catheter were positioned in the proximal stomach of healthy volunteers. After a stabilisation period and when the subjects were in late phase II of the migrating motor complex (MMC), one of four solutions (Table 1) were intragastrically infused at 60 mL/min, three days to one week apart in a single-blind randomised cross-over order. The infusion ended when subjects scored maximum satiation (0-5 scale). IGP was recorded for the duration of the drink infusion and for the following 3 hours. IGP was presented as change from baseline (mean ± SEM). Intensity of epigastric and GI symptoms were rated before the infusion, and then every 15 minutes using a 100 mm VAS. Results were compared using a repeated measures ANOVA.

Results: 15 healthy volunteers (19-32 y, 7 men, 18-30 BMI) were randomised. All were non-smokers with no GI symptoms or history of GI disease. Total ingested volumes at maximal satiation did not differ significantly between solutions (fructan 1376 ± 248 mL; fructose 1080 ± 147 mL, FODMAP mix 1252 ± 154 mL, glucose 1092 ± 126; p = NS). In all subjects and with each infusion, the IGP decreased initially to gradually recover thereafter. The mean IGP drop during infusion was significantly less for fructans (4.71 ± 0.59 mmHg), when compared to all other solutions ($p < 0.001$; fructose -5.86 ± 0.75 mmHg, FODMAP mix -5.38 ± 0.64 mmHg and glucose -5.69 ± 0.70 mmHg). After recovery of the IGP drop, although all solutions remained constantly high in their pressure across the three hours post infusion, the fructans maintained a significantly higher intra-gastric pressure (3.8 ± 0.16 mmHg) compared to the fructose, FODMAP mix and glucose (2.6 ± 0.16, 2.1 ± 0.15 and 1.9 ± 0.1 mmHg, respectively) ($p < 0.0001$). In comparison to the glucose, differences in symptoms were reported for bloating following the fructose, for wind following the fructans, fructose and FODMAP mix and for cramps following the fructose and FODMAP mix solutions ($p < 0.05$).

Table 1: Composition of challenge solutions (in 500 ml water)

		FODMAP total
1. Fructans		19 g
2. Fructose		50 g
3. FODMAP mix	10 g fructans + 5 g galacto-oligosaccharides + 15 g fructose + 5 g sorbitol + 5 g mannitol	40 g
4. Glucose (control)		50 g

Conclusion: This study indicates that fructans induce a significantly lower IGP response in the healthy state, when compared to the other FODMAPs and glucose. Unraveling the sensory, neural and/or hormonal pathways involved in the effect of fructans on gastric physiology require further mechanistic studies. The findings also offer opportunities to identify whether ingestion of fructans contribute to symptoms associated with impaired GA seen in functional GI patients, including IBS.

Disclosure of Interest: None declared

P1231 EXOGENOUS SALSOLINOL TARGETS REGULATORY MECHANISMS CONCERNED WITH ENERGY BALANCE

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Introduction: The digestive system produces a number of hormones to aid energy metabolism, digestion and nutrient uptake into the circulation. Some of them influence gut function, neuronal metabolism, appetite and peripheral energy metabolism, and some of them may be linked with the process of neurodegeneration. Salsolinol (1-methyl-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline), which structurally resembles MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), may be involved in this process, especially if several scientists have been pointing its regulatory role in the central and peripheral neurohormonal circuits.

Aims & Methods: The aim of this study was to evaluate the influence of subchronic intraperitoneal salsolinol administration on body weight, food intake, adipose tissue accumulation, gastric emptying and postprandial serum levels of GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1).

Male Wistar rats were subjected to continuous intraperitoneal low dosing of salsolinol (200 mg/kg in total) with osmotic mini-pumps for two and four weeks with either normal (S1, S2) or high-fat diet (SF1, SF2). Appropriate groups served as the controls (C1, C2, CF1, CF2). Blood samples were collected and gastric emptying was assessed by determination of residual solid food in the stomach at the end of the experiment. Both epididymal fat pads were dissected from each rat and weighted. Serum samples were assayed for GIP and GLP-1 by ELISA method.

Results: Salsolinol significantly reduced animals total body weight, however there were no differences in the cumulative food intake between the groups. The epididymal fat pad/body weight ratio was significantly different between control rats on high-fat diet (CF1 = 15.97 mg/g ± 0.6, CF2 = 21.65 mg/g ± 2.6) and salsolinol-treated rats on high-fat diet (SF1 = 13.09 mg/g ± 0.8, SF2 = 14.54 mg/g ± 2.6). The percentage of mean residual solid food in the stomachs of the S1 group rats (80.24% ± 6.06; $p < 0.05$) was significantly higher than in the C1 group (68.40% ± 6.13). GIP levels were elevated in salsolinol-treated rats in comparison with their controls, especially in groups S2 = 0.42 ng/ml ± 0.12 (C2 = 0.04 ng/ml ± 0.04) and SF2 = 0.36 ng/ml ± 0.19 (CF2 = 0.18ng/ml ± 0.14). GLP-1 levels were lower in salsolinol-treated rats in comparison with their controls, especially in the group SF2 = 0.007 ng/ml ± 0.004 (CF2 = 0.039 ng/ml ± 0.014).

Conclusion: Salsolinol might influence regulatory mechanisms concerned with body weight and fat content through neurohormonal pathways. Our results might suggest that salsolinol targets at least some incretin regulatory circuits.

Disclosure of Interest: None declared

P1232 XYLOGLUCAN FOR THE TREATMENT OF ACUTE DIARRHEA: RESULTS OF A RANDOMIZED, CONTROLLED, OPEN-LABEL, PARALLEL GROUP, MULTICENTRE, NATIONAL CLINICAL TRIAL

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Introduction: There is a strong rationale for the use of agents with film-forming protective properties, like xyloglucan, for the treatment of acute diarrhea. However, few data from clinical trials are available.

Aims & Methods: To assess the efficacy, safety and time of onset of the antidiarrheal effect of xyloglucan (Xilaplus®), in comparison with two widely used antidiarrheal agents, the yeast probiotic *Saccharomyces boulardii* (Ultra-Levura®), and diosmectite (Smecta®), an absorbent activated natural aluminosilicate clay. This randomized, controlled, open-label, parallel group, multicentre, clinical trial included adult patients with acute diarrhea due to different causes.

Patients were randomized to receive a 3-day treatment (4 capsules/6 h of Xilaplus®, 3 sachets/day of Smecta® and 2 capsules/day of Ultra-Levura®), being the first dose administered at visit 1. Presence of symptoms (stools type 6 and 7 on Bristol Scale, nausea, vomiting, abdominal pain and flatulence) was assessed by a self-administered *ad-hoc* questionnaire at 1, 3, 6, 12, 24, 48 and 72 h after the first dose administration. Adverse events were recorded.

Results: 150 patients (69.3% women, mean age 47.3 ± 14.7 years) were included ($n = 50$ in each group). A faster onset of action was observed in the xyloglucan group compared with diosmectite group, in terms of absolute and mean number of stools ($p < 0.05$) during the first 24 h. In the xyloglucan group the highest reduction of the number of type 6 and 7 stools was observed at 6 h with an effect that was statistically significant compared with diosmectite ($p = 0.031$). A higher efficacy was also observed with xyloglucan compared to *S. bouliardii* at 12 and 24 h.

Xyloglucan was the most efficient treatment in reducing nausea throughout the study, particularly during the first hours (from 26% at baseline to 4% after 6 and 12 h).

An important improvement of vomiting was observed in all three treatment groups, with null percentages at 6 and 12 h.

Xyloglucan was more effective than diosmectite and *S. bouliardii* in reducing abdominal pain, with a constant improvement observed throughout the study. At visit 2, the lowest percentage of patients with abdominal pain was recorded in the xyloglucan group (10%), in comparison with diosmectite (22%) and *S. bouliardii* (12%).

The clinical evolution of flatulence followed similar patterns in the 3 groups, with continuous improvement of the symptom. The greatest improvement was shown in the xyloglucan group, with 10% of patients with flatulence at visit 2, compared with diosmectite (30%) and *S. bouliardii* (18%).

All 3 treatments were well tolerated, without adverse events.

Conclusion: Xyloglucan is a fast, efficacious and safe option for the treatment of acute diarrhea, with a rapid onset of action in reducing diarrheal symptoms.

Disclosure of Interest: L. Gnessi Financial support for research: Lucio Gnessi received honoraria from Novintethical, SA to perform the study. X. Llop Directorship(s): Xavier Llop is medical director of Novintethical Pharma, SA, N. Piqué Financial support for research: Núri a Piqué received honoraria from Novintethical, SA to write the abstract

P1233 LOW RATES OF FEEDING GASTROSTOMY ASSOCIATED MORBIDITY AND MORTALITY IN THE COMMUNITY

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Introduction: Morbidity after 30 days and morbidity after 1 year from gastrostomy placement is poorly characterised as patients are discharged into the community. We prospectively recorded morbidity and mortality associated with gastrostomy placement over a five-year period.

Aims & Methods: Community dietitians regularly reviewed all patients with a gastrostomy after hospital discharge, prospectively recording morbidity and mortality between 2008-2012. In addition hospital databases and case notes were examined. Recorded morbidity included insertion site infection, leakage, over granulation, haemorrhage and buried bumper.

Results: There were no deaths and few complications directly related to gastrostomy insertion in 350 patients. We collected a total of 571 years of gastrostomy data. Mortality within 10 days was predominantly from a respiratory cause. 30 day, 3 and 21 month cumulative mortality (and morbidity) were 8% (2%), 16% (10%) and 35% (15%) respectively. 38% of patients required treatment for an insertion site infection with 70% of these having further infections. Overall there was a site infection every 2.1 years a gastrostomy was in situ. Complications such as buried bumpers, persistent fistulas and overgranulation were rare. Few gastrostomies required replacement (11%).

Mortality after gastrostomy placement during study period, median (IQ range) or N (%)

	Time to death after PEG placement				
	< 30 days	1-3 months	3-6 months	6-12 months	> 12 months
Mortality (% of total population)	28 (8%)	29 (8%)	29 (8%)	37 (11%)	66 (19%)
Accumulative mortality	28 (8%)	57 (16%)	86 (25%)	123 (35%)	189 (54%)

Conclusion: This is the first prospective study of morbidity and mortality in a large number of patients undergoing gastrostomy placement over an extended period of time. We have demonstrated reassuringly low rates of gastrostomy-associated morbidity and mortality. There was no direct mortality. The greatest morbidity resulted from gastrostomy-site infection.

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Disclosure of Interest: None declared

P1234 INCREASING SERUM ALBUMIN LEVEL SHORTLY AFTER GASTROSTOMY INSERTION PREDICTS LONGER SURVIVAL IN ELDERLY DEMENTED PATIENTS

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Introduction: A growing proportion of elderly demented patients are now surviving. Thus, at the advanced stages of their illness, swallowing problems are being developed. There is insufficient evidence whether percutaneous endoscopic gastrostomy (PEG) is beneficial in this population (1).

Aims & Methods

Aim: We aimed to evaluate the outcomes of PEG in elderly patients with an advanced dementia.

Methods: Included 194 demented patients who underwent PEG insertion in our unit during 2002-2011. Data regarding their background diseases, age, gender, survival by December 2014, and the level of albumin, hemoglobin, lymphocytes and cholesterol performed 14 days prior the procedure and 90 days after it, were retrieved. Univariate analysis using Cox proportional hazard model was performed to find predicting factors for mortality. Multivariate analysis using Cox regression model for time to death was performed with significant risk factors from the univariate analysis.

Results: Out of 194 demented patients 70% were women. Mean age was 83.28 ± 7.6, range 64-106 years. The median survival rate was 13 months (range 0-105).

32 patients died within 30 days of PEG insertion. Those who died within 1 month of the procedure were older (87 ± 8.6 vs. 83 ± 7.2 years, $p = 0.003$) and had a lower hemoglobin level (10.8 ± 1.5 vs. 11.6 ± 1.5, $p = 0.013$). In addition they had a lower mean baseline albumin as compared to those who survived more than 30 days (2.5 ± 0.6 vs. 3.3 ± 0.5, $p < 0.001$). In 95 patients, a significant increase in serum albumin level was noted within 90 days of PEG insertion. Those patients survived significantly longer than those who failed to improve their baseline albumin levels (24.5 ± 2.5 vs.18.2 ± 2.2, $p = 0.063$). Failure to improve albumin level was a risk factor for mortality (HR: 1.416, 95% CI: 1.029-1.948, $p < 0.001$). Each increment of 1gr/dL of serum albumin, decreased mortality risk by HR = 0.54 (95%CI: 0.41-0.71, $p < 0.001$). An older age and lower hemoglobin level were risk factors for mortality too (HR: 1.17, 95% CI: 1.05-1.31, $p = 0.004$; HR: 0.84, 95% CI: 0.77-0.93, $p < 0.001$). Gender and the absolute count of lymphocytes didn't affect mortality. When we performed multivariable analysis by cox regression, age and albumin level remained the only risk factors for mortality.

Conclusion: Elderly demented patients benefit PEG if their baseline serum albumin is within the normal range or if their albumin level is improved within 3 months after PEG insertion. We believe that when eating problems are developed in demented patients, there is a "window of opportunity" in which PEG should be inserted. Therefore, physicians should follow especially the albumin level of the demented patients and offer them PEG when a decreased level would have noticed. Thus, an improvement of the albumin level will eventually prolong their survival.

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Disclosure of Interest: None declared

P1235 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS: A CASE SERIES

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Introduction: Patients with amyotrophic lateral sclerosis (ALS) and severe bulbar muscle impairment may be at risk of respiratory failure during percutaneous endoscopic gastrostomy (PEG). Non-invasive ventilation (NIV) might reduce the risk of respiratory complications in patients with severe ventilatory impairment (SVI).
Aims & Methods: Our aim was to evaluate the outcomes of PEG placement with NIV in patients with ALS with SVI. It was a retrospective study including ALS patients with dysphagia due to severe bulbar muscle impairment proposed for PEG placement, in the last 5 years. Pre-PEG pulmonary data was analyzed. All the PEG were placed using the pull method and the procedure was performed with the patient under nasal NIV with portable home ventilator in spontaneous timed bi-level mode.
Results: Included 38 patients (63% female) with a mean age of 61 ± 25 years and a mean duration of the disease of 4 ± 3 years. Most patients (92%) performed NIV at home prior to PEG placement, for a median period of 5 months (IQR: 0-15), with an average IPAP: 20 ± 3 mmH2O, EPAP: 6 ± 1 mmH2O and volume current: 887 ± 504 mL. Fifty-three percent of patients had SVI for 24 hours/day. The median time between the onset of bulbar symptoms and the placement of PEG was 7 months (IQR: 2-16). In most of the patients (90%) the procedure was performed without general anesthesia, and in 53% midazolam was given. In 68% of the patients PEG was performed due to dysphagia and in the rest of the patients due to severe ventilator impairment during feeding. There were no complications from PEG placement and the mortality rate at 3, 6 and 12 months was 27%, 42%, 54% respectively.
Conclusion: The placement of PEG with NIV seems to be safe in patients with ALS with SVI. In this cohort no patients complicated or required tracheal intubation. Our results encourage PEG placement even in high-risk patients.
Disclosure of Interest: None declared

P1236 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: SAFETY AND EFFICACY

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Introduction: The percutaneous endoscopic gastrostomy (PEG) is currently considered the best option for enteral feeding in patients requiring enteral nutrition for long periods.
Aims & Methods: This study aimed to evaluate the current indications, technical success, complications and need to repeat procedures.
Methods: Retrospective study of patients referred for our endoscopy unit for PEG placement for a period of 3 years (2012-2014). We reviewed clinical reports in order to evaluate the long term outcome of patients after placement of PEG by the pull method.
Results: Summaries of the results: included 223 patients (60% males) with a mean age of 63 ± 17 years, followed for a median of 18 months (IQR: 8-28). The indications for PEG placement were: cancer (26% of which 80% were head and neck cancers), cerebral vascular accident (23%) and neurological causes (22%). During the analyzed period of time, from the first to the third year, there was an increased rate of PEG placement of 41%. Minor complications occurred in 29 patients (13%) including: inadvertent PEG removal (7%), leakage of the food content (4%) and infection stoma (2%). Five patients had major complications including buried bumper syndrome ($n = 4$) and hemorrhage ($n = 1$). Only 2% of the patients removed the PEG due to complications. There were no deaths related to the procedure and the mortality rate at 30 days 4%. Twenty-two percent of patients replaced the PEG in a median of 10 months (IQR: 5-16). Oral feeding was resumed in 6% of patients at a median of 6 months (IQR: 2-15) after PEG placement.
Conclusion: There was a significant increase in the number of PEGs placed in the last 3 years. This is a safe procedure associated with a low complication rate.
Disclosure of Interest: None declared

P1237 HIGH SERUM MANGANESE LEVELS IN PATIENTS RECEIVING LONG TERM TOTAL PARENTERAL NUTRITION

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Introduction: In patients receiving long-term parenteral nutrition (TPN), high manganese levels have been associated with cholestatic liver disease and nervous system disorders including parkinsonism. Case reports have shown patients on long-term TPN with high manganese levels developing parkinsonism with psychiatric effects. T1-weighted magnetic resonance imaging in these patients demonstrates high-intensity signals in the globus pallidus which regresses on discontinuation of the manganese supplementation. NICE guideline (CG32) recommends checking manganese levels in patients on long-term TPN every 3-6 months.
Aims & Methods: The aim of the study was to assess serum manganese levels in patients on long term TPN and to establish if removing manganese supplements results in normalisation of serum manganese levels.
Serum manganese levels were measured in all patients receiving long-term TPN in the North East of England and Cumbria during the study period from Nov 2013 to Jan 2015. Of those with a high serum manganese, manganese supplementation was withdrawn and the levels were rechecked within 12 months of withdrawal.
Results: In the North East of England and Cumbria, 77 patients were receiving long-term TPN during the study period. Of these, 48 were female and 29 were male. The age range of patients was from 19 to 84 years. The indication for TPN in these patients included; 23 ischaemia, 21 inflammatory bowel disease, 10 intra-abdominal malignancy, 9 post-surgical complication, 5 enteric dysmotility, 4 radiation enteritis, 3 visceral myopathy, 1 connective tissue disorder and 1 congenital abdominal defect. Of the 77 patients, 46 had high serum manganese levels at initial measurement (mean 288nmol/l; range 90-1620). Serum manganese levels were rechecked in these patients within 12 months of manganese withdrawal. When rechecked; 26 patients had normal serum manganese levels and 11 patients had manganese levels reduced but not above the normal limits. 9 patients did not undergo a repeat manganese level due to either acute illness, discontinuation of TPN or death. No patients reported any neurological symptoms or were noted to have cholestatic liver function tests to suggest toxicity.
Conclusion: The study demonstrated that high levels of manganese are found in 60% of all patients receiving long-term TPN. Withdrawing manganese supplementation in these patients results in a normalisation of manganese in levels in 57% and a reduction in manganese level in 20% within 12 months. Although no patients in the study showed signs of manganese toxicity, studies have shown a potential risk of toxicity resulting in neurological disorders. This study highlights the importance of checking manganese levels in keeping with NICE guidance every 3-6 months and adjusting manganese supplementation for those with high levels to avoid potential toxicity. Manganese is supplemented in combination with other trace elements some of which may not be replaced individually including molybdenum, iodine and chromium. Further studies are required to determine the clinical significance of withdrawing these trace elements.
Disclosure of Interest: None declared

P1238 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: WHAT IS ITS REAL IMPACT IN PATIENTS? EXPERIENCE FROM A SPECIALIZED MULTIDISCIPLINARY CONSULTATION

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Introduction: Despite creating an enteric route for administration of food and drugs, the real benefit of a gastrostomy is still matter of debate. We aimed to evaluate the global impact of percutaneous endoscopic gastrostomy (PEG) in patients followed at a specialized multidisciplinary consultation.
Aims & Methods: From the 201 patients submitted to PEG between May/2011 and September/2014, 60 were included in a prospective unicentric study. Age, gender, indication for PEG, Charlson index and mortality were analysed. Number of emergency department (ED) visits or hospitalizations, presence of pressure ulcers, and changes in laboratorial values were collected and compared before and after PEG.
Results: From the 60 analysed patients, 33 (55%) were women and the median age was 79 years (range from 19 to 92). The main indications for PEG were dementia (43.3%), post-stroke dysphagia (30%) and post-traumatic brain injury (8.3%). Mean Charlson Index was 6 and mortality rate during follow-up was 27%. A decrease in the mean number of hospitalizations (1.4 vs. 0.3; $p < 0.001$) and visits to ED (2.2 vs. 1.1; $p = 0.003$) were noted in the next 6 months after PEG, when compared to the previous semester. In 53.8% of patients with pressure ulcers, complete ulcer healing was observed after PEG; however, the number of patients with pressure ulcers before and after PEG did not differ significantly ($p = 0.203$). PEG was associated with significant increases in haemoglobin ($p = 0.024$), lymphocytes ($p = 0.041$), total cholesterol ($p = 0.008$), transferrin ($p < 0.001$), albumin ($p < 0.001$) and total proteins ($p < 0.001$), and significant decrease in serum sodium ($p = 0.001$), which were recognized 4 months after PEG. No significant changes were found on urea ($p = 0.682$), creatinine ($p = 0.146$) or triglycerides ($p = 0.398$).
Conclusion: Percutaneous endoscopic gastrostomy has an early impact in patients. It reduces the need of hospital health care services, facilitates healing of pressure ulcers, and induces metabolic changes that reflect a better nutrition and hydration.
Disclosure of Interest: None declared

P1239 APPROPRIATE RISK STRATIFICATION FOR PERCUTANEOUS ENDOSCOPIC GASTROSTOMY INSERTION MAKES PLACEMENT SAFE AND FEASIBLE IN LATE-STAGE MOTOR NEURONE DISEASE

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Introduction: Weight loss and malnutrition may aggravate muscle weakness, and independently predict survival in Motor Neurone Disease (MND) (1). Gastrostomy placement improves body mass index and offers a small survival benefit (2), but 30-day mortality following PEG insertion has previously been quoted as 10% (3,4) with most risk observed in patients with a forced vital capacity < 50% predicted. Since 2011 we routinely undertook PEG placement in patients with MND. In September 2012 we introduced a risk stratification system prior to PEG placement to guide suitable precautions for those deemed at high risk. These were: a reduction in sedative dose, 30° head-up bed tilt, gently held paediatric mouthguard, and with only experienced operators placing PEGs in the highest-risk patients.
Aims & Methods: Our objective was to evaluate the risk of PEG placement in patients with MND and to evaluate whether risk stratification might reduce complications. We undertook a retrospective systematic search and analysis of a prospectively maintained database of all patients with MND who underwent placement of a PEG between 1/2/11 and 31/3/15. 30-day complication and mortality rate, and dose of sedation given were analysed for the whole cohort and for the pre- and post-risk stratification groups
Results: Data was collected for 90 patients. Overall 30- day mortality was 4/90 (4.4%). None of the deaths were directly related to PEG insertion. 2 patients had complications within 30 days of the procedure (2.2%). The mean (± standard error) midazolam dose was 3.3mg (±0.3) and fentanyl dose was 54.7mcg (±5.8). 39 patients (43%) had PEGs placed prior to the introduction of a risk stratification system and 51 (57%) afterwards. There was a reduction in mortality from 2/39 (5.1%) to 2/51 (3.9%) and a reduction in complications from 1/39 (2.6%) to 1/51 (2%) following introduction of the risk stratification system. Mean sedation rates reduced for midazolam from 4.3mg (±0.6) to 2.6mg (±0.2) ($p < 0.01$) and for fentanyl from 62.2mcg (±5.3) to 49.0mcg (±3.5) ($p < 0.05$).
Conclusion: We have shown a significantly lower 30 day mortality of 4.4% compared to previously quoted mortality of 10% for both PEG and RIG insertion. This suggests that PEG is a suitable and safe choice of feeding tube for patients with MND. We have also demonstrated that with risk stratification, lower doses of sedation and standard precautions taken for all patients with MND the overall mortality rate and complication rate can be reduced to an acceptable level and allows PEGs to be placed in those previously considered unsuitable. Further work needs to be undertaken looking at longer follow-up data and determining the optimal timing of gastrostomy. We would recommend PEG insertion with multi-disciplinary team participation as a safe and effective method of nutritional support in MND.

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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 09:00–14:00
LIVER & BILIARY III – HALL 7

P1240 PROTON-PUMP INHIBITORS AND SPONTANEOUS BACTERIAL PERITONITIS IN LIVER CIRRHOSIS: ANY ASSOCIATION?

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Introduction: Proton-pump inhibitors (PPI) are one of the most commonly prescribed pharmacologic classes, leading to their overuse in clinical practice. They were associated to a high susceptibility for enteric infections. The association between PPI and Spontaneous bacterial Peritonitis (SBP) remains unclear.
Aims & Methods: Retrospective case-control study of 143 consecutive episodes of SBP between 2009-2014, compared with cirrhotic patients without SBP (ratio 1:1). They were divided in 4 groups, according with PPI chronic therapeutic and indications: PPI and approved indication (G1), PPI and non-approved indication (G2), without PPI and approved indication (G3) and without PPI and non-approved indication (G4). The appropriate use is considered for G1 + G4. Patients with primary/second prophylaxis for SBP, previous antibiotic therapy (< 3 months), immunosuppression or recent gastrointestinal bleeding (< 1 month) were excluded.
Results: PPI were prescribed in 45.1% of cirrhotic patients, with non-appropriate indication in 45.1%. In SBP patients, PPI use was superior (53.1% vs 37.2%;$p = 0.016$), with non-appropriate indication in 54.0% (vs 36.3%; $p = 0.008$). In patients with SBP and PPI, the main approved indications were recent endoscopic oesophageal variceal ligation/sclerotherapy (42.8%), Peptic Ulcer Disease (PUD) and Erosive Esophagitis (EE) (28.6%). There is no identification of prescription PPI reason in 50.9% of patients. Some cirrhotic patients without PPI had indication for their prescription (SBP: 7.1% and without SBP: 8.0%), being the most common indication in SBP patients the EE (37.5%), followed by PUD and NSAID use with risk factors (25.0%). After multivariate analysis, PPI use (OR3.395; $p = 0.002$) was the only factor associated with SBP development.
Conclusion: Despite of common PPI use in cirrhotic patients, PPI are inappropriately prescribed in almost half of cases. PPI use is associated with three-fold increased risk for developing SBP. It is necessary new recommendations for a rational prescription of that pharmacologic class in liver cirrhosis.
Disclosure of Interest: None declared

P1241 CAN LIVER STIFFNESS MEASUREMENT BY FIBROSCAN® PREDICT THE PRESENCE AND SIZE OF ESOPHAGEAL VARICES IN HEPATITIS C RELATED CIRRHOTIC PATIENTS?

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Introduction: Liver cirrhosis is the final stage of all chronic hepatopathies. Esophageal varices (EV) and variceal bleeding are feared complications. EV diagnosis is established by periodical upper digestive endoscopy. Gastroscopy in all cirrhotic patients is very expensive, and repeated endoscopies are poorly accepted by patients. The Aim is to predict EV's presence and grading by fibroscan® s in Hepatitis C virus (HCV) related cirrhotic patients.
Aims & Methods: Forty six HCV related cirrhotic patients were recruited in our unit. Inclusion criteria were: age > 18 years, Body Mass Index (BMI) < 35, HCV infection and no history of upper gastro intestinal bleeding. Patients underwent clinical examination, laboratory investigations, abdominal ultrasonography, upper endoscopy and liver measurement with fibroscan®.
Results: There were 25 women (54.3%), mean age was 63.71 years old. Body mass index was 26, 58 kg/m^2, Clinical examination was normal in 80% of patients. Mean HVC viral load was 5.66 log UI/ml, and the most frequent genotype was genotype 2 in 48% of cases. Thirteen patients (28%) had EV. Mean liver stiffness was 23.65 KPa, with a mean Interquartile Range of 4, 26% and a success rate of 93.3%. Mean liver stiffness for patients for patients with small EV (grade I) was 16.54 KPa and for patients with large EV and therefore a risk of variceal bleeding was 22, 86 KPa. The area under the curve ROC was 0.82 with high sensibility and specificity.
Conclusion: Liver stiffness measurement by fibroscan® in our current study is valuable in predicting the presence of large esophageal varices in patients with liver HCV cirrhosis. It may help to select patients for endoscopic screening. A study including a greater number of patients is necessary to confirm those results.
Disclosure of Interest: None declared

P1242 VALIDATION OF ASCITES SPECIFIC PATIENT REPORTED OUTCOME MEASURES IN PATIENTS WITH CIRRHOSIS

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Introduction: Treatment of patients with refractory ascites should focus on symptom relief and quality of life (QoL). No patient reported outcome that assesses symptom relief after treatment for ascites resulting from cirrhosis is validated in US patients.
Aims & Methods: We identified ascites-specific symptoms based on literature, patient interviews (n = 8) and a clinician survey (n = 8) to develop an ascites-specific questionnaire (Ascites-Q). Twelve symptoms were selected; fullness, lack of appetite, early satiety, nausea, abdominal pain, back pain, shortness of breath, limited mobility, tiredness, sleep problems, dissatisfaction with size of abdomen and problems with sexual intimacy. Subsequently, we administered the Ascites-Q, Japanese Ascites Symptom Inventory-7 (ASI-7), FACIT-ascites index for malignant ascites and an overall QoL VAS-scale in cirrhotic patients with refractory ascites scheduled for therapeutic paracentesis; before paracentesis (baseline) and 7 days after paracentesis (target sample size n = 90). Scores are transformed to a 0-100 scale with a higher score indicating more symptoms. We compared baseline scores of patients with refractory ascites with cirrhotic patients without refractory ascites (Mann Whitney U test) recruited at the Mayo liver transplant clinic from January - May 2015. Spearman correlation coefficients of the overall QoL VAS-scale and ascites questionnaires were calculated to assess validity of the questionnaires. Responsiveness of questionnaires to detect changes in ascites-specific symptoms was assessed by comparing questionnaire scores at baseline and 7 days after paracentesis with a paired T-test.
Results: We included 32 patients with refractory ascites (59% male, 61 ± 10 year, MELD-score 15 ± 6 and median tapped volume 3600 mL (IQR 2725 – 6525)) and 61 patients without refractory ascites (controls) (76% male, 57 ± 9 year, MELD-score 11 ± 4). Patients with refractory ascites scored higher than controls on all symptoms of the Ascites-Q and ASI-7, except for back pain ($p = 0.096$) and tiredness ($p = 0.228$). There was no difference between patients and controls in 6/13 FACIT-ascites index symptoms (sleep problems, mobility, nausea, vomiting, frequent urination and emotional distress, $p > 0.05$). Overall QoL correlated with the Ascites-Q and ASI-7 ($r = .497$, $p = 0.008$ and 0.471, $p = 0.013$), but not with the FACIT-ascites index ($r = 0.332$, $p = 0.090$). Symptom scores of the Ascites-Q, (-11.53 ± 18.874, $p = 0.013$), ASI-7 (-35.46, ± 29.22, $p < 0.001$) and FACIT-ascites index (-9.46 ± 10.60, $p = 0.001$) changed significantly 7 days after paracentesis.
Conclusion: The Ascites-Q and the ASI-7 are most sensitive for ascites-specific symptoms in patients with cirrhosis. We will investigate which symptoms are most responsive to treatment to further refine the Ascites-Q.
Disclosure of Interest: None declared

P1243 BLOOD-BRAIN BARRIER DYSFUNCTION ASSESSED BY PROTEIN S-100 BETA LEVELS IN CIRRHOTIC PATIENTS IN ICU

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Introduction: The protein S-100 beta (PS-100) is a small dimeric cytosolic protein synthetized in astrocytes and Schwann cells. High serum levels of PS-100 are associated with brain lesions and altered blood-brain barrier permeability in traumatic brain injury, ischemic stroke, cerebral tumors and subarachnoid hemorrhage. Early brain damage has been detected in patients with cirrhosis. We hypothesized that those insults could be detected by the PS-100 serum levels (normal values < 0.10 µg/L).

Aims & Methods: Hence, the aim of the present study was to assess PS-100 levels in cirrhotic patients, and compare them to PS-100 levels in non-cirrhotic patients followed up in the same department for initial workup of elevated liver enzymes (controls).

We prospectively included a population of cirrhotic patients admitted for complication of cirrhosis in ICU and controls. Baseline data were recorded and levels of ammonemia and PS-100 determined at admission. Overt HE was diagnosed as a West-Haven score ranging between 2 and 4.

Results: Between October 2013 and October 2014, 124 cirrhotic patients (mean age: 63 years, male gender: 73%, etiology of cirrhosis: alcoholic 51%, viral 25%, other 24%, Child-Pugh 11 [8-12], MELD score 21 [14-26]) and 79 non-cirrhotic patients (mean age: 63 years, male 59%, etiology of elevated liver enzymes: alcoholic 5%, viral 44%, NASH 38%, other 13%, mean Fibroscan: 5.3 kPa, mean FibroTest: 0.15) were included. Among cirrhotic patients, 40 patients (33%) displayed HE at admission and 50 (41%) had an infection. Mean PS-100 level were 0.15 ± 0.01 for cirrhotic patients and 0.07 ± 0.01 for non-cirrhotic patients ($p < 0.0001$). In cirrhotic patients, PS-100 was correlated to AST ($p = 0.0027$), bilirubin ($p = 0.0001$), Child-Pugh score ($p = 0.001$) and MELD ($p = 0.0004$) and inversely correlated to albumin ($p = 0.04$), sodium ($p = 0.01$), PTT ($p = 0.001$), and FV ($p = 0.011$). PS-100 levels were not correlated to the presence of overt HE nor to infection. In multivariate analysis, levels of PS-100 were independently associated with MELD score ($p = 0.0006$), whereas overt HE was associated to hyperammonemia ($p = 0.002$) and the presence of infection ($p = 0.008$) but not to PS-100 levels.

Conclusion: Patients with cirrhosis in ICU display neurological insult or blood-brain barrier dysfunction even in the absence of overt HE. Brain damage is more frequent in patients with advanced liver disease.

Disclosure of Interest: None declared

P1244 THE PREVALENCE AND CLINICAL IMPACT OF MULTIDRUG-RESISTANT SPONTANEOUS BACTERIAL PERITONITIS IN CIRRHOTIC PATIENTS

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Introduction: International guidelines recommend third-generation cephalosporins as the empirical therapy of choice in spontaneous bacterial peritonitis (SBP), however, recent studies have challanged this recommendation due to high rates of third-generation cephalosporin-resistant infections and a consequent higher mortality among this patients due to inappropriate empirical antibiotic choice. We present a single-center cohort study analyzing the prevalence, risk factors and the short-term clinical impact of multidrug-resistant (MDR) SBP.

Aims & Methods: Retrospective analysis (Jan 2008 and Dec 2013) of 54 SBP episodies in cirrhotic inpatients. Studied variables: demographics, laboratorial, microbiological and known risk factors for MDR acquisition.

Results: Among a total of fifty-four SBP episodes, 39% ($n = 21$) were aquired in the nosocomial setting. In 43% ($n = 23$) of the SBP, at least one bacteria was isolated and, among those culture-positive SBP, 39% ($n = 9$) were MDR bacteria. Almost 2/3 (67%; $n = 6$) of MDR-SBP were aquired in the nosocomial setting, on the other hand, 2/3 of the non-MDR-SBP were aquired in the community or healthcare-associated. The bacteria most frequently isolated were: *Escherichia coli* non-MDR (30%), Streptococcus non-*viridans* (22%) and vancomycin-sensitive *Enterococcus* (22%). The rate of acute kidney injury (AKI) was higher among MDR-SBP patients (67% vs 49%). Among all study population thirty-day mortality was 35%, higher among MDR-SBP group (67% vs 29%). On a multivariate analysis we found no independent predictors for MDR-SBP acquisition. After multivariate analysis, MDR-SBP, AKI and diabetes mellitus were independent predictors of 30-day mortality.

Conclusion: In this study, we have found an high prevalence of MDR-SBP (39%). Also, the acquisition of this type of infection was independently associated with a very high 30-day mortality rate (67%). Althought independent predictors for MDR-SBP acquisition were not found in our study, it is important to implement preventive strategies in order to minimize the risk of MDR acquisition.

Disclosure of Interest: None declared

P1245 EVALUATION OF THE COST EFFECTIVENESS OF RIFAXIMIN-A 550 MG (XIFAXAN) IN THE REDUCTION OF RECURRENCE OF OVERT HEPATIC ENCEPHALOPATHY IN SWEDEN

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Introduction: The value for money of drugs varies by country mainly due to changes in treatment patterns and related costs. Hepatic encephalopathy (HE) is associated with high morbidity and mortality. Rifaximin-α 550 mg (XIFAXAN) is effective in reducing the recurrence of episodes of overt HE, and reduces hospital utilisation. Our aim was to characterise the cost effectiveness of rifaximin-α 550 mg versus standard care (lactulose) in patients with liver cirrhosis in Sweden.

Aims & Methods: This economic evaluation used a Markov state transition model. The outcome metric was the incremental cost effectiveness ratio (ICER), derived from estimates of the cost/quality adjusted life years (QALYs). The payer perspective was that of the Swedish healthcare system. Outcome data were from two trials of rifaximin-α 550 mg. Population outcome data were from a complementary study of patients with liver cirrhosis treated in Sweden. Swedish Costs data (2012) were derived from published sources. Health-related utility was estimated indirectly from disease-specific quality of life RCT data. The time horizon was five years. Costs and benefits were discounted at 3.5%. Extensive sensitivity analyses were carried out. Real-world data were also applied into the model for length of stay in hospital and the number of admissions.

Results: The average cost of the included elements of care was SEK302,520 (€32,667) in the rifaximin-α 550 mg arm and SEK393,777 (€42,522) in the lactulose arm, a difference of -SEK91,257 (-€9,854). The corresponding values for benefit was 2.38 QALYs and 1.83 QALYs per person, respectively, a difference of 0.55 QALYs over the five-year period. This translated into a dominant base-case ICER at five-years, meaning that rifaximin-α 550 mg was both less costly and more beneficial. Key parameters that impacted the ICER included length of stay in hospital and the number of admissions to hospital. Evaluation to 10 years also resulted in a dominant ICER, although the lifetime ICER was SEK5,918 (€639) per QALY.

Conclusion: In Sweden, treatment with rifaximin-α 550 mg in patients with recurrent HE in the context of liver cirrhosis was cost effective compared to standard care, by reducing episodes of overt HE.

Disclosure of Interest: C. Poole Conflict with: Consultant for Norgine, E. Berni Conflict with: Consultant for Norgine, P. Conway Conflict with: Employee of Norgine, A. Radwan Conflict with: Employee of Norgine, C. Currie Conflict with: Consultant for Norgine

P1246 COST EFFECTIVENESS OF RIFAXIMIN-A 550 MG (XIFAXAN/TARGAXAN) IN THE REDUCTION OF RECURRENCE OF OVERT HEPATIC ENCEPHALOPATHY IN UNITED KINGDOM

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Introduction: Hepatic encephalopathy (HE) is associated with high morbidity and mortality. Rifaximin-α 550 mg (XIFAXAN/TARGAXAN) is effective in reducing the recurrence of episodes of overt HE. Our aim was to determine the cost effectiveness of rifaximin-α 550 mg versus standard care (lactulose) in patients with cirrhosis in the UK.

Aims & Methods: This economic evaluation used a Markov state transition model. The outcome metric was the incremental cost effectiveness ratio (ICER), derived from estimates of the cost/quality adjusted life years (QALYs). The payer perspective was that of UK National Health Service. Outcome data were from two trials of rifaximin-α 550 mg. Population outcome data were from a complementary study of patients with liver cirrhosis treated within the NHS. UK Costs data (2012) were derived from published sources. Health-related utility was estimated indirectly from disease-specific quality of life RCT data. The time horizon was five years. Costs and benefits were discounted at 3.5%. Extensive sensitivity analyses were carried out. Real world data describing the use of rifaximin-α 550 mg in the UK NHS were also applied into the model for length of stay in hospital and the number of admissions.

Results: The average cost for the included elements of care was £22,971 in the rifaximin-α 550 mg arm and £23,545 in the lactulose arm, a difference of -£573. The corresponding values for benefit were 2.56 QALYs and 1.75 QALYs per person, respectively, a difference of 0.81 QALYs. This translated into a dominant base-case ICER. Key parameters that impacted the ICER included length of stay in hospital and the number of admissions to hospital. Evaluation to 10 years and lifetime resulted in ICERs of £3,024/QALY and £5,068/QALY, respectively.

Conclusion: Rifaximin-α 550 mg in patients with recurrent HE in the context of liver cirrhosis represented good value for money compared to standard care, by reducing episodes of overt HE, the likelihood of hospital admission and hospital length of stay.

Disclosure of Interest: E. Berni Conflict with: Consultant for Norgine, C. Poole Conflict with: Consultant for Norgine, P. Conway Conflict with: Employee of Norgine, A. Radwan Conflict with: Employee of Norgine, C. Currie Conflict with: Consultant for Norgine

P1247 D-DIMER LEVEL, LEUCOCYTE COUNT AND AGGREGATION ACTIVITY OF PLATELETS AS PREDICTORS OF PORTAL VEIN THROMBOSIS IN LIVER CIRRHOSIS

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Introduction: Liver cirrhosis is associated with profound disturbances in coagulation system. Portal vein thrombosis (PVT) is being increasingly recognized in patients with advanced cirrhosis and in those undergoing liver transplantation with 10-25% reported prevalence. The presence of PVT is associated with the long-term mortality. Although the pathogenesis of PVT is poorly understood, a reduced flow in the portal vein, portal endotoxemia and hypercoagulability are most often incriminated for the development of PVT.

Aims & Methods: We aimed to investigate several biochemical markers characterizing the coagulation system, platelets aggregation and permeability of the intestinal barrier to determine the high-risk individuals for PVT attending our center.

In total, 49 consecutive patients with cirrhosis (15 in Child-Pugh class A and 34 in class B&C) aged 27-81years were included to the study. They were divided into two groups: those without PVT (n = 33) and those with partial or complete PVT (n = 16) diagnosed by spiral computed tomography. Routine laboratory and coagulation parameters, as concentration/activity of vonWillebrand factor (vWF), factor VIII, D-dimers, protein C, prothrombin and tissue factor (TF) were measured in the serum. Platelets aggregation was tested by Multiplate Analyzer using adenosine diphosphate (ADP, 6.4 μM), arachidonic acid (ASPI, 0.5 mM), ristocetin (Risto, 0.2 mg/ml and 0.77 mg/ml) and thrombin receptor-activating peptide (TRAP, 32 μM). Permeability of gut barrier was assessed by serum levels of lipopolysaccharides (LPS) and zonulin.

Results: In patients with PVT endoscopic banding of esophageal varices was more common (81.2% vs 42.4%; p = 0.02), and these patients had significantly larger size of splenic and superior mesenteric vein, lower count of leukocytes (3.9 ± 1.4 vs 5.5 ± 2.7 G/l; p = 0.01), lower bilirubin level (2.1 ± 1.0 vs 4.0 ± 3.4 mg/dl; p = 0.02), and higher levels of D-dimer (4.45 ± 2.59 vs 3.04 ± 2.97 pg/ml; p = 0.04) and prothrombin (175 ± 98.8 vs 115 ± 72.9 μg/ml; p = 0.01) in comparison with those without PVT. Protein C, vWF, factor VIII and TF showed no significant differences in both groups. There was no significant difference in the concentration of LPS and zonulin between PVT positive and negative patients. Generally, the platelets aggregation activity in patients with PVT was lower compared to those without thrombosis (statistically different in ADP and TRAP tests). D-dimer levels showed 90% negative prediction value for diagnosis of PVT (cut-off 1.82 pg/ml) and in stepwise logistic regression model the D-dimers, bilirubin and TRAP test were independent risk factors for PVT.

Conclusion: 1) Low count of leukocytes as well as high D-dimer level indicate PVT in cirrhotic patients. 2) D-dimer level below 1.82 pg/ml excludes with high probability PVT. 3) The platelets aggregation in patients with PVT is reduced that may be either adaptive response to a decrease in liver perfusion and increase of portal hypertension. 4) Endotoxemia does not seem to play a major role in the development of PVT.

Disclosure of Interest: None declared

P1248 CLIF-AD SCORE VALIDATION FOR PREDICTING MORTALITY IN PATIENTS WITH ACUTE DECOMPENSATED CIRRHOSIS WITHOUT ACUTE-ON-CHRONIC LIVER FAILURE

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Introduction: Recently EASL-CLIF Consortium defined a new prognostic score (CLIF-AD) for patients with acute decompensated cirrhosis without acute-on-chronic liver failure (ACLF).[1]

Aims & Methods: We sought to validate the CLIF-AD score and compare it with the existing scoring systems Model for End-Stage Liver Disease (MELD), MELD-Sodium and Child-Turcotte-Pugh (CTP). Retrospective analysis of demographic, clinical and laboratorial data of patients admitted for acute decompensation of cirrhosis without ACLF criteria between January 2013 and September 2014. Twenty eight (M28), 90-day (M90), 180-day (M180) and 365-day (M365) mortality were evaluated. CLIF-AD performance in predicting mortality in each time-point was compared with MELD, MELD-Sodium and CTP performances.

Results: 90 patients were included (male sex:72.2%, mean age:59 ± 11 years). 82% had alcoholic cirrhosis (with or without viral infection) and 32.2% had active alcoholism. Mean CLIF-AD was 51.8 ± 8.4 and was significantly higher in patients who died at M28, M90 and M180 time-points versus survivors (63.3 ± 7.6 vs. 50.9 ± 7.7, p = 0.001; 56.2 ± 10.3 vs. 50.7 ± 7.4, p = 0.05; 57.2 ± 10.2 vs. 50.3 ± 7.1, p = 0.008, respectively). CLIF-AD ≥ 60 was associated with significantly higher M28, M90, M180 and M365 (60.0 vs. 8.1%, p = 0.006; 80.0 vs. 20.9%, p = 0.008; 80.0 vs. 22.1%, p = 0.01 and 80.0 vs. 32.6%, p = 0.041, respectively). The AUROC of CLIF-AD in predicting M28 (0.891 ± 0.43), M180 (0.723 ± 0.74) and M365 (0.636 ± 0.065) was significantly superior to CTP, MELD and MELD-Sodium.

Conclusion: The application of the new CLIF-AD identifies patients with high mortality (CLIF-AD ≥60). The CLIF-AD score accurately predicts short and long-term mortality and is superior to the existing scoring systems.

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Disclosure of Interest: None declared

P1249 VALIDATION OF THE EASL-CLIF CONSORTIUM DEFINITION OF ACUTE-ON-CHRONIC LIVER FAILURE AND THE CLIF-SOFA SCORE FOR PREDICTION OF MORTALITY IN A WARD

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Introduction: Recently, the EASL-CLIF Consortium defined diagnostic criteria for acute-on-chronic liver failure (ACLF), a frequent syndrome characterized by acute decompensation of cirrhosis, organ failure(s) and high mortality.[1]

Aims & Methods: We sought to validate the ACLF definition and the Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) score in patients admitted in a Gastroenterology ward and compare it with the existing scoring systems Model for End-Stage Liver Disease (MELD) and Child-Turcotte-Pugh (CTP). Retrospective analysis of demographic, clinical and laboratorial data of patients admitted for acute decompensation of cirrhosis between January and September 2014. Twenty eight (M28) and 90-day (M90) mortality were evaluated. Patients with and without ACLF were compared. CLIF-SOFA performance was compared with MELD and CTP.

Results: 82 patients were included (male sex:78%, mean age:63 ± 13 years). 82% had alcoholic cirrhosis (with or without viral infection) and previous episodes of acute decompensation were absent in 27%. At admission 27.1% fulfilled criteria for ACLF (Grade 1 17.6%, Grade 2 9.5%) and 9.8% developed it during hospitalization. M28 e M90 were, respectively, 1.9% and 15% in patients without ACLF and 46.4% and 64.3% in patients with ACLF (p = 0.01). Mortality was > 70% in patients with ACLF grade 2 and 3; 44.4% of ACLF grade 2 patients had median arterial pressure < 65mmHg. Patients with ACLF were older (70 ± 13 vs. 60 ± 12 years, p = 0.038), had more infections (61% vs. 23%, p = 0.001) and higher C-reactive protein, independently of the presence of infection (1.3 vs. 4.1 mg/dL, p = 0.01). The AUROC of CLIF-SOFA in predicting M28 was 0.907 ± 0.0461 (95%CI 0.820-0.961) and M90 was 0.820 ± 0.0504 (95%CI 0.717820-0.897), which was significantly superior to CTP but not significantly superior to MELD.

Conclusion: The application of ACLF criteria in the ward identifies patients with high mortality. The CLIF-SOFA score accurately predicts short-term mortality but was not significantly superior to MELD; this might be related to absence of CLIF-SOFA circulatory and ventilatory failure criteria in the ward setting, leaving only parameters common to other hepatospecific scores.

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Disclosure of Interest: None declared

P1250 PSYCHOMETRIC TESTS FOR DIAGNOSING MINIMAL HEPATIC ENCEPHALOPATHY: APPLICABILITY IN CLINICAL PRACTICE

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Introduction: Minimal hepatic encephalopathy (MHE) has been associated with increased mortality risk and impaired quality of life. Its detection using the Psychometric Hepatic Encephalopathy Score (PHES) is recommended in the treatment algorithm of cirrhotic patients.

Aims & Methods: The aim was to evaluate the applicability in clinical practice of the calculation of the PHES in patients with liver cirrhosis. It was a prospective cohort of consecutive patients with liver cirrhosis without clinical encephalopathy, followed as Hepatology outpatients. Any conditions impeding the completion of the test were registered. When applicable, 5 psychometric tests were performed to calculate the PHE:Trail Making Test A and B, the Digit Symbol Test, the Serial Dotting Test and the Line Drawing Test.

Results: A total of 69 patients were included (78% male). Twenty nine percent of patients proposed to determine the PHES did not perform the tasks due to the following causes: neurological disease/dementia (40%), alcohol consumption >40 g alcohol/day (35%), visual disturbances (15%) and illiteracy (10%). Twenty nine percent of the patirents that completed the psychometric test had MHE. The Trail Making test (Part B) was the test that separately detected more patients with MHE (54%). Four tests (Trail Making Test, the Serial Dotting Test and the Line Drawing Test) detected all cases of MHE diagnosed in this cohort. The mean time to perform the 5 tasks was 13 ± 6 minutes. The time to determine the PHES was statistically significant higher in patients with MHE compared to patients without such cognitive dysfunction (20 ± 1 vs. 11 ± 7 minutes, $p < 0.001$).
Conclusion: A significant proportion of patients were not eligible to determine the PHES due to several limitations to complete the psychometric tests. Despite of being relatively easy to apply, these 5 tasks were time consuming in the presence of MHE.

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Disclosure of Interest: None declared

P1251 DETERMINATION OF PREDICTIVE FACTORS FOR MINIMAL HEPATIC ENCEPHALOPATHY WITH PSYCHOMETRIC TESTS

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Introduction: Minimal hepatic encephalopathy (MHE) encompasses several neuropsychiatric abnormalities in patients with liver cirrhosis (LC). The detection of MHE requires specialized testing as it is not diagnosed on standard clinical examination. The Psychometric Hepatic Encephalopathy Score (PHES) calculated using 5 psychometric tests, shows high sensitivity and specificity for MHE diagnosis. The aims were to determine the prevalence and predictor factors for MHE.
Aims & Methods: It was a prospective study with consecutive patients with LC followed as Hepatology outpatients. Five psychometric tasks were performed: Trail Making Test A and B, the Digit Symbol Test, the Serial Dotting Test and the Line Drawing Test. Patients with clinical encephalopathy and neurological diseases were excluded. PHES normality tables validated for the Portuguese population were used and the final score was calculated for each patient, the total score of -4 points defined MHE.
Results: We included 49 patients (69% men) with a mean age of 57 ± 10 years. The most frequent aetiology of LC was hepatitis C (50%) and 62% had Child-Pugh score A (64%). Eighteen percent of patients were under treatment with lactulose and 3% with rifaximin. The proportion of EHM was 29% and 63% of them were still driving. The presence of MHE was associated with:diuretic therapy ($p = 0.004$), use of benzodiazepines ($p = 0.015$), score Child-Pugh B/C ($p = 0.018$), previous hospital admissions due to cirrhosis descompensatio ($p = 0.015$) and the presence of esophageal varices ($p = 0.002$). Previous episodes of hepatic encephalopathy, INR and albumin levels, MELD score and thrombocytopenia were not significantly different in the group of patients with EHM. In logistic regression, the use of benzodiazepines [OR: 7.812 95% CI (1.242 to 45.287)] was independently related with the presence of EHM.
Conclusion: The presence of EHM was associates with: diuretic therapy, score Child-Pugh B/C, prior hospitalization due to decompensation of LC and esophageal varices. Benzodiazepines therapy was an independent risk factor for EHM.
Disclosure of Interest: None declared

P1252 ALFA PUMP FOR THE TREATMENT OF REFRACTORY ASCITES: A "REAL-WORLD" EXPERIENCE FROM THE UK

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Introduction: Up to 10% of cirrhotic patients with ascites become refractory to diuretic therapy requiring either large volume paracenteses (LVP), transcutaneous intrahepatic portosystemic shunt (TIPSS) or liver transplantation (LT). In patients where TIPSS or LT is contraindicated, repeated LVP is the only option. LVP is an uncomfortable procedure requiring hospital visits and has risk of complications. The ALFA pump is a surgically implanted automated low flow pump system that transports fluid from the peritoneal cavity to the bladder and is an alternative treatment option for patients with refractory ascites. Our aim was to evaluate the early "real world" experience of the ALFA pump for the treatment of refractory ascites from centres in the UK.
Aims & Methods: Retrospective case note review of the outcomes of patients who had an ALFA pump implanted for refractory ascites outside trials at 4 NHS hospitals since Sept 2013.
Results: ALFA pumps were implanted in 9 patients (6 male, 3 female; median age 74, range 41-81) at four centres (4 NCL, 2 UCL, 2 CAM, 1 QEHB). 7 patients had ascites related to cirrhosis (4 Child-Pugh B, 3 Child-Pugh C), 1 due to congestive cardiac failure and 1 with portal hypertension due to arteriovenous malformation. Prior to insertion of the ALFA pump the median frequency of paracenteses was every 10 days (range 7 – 20) and the median volume of ascites drained was 9 litres (range 8 to 12). ALFA pumps were successfully implanted in all patients. Requirement for paracenteses was substantially reduced post ALFA pump implantation with 7 patients no longer requiring any paracenteses. In one patient the pump blocked after 3 weeks and required reimplantation with a second pump that also blocked and the patient has returned to LVP. In another patient the pump blocked after 8 months and a second ALFA pump was successfully implanted. All 9 patients had ALFA pump related complications including 4 post-operative seromas, 3 bladder catheter migrations/occlusions, 5 site related infections, 6 acute kidney injury/electrolyte disturbance and 1 urinary incontinence. 5 of the 9 patients were alive with a functioning pump 6 months after implantation.
Conclusion: The ALFA pump offers an alternative option for patients who have refractory ascites in whom TIPSS and LT are contraindicated. ALFA pump implantation substantially reduces the need for paracenteses in a cohort of patients who had previously required a significant number of LVP. ALFA pump related complications were frequent suggesting the need for careful patient selection in this high risk group. Outcomes of a randomized controlled trial are eagerly awaited.
Disclosure of Interest: None declared

P1254 THE RISK OF HEPATIC ENCEPHALOPATHY FOR ALCOHOL VERSUS VIRAL CIRRHOTIC PATIENTS

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Introduction: Hepatic encephalopathy (HE) is found frequently in the setting of liver cirrhosis (LC). HE worsens the prognostic and impairs the quality of life for patients with LC. The current accepted classification comprises covert (CHE) and overt (OHE) encephalopathy. Alcohol determines changes in the frontal cortex, therefore cognitive function and treatment may be different between alcoholic and viral liver cirrhosis. In this retrospective study, we evaluated the risk of OHE and CHE, in viral versus alcoholic LC.
Aims & Methods: We retrospectively evaluated 642 patients that were hospitalized in our service of gastroenterology from January 2014 to December 2014 (viral: 338 and alcohol: 304) with compensated and decompensated LC. The patients were followed for six months. The diagnosis of CHE and OHE was made according to the West Haven classification.
Results: The mean age of patients with alcoholic and viral LC was 56.45 (10.59) and 55.24 (11.4) years, respectively. The patients with alcoholic etiology of the liver disease had a risk of developing HE that was 1.48 fold higher than the ones with viral etiology ($P < 0.0001$, OR 1.48, CI 1,254-1,747). The patients that were diagnosed with OHE had a higher risk of death than the ones that were diagnosed with CHE ($P < 0.046$, CI 0.938-2,384).
Conclusion: The risk of developing hepatic encephalopathy is higher for the cirrhotic patients with alcoholic etiology than for the ones with viral etiology, therefore the cirrhotics that associate alcohol disease may benefit from a closer monitoring for the diagnostic of HE than the ones with viral etiology.
Disclosure of Interest: None declared

P1255 ERYTHROPOIETIN VALUES IN ACUTE ON CHRONIC LIVER FAILURE-PRELIMINARY DATA

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Introduction: Acute on chronic liver failure (ACLF) is defined as progressive deterioration of hepatic function after an acute insult on an underlying diagnosed or undiagnosed chronic liver disease. It is associated with high short-term mortality due to multiorgan system failure. Therefore ACLF is one of the most clinical challenging health problem. Liver transplantation is the only therapeutical option to improve survival, but a large proportion of patients succumb while waiting on the transplanta list. So other therapeutical options are tried as use of erythropoietin (Epo). Epo is a pleiotropic cytokine known for its role in stimulation of erythropoiesis, but also rise levels of calcium in the blood vesels endothelium, stimulates acting of angiotensin II, whis activate sinthesis of NO with pressor efect. Elevation of blood pressure leads to better perfusion and healing. Epos has an antiinflammatory and cytoprotective effect as well.
Aims & Methods: In this study 54 patients were included, mean age 58.2 ± 1.3 years. The liver disease in majority of patients (83.3%) was caused by alcohol abuse. All patients underwent a complete biochemical workup, including measuring of Epo values. Relevant scores for assing liver functions and outcome in ACLF were measured (Child, MELD, MELD Na, SOFA, APACHE II). We analyzed the values of Epo in correlation to acute insult and outcome.
Results: We devided the patients into two groups according to the acute insult-bleeding due portal hypertension (A-13 pts) and other-icterus, encephalopathy etc. (B-41 pts). The mean Epo, Child, MELD, MELD Na, SOFA, APACHE and CLIF score values were presented in table , and as presented, the Epo values are significantly higher in patients who presented initialy as gastrointestinal bleeding.

	Group A	Group B	p values
Epo (mIU/mL)	327.27 ± 244.19	201.43 ± 200.87	0.03
Child	10.38 ± 2.29	11.2 ± 2.0	0.14
MELD	19.31 ± 4.11	22.71 ± 7.51	0.06
MELD Na	21.23 ± 4.87	22.76 ± 9.75	0.29
SOFA	8 ± 2.71	9.22 ± 3.24	0.11
APACHE II	14.15 ± 4.61	14.93 ± 4.86	0.31

In group A, 6 (78%) patients had lethal outcome, and in group B ,16 (39%) respectively. Further, we analyzed the values of Epo according to outcome. In group A, patients with lethal outcome had statistically significant higher ($p = 0.007$) values of Epo (493.5 ± 242.86 and 184.79 ± 137.07, respectively), while in group B, the Epo values were statistically significant lower ($p = 0.002$) in patients who succumb (89.09 ± 84.32 and 273 ± 221.37, respectively).
Conclusion: Patients suffering from ACLF without bleeding as an initial insult have significantly lower values of Epo. Taking into account benefits of Epo treatment by stimulating hepatic regeneration and improvement of hepatic function, further studies are necessary in order to define which patients will have the optimal benefit of using Epo in treatment of ACLF.
Disclosure of Interest: None declared

P1256 NEUTROPHIL TO LYMPHOCYTE RATIO AS A NONINVASIVE MARKER FOR DIAGNOSIS OF SPONTANEOUS BACTERIAL PERITONITIS

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Introduction: The diagnosis of spontaneous bacterial peritonitis (SBP) based on the presence of ascitic fluid absolute polymorphonuclear leukocyte (PMN) count equal or greater than 250 cells/mm^3 without an evident intra-abdominal, surgically treatable source of infection. Neutrophil-lymphocytic ratio (NLR) may be considered as a simple and inexpensive indicator of inflammation in some diseases.
Aims & Methods: The aim of this study was to evaluate clinical utility of NLR as a noninvasive marker for diagnosis of SBP.126 Consecutive cirrhotic ascitic patients who were diagnosed with SBP and 54 cirrhotic ascitic patients without SBP were enrolled in this study. NLR was calculated and high-sensitive CRP (hsCRP) values were determined for all patients. The ability of NLR values as a marker for diagnoses of SBP in ascitic patients was analyzed using receiver operator characteristic (ROC) curvature analysis.
Results: NLR and hsCRP were significantly higher among cirrhotic ascitic patients with SBP versus non SBP patients ($p < 0.001$) for each one. ROC was computed between blood NLR and hsCRP in patients with SBP. At the cut of blood NLR (>2.89) in patients with SBP the sensitivity was (80.3%) and specificity (88.9), whereas hsCRP (>11.3) had a sensitivity of (88.9) and specificity (92.6). In logistic regression analysis model combining both NLR and hsCRP, the sensitivity was (95.1) and specificity (96.3).
Conclusion: The findings indicate that the combination of NLR and hsCRP could be used as a novel noninvasive marker for the diagnosis SBP.
Disclosure of Interest: None declared

P1257 POTENTIAL RISK FACTORS IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS: A FIVE-YEAR SINGLE CENTER EXPERIENCE

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Introduction: Aetiology of primary biliary cirrhosis (PBC) is unknown, but it is associated with frequent bacterial and viral infections, autoimmune conditions, reproductive hormone replacement therapy, cigarette smoking and use of nail polish.
Aims & Methods: To analyse potential risk factors in patients with confirmed PBC diagnosis in Latvia. Retrospective medical documentation study of all PBC patients admitted to Riga East Clinical University Hospital – the biggest, 2270-bed medical centre in Latvia, from 2010 to 2015. An originally created study protocol, containing more than 35 parameters, including the most likely risk factors as infection diseases, autoimmune conditions and exogenous agents, was completed for each patient and data was entered into database with consecutive statistical analysis using SPSS 20.0.
Results: 34 patients, 33 (97%) female and 1 (3%) male patient, were admitted 54 times. 19 (55.88%) of all 34 patients had no identified potential PBC risk factors in the past. 5 (14.71%) of all patients have been diagnosed with urinary tract infection. 12 (35.29%) of all patients have had other bacterial infections. 11 (32.35%) of all patients have had viral infections in the past and 2 (5.88%) patients have had contact with chemical agents and previous reproductive hormone replacement therapy. No data about pesticides, food additives, use of certain cosmetics, including nail polish, no data about genetic variants of HLA class II, IL12A, and IL12RB2 loci and no data about family history was found during the study. Statistically significant differences were not found between patients who had bacterial or viral infection in the past and patients who did not have any potential PBC risk factors in the past, when comparing MELD, CTP and length of the hospitalization period.
Conclusion: 1. Bacterial infections, viral infections, urinary tract infections, contact with chemical agents and reproductive hormone replacement therapy are the most frequently found risk factors that are consistent with the literature data. 2. Additional study, including more detailed lifestyle and environmental factor analysis in combination with genetic analysis should be performed to analyse PBC risk factors more profoundly. 3. Statistically significant differences were not found between patients who had and patients who did not have any bacterial or viral infections in the past.
Disclosure of Interest: None declared

P1258 IMPACT OF POLYMORPHISMS IN IFNL3 AND IFNL4 GENES AND MXA GENE EXPRESSION ON RESPONSE TO INTERFERON/ RIBAVIRIN TREATMENT IN CHRONIC HEPATITIS C-4 EGYPTIAN PATIENTS

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Introduction: Host genetic factors have a role in the clearance of HCV infection in patients under treatment with PEG/RBV. Several studies have reported that interferon Lambda (IFNL) gene polymorphism is the best baseline predictor of response to interferon alfa(IFNα)-based antiviral therapies in chronic hepatitis C. Recently, a new IFN-L4 polymorphism was identified as first potential functional variant for induction of IFNL4 expression. Myxovirus resistance gene A (MxA) expression is induced by IFNs and Ribavirin (RBV) treatment.
Aims & Methods: In this study polymorphism of interferon lambda 3 (IFNL3) and IFNL4 and their association with MxA RNA expression have been evaluated in respect to sustained virological response (SVR) in IFNα/RVB treated hepatitis C-4 patients. A Total of 442 hepatitis C-4 Egyptian patients (male/female = 272/170; mean age: 45 [20-65] y) were investigated. Liver fibrosis was assessed by liver biopsy. Treatment was standard pegIFNα/RBV for 48 Weeks. SNPs rs12979860, rs8099917, rs12980275 were analyzed by Real time-PCR system and and ss469415590 mutations was analyzed by DNA sequencing. Relative Expression of MxA RNA was evaluated by qPCR. Fifty healthy people were served as a control.
Results: Distribution of variants of INFL3 (rs12979860) was: CC (27%), CT (46.5%) and TT (26.5%) variant. For rs8099917: GG (4.5%), GT (35.7%) and TT (59.8%) variant. For rs12980275: AA (29.2%), AG (56.4%) and GG (15.4%) variant. For ss469415590: ΔG/ ΔG (6.5%), ΔG/TT (54.4%) and TT/TT (39.1%) variant. Highly significant higher percentage of SVR rates was found among cases with CC subtype of rs12979860 ($p = 0.0001$) and cases with AA subtype of rs12980275 ($p = 0.001$), while SNPs rs8099917 and ss469415590 had no significant impacted on SVR ($p = 0.6$, 0.2 respectively). Expression of MxA (thatenhance IFN-α anti-viral activity against HCV) was highly significant ($p = 001$) in SVR cases than non-responders.
Conclusion: Polymorphisms in IFNL3/4 genes and expression of MxA gene have a different impact effects on response to IFNα/RBV treatment in HCV-4 infected patients. Although there are significant correlation between some subypes of polymorphisms and MxA expression and prediction of response to treatment, but on indivedual levels, there is no absolute predictor factor for response to IFNα/RBV therapy.
Disclosure of Interest: None declared

P1259 DEPLETION OF CD4+CD25+REGULATORY T CELLS ATTENUATE THE DEVELOPMENT OF CCL4-INDUCED LIVER FIBROSIS IN HCV NONSTRUCTURAL PROTEIN 3/4A TRANSGENIC MICE

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Introduction: Regulatory $CD4^+CD25^+$ T cells (Tregs) are considered to affect the disease outcomes of Hepatitis C virus (HCV) infection and appear to play a crucial role in viral persistence by suppressing HCV-specific T cell responses. But the role of Tregs in HCV infection, particularly in inflammation and fibrogenesis is still debated.
Aims & Methods: In this study, we aimed to understand the role of $CD4^+CD25^+$ Tregs in CCl_4-induced fibrosis progression in HCV (NS3/4A) transgenic mice. We used transgenic (Tg) mice with hepatic-specific expression of the HCV non-structural NS3/4A protein complex. Tregs were depleted for 4 weeks using anti-CD25 and anti-GITR antibodies and control group received isotype control antibodies. After 2 weeks of antibodies administration, mice were treated either with olive oil or CCl_4 (1ml/kg) for 2 weeks to induce liver fibrosis. Liver damage, HSC markers, inflammatory markers (M1 and M2 macrophages) and Th1/Th2/Th17 responses were examined using immune-histological stainings and quantitative gene expression PCR analysis.
Results: Hepatic expression of NS3/4A did not induce spontaneous liver disease. Following Treg depletion, NS3/4A-Tg mice exhibited significantly reduced Collagen I protein and mRNA expression showing reduced fibrogenesis in comparison to non-depleted NS3/4A-Tg mice. Furthermore, in Treg-depleted mice, significant inhibition of hepatic stellate cells proliferation (desmin) and activation (a-SMA) was observed. No significant differences in intra-hepatic macrophages was found as determined by F4/80 staining. Strikingly, YM1-positive macrophages and MMP-13 levels were drastically increased in Treg-depleted mice as compared to isotype (non-depleted) control mice. IL-1b and IL-6 gene expression was also significantly reduced suggesting inhibition in inflammation in Treg-depleted animals. Furthermore, in Treg-depleted NS3/4A-Tg mice, strong bias towards Th2 was observed as compared to Th1 response together with reduced Th17 response.
Conclusion: In conclusion, these results suggests that $CD4^+CD25^+$ Tregs depletion in chronic HCV infection attenuates hepatic fibrogenesis by inhibiting HSC activation, suppressing liver inflammation and modulates Th1/Th2 balance toward a Th2 dominant response.
Disclosure of Interest: None declared

P1260 QUANTITATIVE ANALYSIS OF HEPATITIS B SURFACE ANTIGEN AFTER TWO YEARS OF ENTECAVIR TREATMENT IN PATIENTS WITH CHRONIC HEPATITIS B

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Introduction: Anti-hepatitis B e antigen (anti-HBe) seroconversion and hepatitis B surface antigen (HBsAg) loss are important therapeutic endpoints in patients with hepatitis B virus (HBV) infection. Quantitative measures of HBsAg have been identified as potentially useful indicators of therapeutic response in HBV monoinfection. A rapid HBsAg decline during nucleoside/nucleotide analogue therapy may identify patients who will show clearance of HBsAg. In the present study, we examined HBsAg levels in patients who received entecavir for chronic HBV in our hospital.
Aims & Methods: A total of 54 patients who received entecavir for chronic HBV, were screened for study inclusion and 25 patients were excluded due to inadequate data. In 29 patients (14 males and 15 females), biochemical values and HBV-DNA and HBsAg levels were determined at the start, six months, and 1 and 2 years after the start of entecavir treatment.
Results: At the start, the patients' mean age was 55.7 ± 15.6 years, HBV-DNA levels were 6.6 ± 1.6 log copies/mL, median alanine aminotransferase (ALT) level was 268 IU/L, and median HBsAg level was 11,123 IU/L. No patient became negative for HBsAg at two years. After two years of entecavir treatment, HBsAg levels showed no significant difference (>0.5 log) in 20 patients (69%), but decreased in 7 patients (24%) and increased in 2 patients (7%). HBeAg-positive patients showed significantly decreased HBsAg levels compared with HBeAg-negative patients (35.7 vs. 14.3%, respectively, $P = 0.002$). High levels of HBV-DNA (7.98 vs. 6.17 log copies/mL, respectively, $P = 0.01$), ALT (289 vs. 126 IU/L, respectively, $P = 0.026$), and prothrombin time (PT) (113 vs. 86%, respectively, $P = 0.002$) at baseline were found in patients with significantly decreased HBsAg, compared with patients with no significant decrease in HBsAg. At two years, 27 of the 29 patients (93.1%) became negative for HBV-DNA, and 6 of 14 patients (42.9%) showed HBeAg seroconversion. In those with seroconversion, there was no significant correlation among ALT, HBsAg, and HBV-DNA levels at baseline. In addition, there was no significant difference in the seroconversion rates between patients with or without significantly decreased HBsAg levels at six months (40.0 vs. 33.3%, respectively, $P = 0.297$).
Conclusion: HBV-DNA proliferation was inhibited by entecavir treatment, and most of the patients became negative for HBV-DNA. However, most patients showed no significant decrease in HBsAg levels. Patients with significant HBsAg reduction after two years of entecavir treatment had higher HBV-DNA levels, ALT levels, and PT levels at baseline. The significantly decreased HBsAg levels at six months were not correlated with the seroconversion rates at two years.
Disclosure of Interest: None declared

P1261 PREVALENCE AND RISK FACTORS OF HEPATITIS B INFECTION IN PREGNANT WOMEN AT THE PRENATAL CLINIC OF THE UNIVERSITY OF THE PHILIPPINES- PHILIPPINE GENERAL HOSPITAL

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Introduction: Perinatal transmission remains to be the leading cause of spread of hepatitis B virus in the Philippines. This study assessed the prevalence and associated factors for hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) in pregnant subjects seeking prenatal care at the Philippine General Hospital (PGH).
Aims & Methods: Outpatient charts of consecutive pregnant subjects at the prenatal clinic of PGH from January to July 2014 were reviewed. Information on age, marital and employment status, educational attainment, residence, gravidity, history of abortion or stillbirth, number of sexual partners, history of surgery and sexually transmitted infection, and results of screening test for syphilis were recorded. STATA SE version12 for Windows was used for statistical analyses. Univariate analysis and simple logistic regression were used to determine independent predictors of HBsAg positivity. A p-value of < 0.05 was considered as statistically significant.
Results: A total of 768 outpatient charts were reviewed. The prevalence of HBsAg seropositivity was 9.6%. HBeAg positivivity was 15.9%. HBsAg positive subjects compared with HBsAg negative subjects, tend to be older ($p = 0.016$), married ($p = 0.0032$), have multiple (≤ 3) pregnancies ($p = 0.0157$), and have history of spontaneous abortion ($p = 0.0458$). The odds of having hepatitis B infection was 1.05 times higher in older subjects; 2.22 times higher among married; 1.83 times higher among those with history of abortion; and 2.00 times higher among those with multiple pregnancies.
Conclusion: Prevalence of HBsAg seropositivity in pregnant women in PGH remains to be high despite screening guidelines and nationwide HBV vaccination.
Disclosure of Interest: None declared

P1262 IS STANDARD HEPATITIS B VIRUS VACCINATION ADEQUATE FOR LYMPHOMA PATIENTS?

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Introduction: Reactivation of hepatitis B virus (HBV) infection is a well-recognized complication of systemic chemotherapy, including chemotherapy regimens with corticosteroids and/or rituximab. Traditionally, hepatitis B surface antibody (anti-HBs) is considered a protective antibody. The effect of rituximab on these antibodies has not been established.
Aims & Methods
Aim: To ascertain the clinical features of patients who lost anti-HBs during treatment of lymphoma.
Methods: Four non-Hodgkin's lymphoma (NHL) patients previously vaccinated for HBV and became negative for anti-HBs after treatment were analyzed, regarding their clinical and demographic data. Serological HBV tests (HBsAg, anti-HBs and anti-HBc) were performed at the initial screening and throughout NHL treatment. It was considered loss of immunity when anti-HBs was less than 10 IU/mL.
Results: Four patients were included, 1 man, with a mean age of 47 ± 28 years (15-75 years). Two patients were diagnosed with a diffuse large B cells NHL, one had a mantle cell lymphoma and one had a lymphoma with intermediate features of Burkitt lymphoma/Diffuse B Large cells NHL. All patients were treated with chemotherapy (3 RCHOP and 1 protocol LMB-95). Two patients underwent further treatment: R-ESHAP followed by bone marrow transplantation (1) and radiotherapy (1). All patients received steroids and rituximab. The median pre-treatment anti-HBs titer was 19.17mIU / ml (11.9-25.8mIU / mL). The median interval between the beginning of treatment and the loss of anti-HBs was 5 months (range, 2–9 months). No patient was infected by HBV.
Conclusion: Chemotherapy for NHL has an important role in reducing the anti-HBs titers and loss of immunity, which my lead to an increased risk of developing a new HBV infection. In vaccinated patients it seems reasonable to perform a systematic determination of anti-HBs while under immunosuppressive therapy and to consider re-vaccination if immunity is lost.
Disclosure of Interest: None declared

P1263 QUANTIFICATION OF SERUM HBSAG IS A USEFUL PARAMETER TO OPTIMIZE ANTIVIRAL NUC THERAPY IN CHRONIC HBV INFECTION

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Introduction: Serum HBsAg loss is the recommended stopping rule in NUC responders, yet this event occurs rarely. Decreasing serum HBsAg levels, preceeding HBsAg seroclearance, has not been investigated sufficiently and the predictive value of baseline and on-treatment quantitative serum HBsAg levels in the therapeutic response to NUC in chronic hepatitis B (CHB) patients remains unclear. We aimed to investigate the kinetics of HBsAg levels during NUC therapy to predict the treatment period to achieve HBsAg seroconversion.
Aims & Methods: Patients with CHB, receiving NUC antiviral therapy with stable viral suppression (HBV-DNA < 20 UI/ml), were recruited at the Gastroenterology Unit of the University of Naples ''Federico II''. Sequential serum samples from these patients were tested for HBsAg with the ''HBsAg II quantitative immunoassay''(Roche). HBsAg levels were determined at baseline, where possible, and during antiviral therapy every 12 months.
Results: A total of 63 patients (male/female: 50/13, median age 58yrs, range 35-80yrs,27% cirrhosis) with CHB, HBeAg-negative, responder to different NUC therapies, were enrolled. Currently, 38 patients were in therapy with Tenofovir, 11 with Entecavir, 14 with Lamivudine. The median treatment duration was 110 months, range 48-183 months. There was a significant decrease of the HBsAg levels during at least 4 years of monitoring (p value < 0.05); in particular, at time of enrollment, the HBsAg baseline mean value was 3372 UI/ml (26.6-28948 UI/ml), while the mean value of the last determination of HBsAg was 1496 UI/ml (<20-9700 UI/ml). The statistically significant decrease of HBsAg levels was also maintained in different patient'subgroups in relation to different antiviral therapy and presence/absence of cirrhosis. HBsAg seroclearance, with HBsAb seroconversion, occurred in 12.6% of patients. Undetectable HBsAg was evidenced at least two years before the HBsAb seroclearance.
Conclusion: The results of this study suggest a role of on-treatment HBsAg quantification in the management of NUC-treated patients. If validated, prospectively in a larger patient cohort, HBsAg measurements would be a useful parameter to optimize antiviral treatment schedule.
Disclosure of Interest: None declared

P1264 PREVALENCE OF FAMILIAL AGGREGATION IN CHRONIC HEPATITIS B AND CORRELATION WITH CLINICAL CHARACTERISTICS AND INFLUENCE ON PATHOGENESIS OF OFFSPRING: A CROSS-SECTION STUDY FROM A HIGH EPIDEMIC AREA IN CHINA

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Introduction: Family infection is one of the most remarkable characteristics in pathogenesis pattern of hepatitis B in China. Family aggregation of hepatitis B varies from geographic distribution and the impact on disease remains controversial.
Aims & Methods
Aims: To investigate the prevalence of familial aggregation in Guangzhou area of which population prevalence rate of Chronic hepatitis B (CHB) is 12.45%[1] and study the relationship between clinical characteristics, influence on pathogenesis of offspring and family assemble chronic hepatitis B.
Methods: We conducted a cross-sectional survey in the First Affiliated Hospital of Sun Yat-sen University from January 2009 to January 2015. 853 consecutive subjects with established CHB were investigated at our out-patients clinic. Information of their core family members on status of HBV infection was collected with specific designed questionnaires and from the treating doctor. HBV serologic indicators, HBV DNA levels, liver function, blood cells count and imaging examination were assessed. Univariate logistic regression model were used to analyze the risk of HBV transmission.
Results: Of 668 patients with available family member data, 441 (66.0%) patients were male and the median age was 38.5 (26~68) years. Positive HBV family history was found in 331 patients (49.5%); Negative family history in 337 patients (66.02%). Two group patients were stratified according to age, as young subgroup (16~30y), middle age subgroup (31~45y), older subgroup (>45y). A significant difference was observed in the rate of diagnose with cirrhosis decompensated in HBV family history positive patients with 6.89%, 41.38%, 51.73% in young subgroup, middle age subgroup, older subgroup respectively, compared with 6.25%, 15.63%, 78.3% in HBV family history negative patients ($P = 0.046$). The rate of middle age subgroup with family history was significantly greater than that of control group (p = 0.027), while the differences in the other 2 subgroups were not significantly (p > 0.05). The groups did not differ in gender, estimated duration of infection, HBV serologic indicators, liver function and PLT ($P > 0.05$). In HBV family history positive group, children with HBsAg positive brothers was the most common aggregation pattern(30.51%), followed by children with HBsAg positive mothers (29.60%) and children with HBsAg positive fathers (23.56%). Adjusted odds ratios (OR) of risk of HBV transmission to offspring were elevated for father infected alone with HBV compared with for mother alone (OR = 2.92, 95%CI = 2.38~3.96, p = 0.009), parents both (OR = 9.54, 95% CI = 4.12~13.62, p = 0.0062).
Conclusion: Patients with HBV family history may develop cirrhosis decompensated earlier than those without. CHB children with HBsAg positive brothers is the predominant pattern in familial CHB. Mother alone or parents both infected with HBV may be at higher risk of HBV transmission to offspring than father alone.

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Disclosure of Interest: None declared

P1265 THE OUTCOME OF HEPATITIS B IMMUNOPROPHYLAXIS ON VERTICAL TRANSMISSION: A 5-YEAR OBSERVATIONAL HOSPITAL-BASED STUDY

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Introduction: Hepatitis B virus (HBV) infection is a global health problem with significant morbidity and mortality. Mother-to-child transmission is a major mode of transmission, against which immunoprophylaxis confers protection. The United Kingdom's (UK) public health strategy to prevent HBV transmission has hitherto been to offer babies born to HBV carriers immunoprophylaxis, as opposed to universal vaccination. More recently, recommendations have been proposed to introduce direct acting antiviral therapy in the third trimester of pregnancy in highly replicating mothers as an additional strategy to reduce vertical transmission. We set out to observe the effectiveness of the UK immunisation strategy, in order to quantify the risk of mother-to-child transmission despite immunoprophylaxis and introduce this into the debate on the use of direct acting antivirals in pregnancy.
Aims & Methods
Aims: To evaluate the effectiveness of our current HBV vaccination protocol in preventing mother-to-child transmission and identify risk factors for vaccination failure.
Methods: An HBV perianatal vaccination programme at a single UK London district general hospital within an area of high HBV endemicity. Children born to HBV carriers identified by universal screening were offered an accelerated immunisation schedule with 0.5ml Engerix B (GSK Pharma, UK) at birth, one month and two months of age, with a booster at 12 months of age and assessment of HBV immunity. Children born to HBV e antigen positive mothers were in addition offered HBV Immunoglobulin (HBIG, 20 IU, Colindale, UK) at birth. A dedicated HBV post-natal screening programme ensured a high patient compliance rate.
The serological records of all ante-natal patients registering within our hospital were retrospectively examined and HBV carriers identified. The serological records of children born to these carriers were used to identify vaccination failures. The case records of case failures were studied to identify risk factors for vaccination failure.
Results: Of 37,662 women registering in the Antenatal Clinic for the period 2008-2012, 805 (2.12%) patients were found to be HBV carriers, giving a much higher prevalence than the national average (0.54%). Seventy women (8.7%) were HBV e antigen (HBeAg) positive carriers. 98% compliance rates were recorded for the post-natal immunisation clinics. Two infants born to HBeAg positive mothers with high viral titres (above 6 $\log_{10}$ IU/ml) were deemed as vaccination failures (0.24% of the total born to HBV carriers and 2.86% of those born to HBeAg positive carriers) despite both passive and active immunisation. The numbers needed to treat (NNT) with direct acting antivirals in the third trimester of pregnancy in patients with high viral titres is 55 (95% CI, 45.1 – 67.9).
Conclusion: There are areas of high HBV endemicity within London (2.12%) which merit special public health attention. Current strategies to prevent HBV mother-to-child transmission are not without a significant failure rate (2.86%). The health economic debate can now take place to convince the medical community of the cost-effectiveness of the use of direct acting antivirals in the third trimester of pregnancy.
Disclosure of Interest: None declared

P1266 OUTCOMES OF THERAPEUTIC RESPONSE TO TENOFOVIR DIPIVOXIL FUMARATE (TDF) IN CHRONIC HEPATITIS B PREGNANT PATIENTS

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Introduction: Antiviral therapy may be required during pregnancy to control maternal disease and to prevent vertical transmission at third trimester. We prospectively studied the efficacy and safety of TDF in managing these patients.
Aims & Methods: Chronic Hepatitis B mothers who required antiviral treatment during pregnancy were screened. Those with ALT 50 and above and HBDNA more than 10,000 IU were treated with TDF until 52 weeks postpartum.
Primary endpoints in mother were HBV DNA < 5log10 copies/mL at delivery and the percentage of patients with HBV DNA undetectable at postpartum week 52.
Primary end points in infants were incidence of Hep B surface antigen positivity. Secondary endpoints were safety, tolerability of the drug.

Results: During 3/2012-3/2013, 30 consecutive chronic hepatitis B mothers were enrolled. All subjects received TDF 300 mg daily with a mean (range) duration of 17.1 (9-39) weeks prior to delivery. At delivery, a significant reduction of HBV DNA was observed when compared to those at the baseline (2.8 vs. 7.1 log10 copies/mL, $p < 0.001$), all mothers achieved HBV DNA reduction to the levels below 5log10 copies/mL. The treatment was well tolerated with no viral breakthrough. At postpartum week 4, four patients self-discontinued TDF without severe ALT flares. At postpartum week 52, 57% of mothers had undetectable HBV DNA levels; 64.3% of patients achieved normalization of alanine aminotrans-ferase; The adverse events were mild in severity.
Conclusion: In our cohort, mothers with chronic hepatitis B had excellent response to TDF during pregnancy. The therapy was well tolerated with no safety concerns. TDF treatment is effective not only in managing maternal disease, but also in preventing vertical transmission in mothers with high level of viremia. Further large multicenter studies are needed to verify our findings.
Disclosure of Interest: None declared

P1267 ASSOCIATION BETWEEN IL28B POLYMORPHISMS AND SPONTANEOUS HBSAG SEROCONVERSION IN PATIENTS WITH CHRONIC HEPATITIS B VIRUS (HBV) INFECTION

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Introduction: The clinical relevance of single nucleotide polymorphisms (SNPs) of the IL28B gene (interferon [IFNλ3]) is controversial in patients with hepatitis B virus (HBV) infection. Our objective was to evaluate the role of viral and host factors, including IL28B polymorphism (rs12979860), in the outcome of HBV infection in HBV patients followed up at the Hepatitis Outpatient Clinic of the University Hospital, Faculty of Medicine of Ribeirão Preto, University of São Paulo, Brazil, from 2001 to 2013.
Aims & Methods: SNPs of IL28B were determined by polymerase chain reaction in 224 chronic HBV patients, 178 males and 87 females, aged 12-69 years (128 chronic hepatitis B HBeAg (-), 52 chronic hepatitis B HBeAg (+) and 44 inactive carriers) and 41 patients with spontaneous HBsAg seroconversion. All patients were submitted to serial blood tests (the results used for analysis are given in brackets): HBV-DNA (average of 3 measurements/year) [$\leq 2x10^3$ IU/ml and $>2\ x10^3$ IU/ml], ALT (average of 4 determinations/year) [elevated ALT (ALT $\geq$ 1.5 x LSN) and normal/elevated ALT ($<$1.5 x LSN)] and HBV serology (once a year) [HBsAg, HBeAg and Anti-HBeAg].
Results: The distribution of the different genotypes of IL-18 was: chronic hepatitis B infection(C/C: 95 patients; C/T: 94 patients and T/T: 35 patients) and spontaneous HBsAg seroconversion (C/C: 13 patients; C/T: 25 patients and T/T: 3 patients). The frequency of the IL28B C/T genotype was significantly higher in patients with spontaneous HBsAg seroconversion than in patients with chronic hepatitis B infection ($p = 0.027$; OR = 0.462; 95%CI = 0.234 to 0.914). No association was observed between the IL28B genotypes (C/C, C/T, T/T) and ALT levels, viral load and HBeAg status. Spontaneous HBsAg seroconversion was associated to inactive carrier status (67.5% inactive carriers vs 32.5% chronic hepatitis, $p<0.0001$; OR: 0.24; 95%CI: 0.123 to 0.455) and age higher than 40 years ($p=0.0007$).
Conclusion: IL28B C/T genotype appears to be associated with spontaneous HBsAg seroconversion. Additional studies are needed to understand the mechanisms of IL28B polymorphisms in the evolution of HBV infection.
Disclosure of Interest: None declared

P1268 AUDIT ON ANTE NATAL CARE OF PATIENTS WITH HEPATITIS B IN A MULTI-PROFESSIONAL CLINIC IN A NON-REGIONAL CENTRE

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Introduction: Vertical Hepatitis B (HBV) transmission is the commonest mode of transmission. Antenatal screening for HBV was introduced in the UK in 2000[1]. Our hospital serves half a million population with predominantly Caucasian population. Prior to establishing antenatal Hepatitis B service, the service was haphazard due to a combination of non-referral to Hepatologist by GP and maternal non-attendance. Henceforth multi-professional antenatal HBV clinic for screen detected patients during their ante-natal visits was established in 2009 with Obstetrician, Hepatologist, Midwife in attendance. Antenatal Hepatitis B services are available at regional centres in UK but 25% rate of non-attendance are barriers to the delivery of high-quality service[2, 3].
Aims & Methods: We aimed to determine the prevalence of active HBV disease that requires treatment and to review the management of mothers during pregnancy by comparison of our attendance rate to regional centres. We did a retrospective database review of 5 years from 2009-2014 of all HBV-infected pregnant women who attended the multi-professional clinic. Demographics, clinical information, vaccination and immunoprophylaxis were reviewed electronically.
Results: 81 patients were screen detected: 3 patients' records not retrievable; 5 had miscarriages; 4 patients did not attend hospital ante-natal clinic and 3 did not see Hepatologist. We reviewed the records of 62 patients. Mean age was 29. Only 3% of mothers were white British, rest were ethnic minority with Chinese being the majority (35%). 97% (60/62) were surface antigen positive, 89% (55/62) were HBe Ag negative, 15% (9/62) were HBe Ab negative, 16% had viral DNA $> 10^6$ (10/62, 7 HBe Ag positive and 3 HBe Ag negative). 19% infants (12/62, 2 infants born to mother with HBe Ab negative state and 10 infants born to mother with viral load $> 10^6$ in 3rd trimester), received Immunoglobulin and vaccination as per DOH guidelines[3, 4]. 16% (10/62) mothers with viral load more than 10^6 received anti-viral treatment in the 3rd trimester. Vaccination uptake was complete in all infants.
Conclusion: 16% mothers having active Hepatitis B requiring treatment and 19% infants requiring immunoglobulin does validate the need for a specialist service. The non-attendance rate of 9% substantiates the need for locally established multi-professional clinic to prevent vertical transmission compared to nearly 25% rate of non-attendance in regional service.

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Disclosure of Interest: None declared

P1269 REACTIVATION OF OCCULT OR PAST HEPATITIS B VIRUS INFECTION IN A NON-HODGKIN B CELL LYMPHOMA POPULATION

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Introduction: Reactivation of hepatitis B virus (HBV) infection is a life-threatening complication in patients undergoing systemic chemotherapy. Rituximab is a risk factor for reactivation of occult or past HBV infection (antibody to hepatitis B core antigen [anti-HBc] positive and hepatitis B surface antigen [HBsAg] negative) in patients with B cell non-Hodgkin lymphoma (NHL-B). Recently published guidelines recommend HBV prophylaxis in these subgroup of patients.
Aims & Methods: We aim to characterize clinical and demographically anti-HBc positive/HBsAg negative NHL-B population and determine the HBV reactivation rate. All patients with the diagnosis of NHL-B are routinely tested for HBsAg, anti-HBc and antibody to HBsAg (anti-HBs). We performed an observational, retrospective, single-center study of anti-HBc positive/HBsAg negative NHL-B patients, diagnosed between 2003 and 2014. Clinical data, demographic characteristics and HBV reactivation were analysed. HBV reactivation was defined as seroconversion to HBsAg with or without detection of HBV-DNA.
Results: We included 202 patients, 120 male, mean age 73.0 ± 14.7 years. Seventy-sixt percent (n = 154) were anti-HBs positive and 30.2% were tested for HBV-DNA level (all negative). Seventy percent (n = 141) underwent chemotherapy, which included rituximab in 84.3% and corticosteroids in 97% of the cases. During chemotherapy, 10 patients performed antiviral prophylaxis with lamivudine (n = 6) or entecavir (n = 4), with suspension 5.5 ± 4.5 months after chemotherapy discontinuation. Two patients (1%), one with diffuse large B cell lymphoma and other with chronic lymphocytic leukemia, had HBV reactivation during follow-up. Both were anti-HBs negative before chemotherapy, were treated with rituximab, and none performed antiviral prophylaxis. Reactivation was detected 2.8 and 5.4 months after discontinuation of rituximab. These patients were managed with entecavir, one of them successfully (sustained virological response); the other one died of variceal bleeding.
Conclusion: This is one of the largest series evaluating anti-HBc positive/HBsAg negative B cell lymphoma population. In this study, patients with occult or past HBV infection had a small (1%) but potentially fatal risk of HBV reactivation after rituximab therapy if no antiviral prophylaxis was performed. With the implementation of the new guidelines, prospective studies are expected to validate antiviral prophylaxis in these high-risk patients.
Disclosure of Interest: None declared

P1270 CLINICAL SIGNIFICANCE OF QUANTITATIVE HBSAG TITRES AND ITS CORRELATION WITH HBV DNA LEVELS IN THE NATURAL HISTORY OF HEPATITIS B VIRUS INFECTION

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Introduction: Quantification of serum hepatitis B antigen (HBsAg) is an important test that marks active infection with hepatitis B and helps in the prediction of the clinical outcome and management of hepatitis B virus (HBV) infection.

Correlation with HBV DNA quantitative levels may help in developing strategies for antiviral treatment.

Aims & Methods: The study was to evaluate HBsAg titres in various phase of HBV-infection in HBsAg-positive patients. 976 HBV related patients were analyzed in this retrospective cross-sectional study. Patients were categorized based on the phase of HBV infection: immune tolerant phase (IT, n = 123), immune clearance phase (IC, n = 192), low-replicative phase (LR, n = 476), and HBeAg-negative hepatitis (ENH, n = 185). HBsAg titers were quantified and correlated with HBV-DNA levels and clinical parameters.

Results: Median HBsAg titres were different between each phases of HBV infection ($p < 0.001$): (4.62 log10 IU/ml), IC (3.88 log10 IU/ml), LR (2.76 log10 IU/ml) and ENH (2.94 log10 IU/ml). HBsAg and HBV DNA levels showed significant correlation in the whole group ($r = 0.694$, $p < 0.001$), and this was also observed in different phases of HBV infection. Strong correlation in IT phase ($r = 0.603$, $p < 0.001$) and IC phase ($r = 0.523$, $p < 0.001$), moderate in LR phase ($r = 0.362$, $p < 0.001$) and week in ENH ($r = 0.110$, $p = 0.04$). No correlation was observed between serum HBsAg levels and biochemical parameters.

Conclusion: The study demonstrated significant difference in the median baseline values of serum HBsAg titres in different phases of HBV infection. These results may provide additional information in understanding the natural history of HBV-infection.

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P1271 PREEXISTING CO-MORBIDITIES AND CO-MEDICATIONS OF PATIENTS UNDERGOING TREATMENT OF CHRONIC HCV G1 INFECTION IN GERMAN REAL-LIFE

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Introduction: Information about co-morbidities of patients (pts) currently treated for chronic HCV genotype 1 (G1) infection in real-life is scarce. The present interim analysis of the NOVUS observational study was therefore aimed to investigate the frequency of preexisting and ongoing co-morbidities of pts treated for chronic HCV G1 infection in German real-life and to determine the frequency of co-medications.

Aims & Methods: From April 2012 until January 2014, 536 pts with HCV G1 infection were recruited in the ongoing NOVUS study by 97 practices and hospitals in Germany. Until now, pre-existing co-morbidities before triple therapy of HCV G1 infection with boceprevir were documented for 469 pts (treatment-naïve N ± 306, pretreated N ± 154).

Results: Ongoing co-morbidities were reported for 329 of 469 pts (70%) before treatment of HCV G1 infection. Overall, 599 ongoing co-morbidities (multiple answers allowed) were documented. The most frequently reported co-morbidities were obesity (BMI > 30 kg/m^2) (19 %), cardiovascular diseases (18%), psychiatric disorders (14%), opiate substitution (13%), gastrointestinal diseases (11%), metabolic disorders (8%), thyroid gland diseases (7%), bone and joint diseases (6%), skin diseases (5%), HIV-co-infection (4%) and kidney diseases (2%). When co-morbidities were analyzed by gender (female vs. male), thyroid diseases occurred more frequently in females (13% vs. 3%, $P < 0.0001$), while opiate substitution (9% vs. 15%, $P < 0.04$) and HIV- co-infection (1% vs. 6%, $P < 0.01$) occurred less frequently in female pts. Regarding age (≤ 50 vs. > 50 years), cardiovascular (9% vs 28%, $P < 0.0001$), thyroid (3% vs. 12%, $P = 0.0002$) and kidney diseases (0.4% vs. 5%, $P = 0.0025$) were more frequently reported in pts older than 50 years, while opiate dependence (20% vs. 4%, $P < 0.0001$) and HIV-co-infections (6% vs 1%) were less frequently reported in elder pts. In contrast, obesity, psychiatric disorders and diseases of skin and bone/joints showed no association with gender and age. Co-medications were documented for 233 of 469 pts (50%). According to the frequency of co-morbidities, 39% of overall 564 co-medications were related to treatment of neuropsychiatric disorders including opiate dependency, 19% were cardiovascular drugs, 14% were agents for gastrointestinal and metabolic diseases and 6% for thyroid diseases.

Conclusion: The present analysis demonstrates that preexisting co-morbidities are a frequent problem in pts undergoing treatment of HCV G1 infection in German real-life and that several co-morbidities are related to gender or age. As a consequence, there is a high frequency of co-medications which needs attention with regard to possible interactions between co-medications and direct-acting antivirals.

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P1272 BOCEPREVIR TRIPLE THERAPY OF HCV GENOTYPE 1 (G1) INFECTION IN GERMAN REAL-LIFE: COMPARABLE HIGH SVR RATES UP TO 87% IN TREATMENT-NAÏVE AND PREVIOUSLY TREATED PATIENTS WHO ACHIEVE AN EARLY VIROLOGIC RESPONSE

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Introduction: Since 2011, triple therapy with the HCV protease inhibitor boceprevir (BOC) is widely used as standard of care for patients (pts) with chronic HCV G1 infection. The present interim analysis of the German NOVUS observational study was aimed to compare the efficacy of BOC triple therapy in previously untreated and previously treated patients in German real-world and, in particular, to compare the virologic outcome of pts who achieve an early virologic response (EVR) at treatment week (TW) 8.

Aims & Methods: From April 2012 until January 2014, 536 pts with genotype 1 infection were recruited in the ongoing NOVUS study by 97 practices and hospitals in Germany. Pts were treated with pegylated interferons (PegIFN) and ribavirin (RBV) together with BOC up to 44 weeks after a 4 weeks lead-in period with PegIFN/RBV. The present interim analysis was restricted to 275 treatment-naïve pts and 140 previously treated pts who started triple therapy at least 12 months ago.

Results: Overall 275 previously untreated pts were compared with 140 previously treated pts (37% relapsers, 14% partial responders, 19% null-responders, 6% breakthrough and 21% with unknown previous response to dual therapy) who showed the following characteristics (untreated vs. treated): Mean age: 45 vs. 51 years ($P < 0.0001$); male gender: 59% vs. 60%; baseline viral load > 400,000 IU/mL: 68% vs. 72%; G1b: 50% vs. 49%; liver cirrhosis: 5% vs. 11% (not significant, ns); co-infection with HIV: 4% vs. 4%; opioid substitution: 12% vs. 10%. Previously untreated pts achieved more frequently undetectable HCV-RNA levels at TW8 (72% vs 59%, $P = 0.014$), at TW12 (87% vs. 77%, $p = 0.020$) and at end of treatment (88% vs. 77%, $P = 0.009$) than pretreated pts. Until now, follow-up data available from 199 untreated and 108 pretreated pts indicated significantly higher SVR rates in treatment-naïve pts (76% vs. 57%, $P = 0.0008$). Notably, comparable high/low SVR rates were observed in untreated and pretreated pts with EVR (87% vs. 86%, ns) or without EVR (46% vs 34%, ns). Regarding EVR together with the virologic response to PegIFN/RBV lead-in at the end of TW4, untreated pts showed more frequently a HCV-RNA decline > 1log$_{10}$ than previously treated pts (79% vs. 67%, $P = 0.0143$), while no difference in HCV-RNA decline > 1log$_{10}$ at TW4 was observed when untreated or pretreated pts achieved EVR (84% vs. 89%, ns).

Conclusion: Untreated and previously treated pts undergoing BOC triple therapy for HCV G1 infection in German real-world attain SVR rates of 76% and 57%. When pts achieve an EVR, SVR rates are comparably high in untreated (87%) and pretreated pts (86%). Sensitivity to PegIFN/RBV as assessed by HCV-RNA decline at the end of lead-in seems to be higher in untreated pts but comparable in previously untreated and previously treated pts who achieve an EVR.

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P1273 SAFETY AND EFFICACY OF INTERFERON/RIBAVIRIN-FREE THERAPY IN SEPTUAGENERIANS AND OCTOGENERIANS WITH CHRONIC HEPATITIS C

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Introduction: Direct acting antivirals (DAA) have revolutionized treatment of chronic hepatitis C. Septua- and octogenarians were not included in clinical studies and therefore data on efficacy and safety of IFN-free treatments in elderly are missing. Elderly patients may have a decrease of renal and hepatic function and are at risk for drug-drug interactions with DAA with drugs required for long-term treatment for other medical conditions.

Aims & Methods: The aim of this study was to investigate safety and efficacy of inferferon (IFN) and ribavirin (RBV)-free treatments in patients > 70 years with advanced chronic hepatitis C.

44 otherwise healthy patients > 70 years (cirrhosis: 32, F3:12, mean age: 74.6, range 70-88, m/f: 19/26, median HCV RNA $1.18x10^6$ IU/ml, HCV-genotype: GT-1a:6; 1b:35; 3:1; 4:2; missing:1; treatment experienced: 25; median platelet count: 137 G/l; median albumin: 39.5 g/l; median bilirubin: 0.86 mg/dl; median GFR using Cockroft-Gault formula: 66.6 ml/min) were enrolled. The patients were treated with sofosbuvir (SOF) 400mg/day combined either with daclatasvir (DCV) 60mg/day, simeprevir (SMV) 150mg/day, or ledipasvir (LDV) 90 mg/day. HCV RNA quantification was carried out with Abbott RealTime HCV (ART) assay (LLOQ < 12IU/mL). Treatment duration was 12 weeks, and was prolonged to up to 24 weeks in patients with detectable HCV-RNA at week 8.

Results:

	N	Completed treatment N	Completed Follow Up N	SVR	On treatment N	TND*	<12**
SOF/SMV	**21**	**18**	**8**	**7**	**3**	**2**	**0**
SOF/DCV	**17**	**13**	**6**	**6**	**4**	**0**	**1**
SOF/LDV	**6**	**3**	**2**	**2**	**3**	**3**	**0**
Total (%)	**100**	**77.2**	**36.0**	**34.0**	**22.7**	**11.3**	**2.2**

*HCV-RNA: TND = Target not detected. ** HCV-RNA at least 4 weeks of treatment (IU/ml)

Currently, 34 patients completed treatment of which 15 reached end of follow up. No severe adverse events were observed. The most frequent adverse events (AE) were fatigue (27.2%), cephalea and pruritus (6.8% and 13.6). Other less common side effects observed were insomnia (11.4%), mood changes (4.5%), but also dyspnoe, arthralgia, nausea and cough (< 5%). No dose modifications were required. One patient treated with SOF/SIM had a relapse after reaching end of treatment.

Conclusion: IFN/RBV-free treatment regimens are safe and effective in elderly chronic hepatitis C patients with advanced liver disease.

Disclosure of Interest: None declared

P1274 DECOMPENSATION, HEPATOCELLULAR CARCINOMA, LIVER RELATED HOSPITAL ADMISSION AND LIVER RELATED MORTALITY AFTER ANTIVIRAL TREATMENT; A POSTSCRIPT AT THE END OF ERA OF CONVENTIONAL DUAL THERAPY FOR CHRONIC HEPATITS C

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Introduction: There are only limited large-scale data to show the impact of conventional dual antiviral therapy with pegylated interferon and ribavirin (CDAVT) on natural history of chronic hepatitis C (CHC).

Aims & Methods: We aim to evaluate development of decompensation, hepatocellular carcinoma (HCC), liver related hospital admission (LRA) and liver related mortality (LRM) in patients who had received CDAVT.

Methods: 1605 patients (from January 2002 to December 2013) with CHC who underwent liver-biopsy (LB) and received CDAVT were retrospectively analyzed for development of decompensation, HCC, LRA and LRM.

Results: Mean age of patients was 41.9± 9.7 years (85% males), predominantly genotype 4(65%) and genotype 1(11%). Pre treatment LB showed (Scheuer classification) stage-0 fibrosis in 1.9%, stage-1 in 32.9%, stage-2 in 39.5%, stage-3 in19% and stage-4 in 6.6% patients. Median follow-up was 3.5 years (5617.5 patient-years). There were 1079 (67.6 %) responders, 482 (30.2%) non-responders and 34 (2.1%) relapsers. Among responders, 1017 (63.3%) patients had persistent sustained virologic response (SVR) and 62 (3.8%) had recurrence (non persistent SVR) on quantitative PCR assay. 86 (5.3%) patients developed decompensation [bleed (n = 16), ascites (n = 55), jaundice (n = 28), hepaticencephalopathy (n = 2), spontaneous bacterial peritonitis (n = 1) and hepatorenal syndrome (n = 1)]. Esophageal varices developed in 47(2.9%) patients, gastric varices in 1 and both in 1. 15(0.9%) patients developed HCC,28 (1.7) had LRA and 4 (0.2%) had LRM. Non liver related hospital admissions (n = 131, 8.1%) was significantly higher than LRA($p = 0.04$). Non liver related mortality (n = 5, 0.3%) and LRM were comparable ($p = 0.30$). The development of all outcome measures were significantly lower in patients who had persistent SVR compared to non persistent SVR, relapsers and non-responders (Table 1). On comparing patients with persistent SVR and the rest of the patients, the risk of overall decompensation (2% v/s 11.6% $p < 0.001$), bleed (0.2 v/s 2.4%, $p < 0.001$) ascites (1% v/s 7.8%, $p < 0.001$), jaundice (0.6% v/s 3.8%, $p < 0.001$), development of HCC (0.1 v/s 2.4%, $p < 0.001$) and LRA (0.4% v/s 4.2% $p < 0.001$) were significantly lower in the former. LRM showed a similar trend (0.1% v/s 0.5%, $p = 0.06$).

Conclusion: In chronic hepatitis C decompensation, development of HCC, LRA and LRM occur despite treatment and attainment of SVR. However, patients with loss of SVR on follow up, nonresponders and relapsers are at higher risk of these complications.

Disclosure of Interest: None declared

P1275 METABOLIC FACTORS ASSOCIATED WITH HEPATIC STEATOSIS AND FIBROSIS IN CHRONIC HEPATITIS C PATIENTS

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Introduction: Liver steatosis is a common finding in patients infected with hepatitis C virus (HCV)[(1)]. HCV steatosis was recently identified as a risk factor for progression to extensive fibrosis[(2)]. Chronic HCV infection is closely related to the metabolic syndrome (MS). Accordingly, CHC should be classified into CHC with and CHC without MS. Insulin resistance (IR) is the main feature of the MS. In CHC, there is a close association between IR, hepatic steatosis[(3)], and progression of fibrosis[(4)].

Aims & Methods: Evaluate metabolic factors associated with hepatic steatosis and fibrosis in patients infected with CHC, and to assess the impact of insulin resistance (as measured by HOMA-IR score) and serum adipocytokines levels on hepatic steatosis and fibrosis relative to other factors. Finally, to evaluate the relationship between CHC and metabolic syndrome.

Results: Significant steatosis (> 33%) was detected in 54% of the patients, while 21.12% of the patients had stage 3/4 fibrosis. Higher degree of steatosis was significantly associated with higher BMI, serum insulin, HOMA index and TNF-α ($P < 0.0001$, $P < 0.0006$, $P < 0.0001$, and $P < 0.01$ respectively). Higher stages of fibrosis were significantly associated with higher BMI and serum triglycerides ($P < 0.04$, $P < 0.02$ respectively). Multivariate analysis of the metabolic factors showed that HOMA index ($P < 0.001$) and TNF-α ($P < 0.03$) were the factors mostly predicting higher degree of steatosis. While, BMI index ($P < 0.01$) and serum triglycerides ($P < 0.03$) were the factors mostly predicting higher stage of fibrosis. We also found that CHC is closely related to MS, and we recognized that olderage ($P < 0.011$), higher BMI ($p < 0.0001$), lower, serum adiponectin ($P < 0.0001$), higher TNF-α ($p < 0.0001$) and higher steatosis degree ($p < 0.04$) are significantly associated with MS in these patients.

Conclusion: In patients with CHC, steatosis is of metabolic origin as it is closely associated with the presence of metabolic syndrome. Higher BMI, HOMA-IR, lower serum adiponectin and higher serum TNF-α and triglycerides were associated with HCV hepatic steatosis and metabolic syndrome, while higher BMI and serum triglycerides are the predictors of more advanced fibrosis stage in CHC patients.

Abstract number: P1274. Table 1: Development of decompensation, hepatocellular carcinoma liver-related hospital admission and liver-related mortality in patients with CHC after CDAVT

	Decompensation, (total N ± 86) N (%)	Bleed, (total N ± 16) N(%)	Ascites, (total N ± 55) N(%)	Jaundice, (total N ± 28) N(%)	Hepatocellular carcinoma, (total N ± 15) N(%)	Liver-related hospital admission, (total N ± 28) N(%)	Liver-related mortality, (total N ± 4) N(%)
Persistent SVR (n = 1017)	24(2.4)	2(0.2)	10(1)	6(0.6)	1(0.1)	4(0.4)	1(0.1)
Non persistent SVR (n = 62)	2(3.2)	2(3.2)	2(3.2)	1(1.6)	3(4.8)	3(4.8)	1(1.6)
Non responders(n = 482)	50(10.4)	10(2.1)	36(7.5)	20(4.1)	8(1.7)	16(3.3)	1(0.2)
Relapsers (n = 34)	10(29.4)	2(5.9)	7(20.6)	1(2.9)	3(8.8)	5(14.7)	1(2.9)
pvalue	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.006

N ± number of patients.

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P1276 FIB-4, A SIMPLE FIBROSIS TEST, ACCURATELY PREDICTS METAVIR F3/F4 STAGE IN CHRONIC HEPATITIS C

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Introduction: Several interferon-free treatments of chronic hepatitis C have recently become available. Due to their high cost, reimbursement by health insurance has been mostly restricted to patients with severe fibrosis (F3) and cirrhosis (F4). Transient elastography (Fibroscan®) has been widely used to detect ≥F3 using a cut-off of 9.5 kPa, but reliable measurements can be obtained in only 80% of patients approximately. Simple fibrosis tests including FIB-4, APRI and platelet count are readily available and have been found useful to detect significant fibrosis (F2) and cirrhosis (F4) but data on detection of severe fibrosis (F3) are scarce.

Aims & Methods: Consecutive patients with chronic hepatitis C (n = 614) who underwent liver biopsy prior to antiviral treatment were included in two Austrian centers. Exclusion criteria were prior antiviral treatment, presence of hepatocellular carcinoma, previous liver transplantation, and lack of a representative biopsy specimen. METAVIR fibrosis stage was used as reference. Routine laboratory values including AST, ALT, and platelet count (PLT) were collected at the time of liver biopsy; APRI and FIB-4 were calculated using published formulas. Diagnostic accuracy of APRI, FIB-4, and PLT for detection of METAVIR ≥F3 was assessed by ROC analysis and best cut-offs were determined by Youden index.

Results: In our cohort, METAVIR fibrosis stage was distributed as follows: F0: n = 17 (3%), F1: n = 204 (33%), F2: n = 202 (33%), F3: n = 58 (9%), F4: n = 133 (22%). APRI and FIB-4 progressively rose and PLT progressively declined with increasing fibrosis stage. ROC analysis revealed high diagnostic accuracies (AUC, 95% CI) of FIB-4 (0.84, 0.81-0.88), APRI (0.81, 0.77-0.85), and PLT (0.83, 0.79-0.86) for detection of METAVIR ≥F3. Youden index revealed an optimal FIB-4 cut-off of ≥1.77 (sensitivity 77%, specificity 83%, PPV 67%, NPV 89%) for detection of METAVIR ≥F3.

Conclusion: In treatment-naive patients with chronic hepatitis C, severe fibrosis or cirrhosis (METAVIR ≥F3) may be accurately detected by simple fibrosis tests based on routine laboratory values. Highest diagnostic accuracy was found for FIB-4.

Disclosure of Interest: None declared

P1277 VALIDITY OF UPPER GASTRO-INTESTINAL ENDOSCOPIC SCREENING IN HCV CIRRHOTIC PATIENTS AWAITING ANTIVIRAL THERAPY

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Introduction: The Egyptian Ministry of Health initiated a nationwide HCV treatment program with the newly developed oral antiviral therapies and formulated national guidelines for treatment allocation which gives favor for patients with advanced fibrosis and early cirrhosis. One of the prerequisites for treatment was upper Gastro-intestinal (GIT) endoscopy.

Aims & Methods: This study aimed at judging the validity of the national recommendation of upper GIT endoscopic screening before enrollment in HCV antiviral therapy and to assess the work load on the endoscopic units met by this recommendation. This study was carried out at gastrointestinal endoscopy units, Zagazig University Hospitals starting in January 1st and followed to December 31st 2014. The epidemiologic and clinical features of patients undergoing preparation for HCV therapy were examined. Endoscopic findings were analyzed and were compared to other cirrhotic HCV patients on regular endoscopic follow up. Endoscopic classification of esophageal varices was carried out after the Italian liver cirrhosis project while gastric varices were classified according to Sarin classification.

Results: A total of 1143 patients sought upper GIT endoscopy at our units in preparation for HCV treatment during the study peroid. This comprised 22% of all patients undergoing upper GIT endoscopy over that year. There was a four-fold rise in percentage of patients undergoing endoscopy for therapy in this year (22%) after starting enrollment for sofosbuvir-based therapy when compared to assessment for Interferon/Ribavirin combination therapy (5%) in the last year. A total of 361 patients had no esophageal or gastric varices. Small sized varices (grade I) were present in 301 patients while medium sized varices (grade II) were reported in 188 patients and 291 patients encountered in large sized varices (grade III). Thirty patients (2.6%) had gastric varices, of them 17 were GOV type 1, 9 were GOV type 2 and 4 were IGV type 1 (only 2 patients had isolated gastric varices without associated esophageal varices). Endotherapy (band ligation and/or gastric variceal injection) was performed in 320 patients. Follow-up for these patients was arranged according to the established guidelines.

Conclusion: According to the results of this study screening endoscopy for early cirrhotic patients awaiting oral anti-HCV therapy seems to be valid. Endoscopic work burden is expected to rise with increased demand on newer sofosbuvir-based regimens. More cases eligible for endotherapy are detected earlier with shifting of workload from advanced to earlier stages of CLD.

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P1278 DIFFICULTIES IN DIAGNOSE AUTOIMMUNE HEPATITIS IN NAFLD PATIENTS

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Introduction: The diagnosis of AIH needs to be considered in any patients with elevated aminotransferases. NAFLD is an exclusion diagnosis and there are no specific serum markers for these two diseases. Most patients may be asymptomatic or have nonspecific symptoms in both diseases. In our study we want to evaluate the role of AIH score (after Hennes) in NAFLD patients.

Aims & Methods: We included 152 patients with high levels of aminotransferases or bright liver on ultrasonography , 40 males (26.31%) and 112 females with age from 23 to 79 years.35 patients (23.02%) were overweight, 9 patients had normal weight and 24 (15.79%) had severe obesity. Blood samples were collected to determinate aminotransferases, alkaline phosphatase, IgG level, gamma-globulin, anti-nuclear antibody (ANA), albumin, bilirubin, platelet count. We excluded the patients with other known cause of liver disease : viral, alcohol, genetic or drug-induced and others autoimmune diseases. The abdominal ultrasonography was performed by the same physician and steatosis was graded using a semi-quantitative scale of 1 (mild) to 3 (severe). 54 patients accepted liver biopsy. Histological samples were evaluated by one pathologist who was not blinded to the patient's history. We considered AIH probable if the score was > 6 and definite if the score was > 7.

Results: 28 patients (18.42 %) were positive for ANA with median titer > 1:40 (20 patients) or > 1:80 (8 patients). IgG levels were upper normal limit in 19 patients and > 1.1 normal limit in 6 patients. Only 12 patients were both positive for ANA and had IgG levels upper normal limit. All these patients ANA positive or abnormal IgG levels accepted liver biopsy. Before the liver biopsy 4 patients had AIH score equal to 6, after the liver biopsy only 1 patient had portal tract plasma cell infiltration, a characteristic feature for AIH but not specific. We could not find any independent factor predictive(gender, age, weight, gamma globulin, aminotransferases, bilirubin or alkaline phosphatase level) for ANA presence.

Conclusion: AIH score is not very strong for predicting the disease, especially for borderline diagnosis.

Disclosure of Interest: None declared

P1279 ALKALINE PHOSPHATASE AS BIOMARKER IN PRIMARY SCLEROSING CHOLANGITIS: BETTER PROGNOSTIC VALUE ONE YEAR AFTER DIAGNOSIS

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Introduction: In a chronic orphan disease such as primary sclerosing cholangitis (PSC) it is important to identify biomarkers for disease progression. Biomarkers can be used to measure treatment effect in clinical trials and improve patient management and counselling. Several recent publications have assessed the prognostic value of alkaline phosphatase (ALP), using various thresholds over various periods of follow up (FU).

Aims & Methods: With this study we aimed to assess the prognostic value of alkaline phosphatase at diagnosis (T0) and 1 year FU (T1) at different follow-up times in a large-population based PSC cohort. Furthermore we aimed to determine the most optimal threshold value of ALP.

Patient charts of PSC patients that were included in the population based Epi PSC PBC cohort were reviewed for ALP values at T0 and T1 (range +/- 3 months). ALP values were expressed in times upper limit of normal (xULN). A combined clinical endpoint was defined as development of cholangiocarcinoma, liver transplantation (LTx), or PSC-related death. The association between ALP level (measured as xULN at T0 and T1 as well as relative change ((T1-T0)/T0*100%)) and the hazard of reaching a clinical endpoint was assessed using cubic spline functions. The Uno's C-statistics were calculated for each month of FU to assess the discriminatory power of ALP at T0 and T1 and relative change at T1. The Harrell's C-statistics were calculated for each threshold ranging from 0.5xULN to 3.0xULN with a step of 0.1 at T0 and T1 and relative change ranging from -100% to 100% with a step of 5%, from which the optimal threshold was determined. Kaplan Meier survival curve was used to

present the survival probability of the two groups classified by the optimal threshold.

Results: A total of 367 patients were included, with a median FU of 100 months (IQR 67-150). The mean age at diagnosis was 40 (±14), 66% was male. ALP values at T1 were missing for 21 patients, 8 patients were excluded for T1 analyses as they reached an endpoint within 1 year FU. Median ALP at T0 was 1.99xULN (IQR 1.38-3.37) vs 1.22xULN (IQR 0.80-1.89) at T1. A total of 72 patients (20%) reached an endpoint; 15 (4%) PSC-related death, 41 (11%) LTx, 16 (4%) cholangiocarcinoma. A positive association was observed between the hazard of reaching an endpoint and ALP level in the range of 0-3xULN at T0 and T1, as well as reduction in relative change at T1. ALP measured at T1 had better predictive value than at T0 or the relative change in most of the FU time. With the optimal threshold of 1.3xULN at T1 (C-statistic 0.61 (95%CI 0.55-0.68)), the difference in endpoint-free survival between the two groups was statistically significant (log-rank test $p < 0.001$). Patients with ALP above 1.3xULN at T1 had a 1.47 times higher probability of reaching an endpoint compared with patients with ALP below 1.3xULN at T1.

Conclusion: The use of ALP to predict endpoint-free survival in PSC patients holds best prognostic value at T1, with an optimal threshold of 1.3xULN. These results confirm the usefulness of ALP as surrogate endpoint in clinical intervention studies in PSC. Furthermore, ALP at T1 may be an important factor to include in prognostic modeling for PSC.

Disclosure of Interest: None declared

P1280 THE FIRST NEW TRIALS FOR PRIMARY BILIARY CIRRHOSIS IN A DECADE: AN INTERNATIONAL PROGRAM EVALUATING THE FARNESOID X RECEPTOR AGONIST OBETICHOLIC ACID

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Introduction: Primary biliary cirrhosis (PBC) is a chronic autoimmune cholestatic liver disease which can lead to cirrhosis, liver transplant or death. Hepatobiliary injury is reflected by increased plasma alkaline phosphatase (ALP) and bilirubin that correlate with disease progression. Obeticholic acid (OCA), a modified bile acid and farnesoid x receptor (FXR) agonist, has been evaluated in three international double-blind placebo-controlled PBC studies.

Aims & Methods: Two Phase 2 studies evaluating OCA as monotherapy (Study 201; N = 59) or in conjunction with UDCA (Study 202; N ± 165) recruited subjects with ALP ≥1.5 xULN, randomized to receive OCA 10 mg, OCA 25 mg (Study 202 only), OCA 50 mg or placebo. The Phase 3 POISE study enrolled subjects (N ± 216) with an inadequate response to UDCA who were randomized to receive placebo, OCA 10 mg, or OCA 5 mg uptitrated to 10 mg based on clinical response. This analysis evaluated the three studies for the Phase 2 primary endpoint (mean % change in ALP) and the Phase 3 primary composite endpoint (ALP < 1.67xULN with a minimum 15% reduction and normal bilirubin, shown to correlate with survival (Lammers 2014)).

Results: Baseline characteristics were generally similar between treatment groups. All 3 studies met their pre-specified primary endpoints. Statistically significant reduction in ALP compared to placebo was seen in all 3 studies and at all doses (Table 1). At three months of treatment, significantly more OCA-treated subjects also achieved the composite POISE endpoint in all three studies (Table 1). OCA treatment was also associated with statistically significant decreases in other liver enzymes including GGT, ALT and AST. While the subjects in the monotherapy group had higher ALP at baseline than the OCA plus UDCA group, the two groups reached similar ALP levels by end of the double-blind period. Pruritus was the most common adverse event with a dose-related increase in incidence with OCA.

Conclusion: A significantly larger percentage of subjects treated with OCA, with or without UDCA, achieved both lower ALP and a composite endpoint shown to correlate with long-term, transplant-free survival compared to placebo-treated subjects. The efficacy of OCA compared to placebo was consistent across the 3 studies, spanning doses from 5 to 50 mg over 3-12 months of treatment. Safety & tolerability profile of OCA showed consistent results across studies.

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P1281 FACTORS PREDICTING RELAPSE FOLLOWING TREATMENT WITHDRAWAL IN PATIENTS WITH AUTOIMMUNE HEPATITIS

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Introduction: Relapse after the withdrawal of corticosteroids occurs in 50–87% of patients with autoimmune hepatitis (AH). The ultimate goal of complete remission after treatment withdrawal can be achieved in a small proportion of patients. We aimed to investigate the predictive factors for relapse after treatment withdrawal in patients with AH

Aims & Methods: We retrospectively evaluated the patients who had diagnosed AH with clinical and laboratory and histological findings in our outpatient clinic. Inclusion criteria were >1 year follow-up, reliable demographic and laboratory data at baseline and 3 months interval. Exclusion criteria were HIV infection, suspected other liver diseases (eg. steatohepatitis), and missed follow-up more than 6 months. Treatment stopped in patients with >1 year biochemical remission, if they have no cirrhosis, no evidence of advanced liver disease. When suspected, liver biopsy was performed. Demographic data, baseline laboratory values, baseline biopsy findings, changes of the blood tests at 6 months of treatment, the time of biochemical remission, drug dosages and types were investigated as the predictors of relapse after drug discontinuation.

Results: Eighty-one of a total of 158 patients with AH were enrolled into the study. Treatment was discontinued in 39 (48%) patients (M/F:4/35, age 54 + 14.). In these 39 patients treatment duration after ALT normalization was 41.4 ± 23.6 month. Control liver biopsies were performed in 25 (64%) patients. Relapse occurred in 17 patients (43%) at a median time of 20 months (4-48). Age and gender were not related to relapse. Among several parameters basal globuline and platelet count were found to be related to relapse. Basal globuline was 4.21 ± 0.9 and 3.43 ± 0.76, platelet count $287 \pm 101 \times 10^3/\mu l$ and $207 \pm 61 \times 10^3/\mu l$ in relapsers and non-relapsers, respectively. Focal necrosis (FN) and bile duct injuries (BDI) were more prevalant in relapsers comparing to those remained in remission (FN 100% vs. 57%; BDI 50% vs. 4%). The parameteres in control biopsies were not found to be related to relapses. ALT normalization time under the treatment was longer in relapsers (median 4 months vs. 2 months).

Conclusion: Relapse rate in our population (43%) was low, probably due to the strict selection of the patients to discontinue the treatment and longer duration of treatment after ALT normalization. Basal biopsy findings and ALT normalization time under the treatment should be taken into consideration before cessation of treatment. Control biopsies may not be performed before drug discontinuation.

Disclosure of Interest: None declared

P1282 IL-6 AND CALPROTECTIN LEVELS IN BILE ARE GOOD SURROGATE MARKERS OF BILE DUCT INFLAMMATION IN PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic nonsuppurative inflammation of extra- and intrahepatic bile ducts leading to ductal fibrosis and strictures and eventually to cirrhosis. Furthermore, PSC is associated with a markedly increased risk of cholangiocarcinoma (CCA). At present good surrogate markers for bile duct inflammation for estimating disease activity and risk for progression and CCA are not available. IL-6 is a inflammatory cytokine and plays a major role in the response of bile duct epithelia to inflammation. It has been implicated as an autocrine promoter of growth for several cancers such as CCA (1). A significant increase in serum IL-6 levels has been shown in association with CCA (2). Calprotectin, a heterodimer of S100A8 and S100A9, is a calcium binding protein released from neutrophils and monocytes, is widely used as a fecal marker of inflammation in IBD (3). We have previously shown a

Abstract number: P1280 Table 1: Response at Month 3 (P1280)

	747-201Monotherapy		747-202UDCA		747-301+/- UDCA	
Placebo(N = 23)	OCA 10 mg(N = 20)	Placebo(N = 38)	OCA 10 mg(N = 38)	Placebo(N = 73)	OCA 10 mg(N = 73)	
Composite Endpoint: ALP < 1.67x ULN and Total Bilirubin ≤ULN, and ALP Decrease of ≥15% from Baseline						
Responder, n (%)	1 (4)	8 (40)	3 (8)	16 (42)	7 (10)	35 (48)
CMH p-value[a]	NA	0.0026	NA	0.0002	NA	<0.0001
ALP Values Absolute Change from Baseline						
Absolute Change, LS Mean (SE)	-18.98 (35.24)	-250.76 (34.87)	12.41 (15.55)	-57.52 (13.95)	-5.13 (11.56)	-114.40 (11.45)
p-value	NA	<0.0001	NA	<0.0001	NA	<0.0001

close correlation between neutrophilic inflammation in brush cytology (BC) and the risk of biliary dysplasia and CCA.

Aims & Methods

Aims: To evaluate the diagnostic value of several inflammatory markers (IL-6, calprotectin, CRP, α1-acid glycoprotein) in bile and serum as surrogate markers of inflammation compared to neutrophils in bile duct BC in PSC.

Patients and Methods: In total, 53 patients (18 females/35 males) with confirmed PSC referred for ERC for disease surveillance were included. After cannulation of the common bile duct with papillotomy knife with guide wire a bile sample was aspirated using balloon catheter and immersed immediately in liquid nitrogen and then stored in -20°C. Serum and bile concentrations of IL-6, calprotectin, CRP, MMP-9, α1-acid glycoprotein were quantitated using commercially available ELISA kits. BC was collected both from extra- and intrahepatic bile ducts for Papanicolau staining for grading dysplasia and inflammation. Neutrophilic inflammation in BC was evaluated semiquantitatively (0 = neutrophils/epithelial cells <0.05, 1 = neutrophils /epithelial cells 0.05-0.4, 2 = neutrophils/epithelial cells >0.4).

Results: Serum levels of CRP, IL-6, calprotectin and α1-acid glycoprotein did not correlate with disease activity assessed by neutrophilic inflammation in BC. However, in bile both IL-6 (AUC = 0.829) and calprotectin (AUC = 0.987) levels were significantly associated with neutrophilic count in BC (neutrophils 0 or 1 vs 2).

Conclusion: Both biliary calprotectin and IL-6 levels can be used as surrogate markers of bile duct inflammation to monitor disease activity and progression. The may serve tools for assessing treatment response for medical and endoscopic therapy for PSC.

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P1283 THE MOLECULES OF INTERCELLULAR ADHESION AND HIGH-SENSITIVITY C-REACTIVE PROTEIN IN PRIMARY BILIARY CIRRHOSIS

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Introduction: The goal of the research is to study the role of the molecule of intercellular adhesion (sVCAM and sP-selectin) and the high-sensitivity C-reactive protein (HCRP) in the genesis of the primary biliary cirrhosis (PBC) to determine the severity of the autoimmune process and the severity of the disease.

Aims & Methods: 22 patients (22 women) with primary biliary cirrhosis (PBC) were examined. The patients' age was 38-74 years, the average age – 52.7 ± 4.0 ($M \pm \sigma$). The diagnosis was verified using data of clinical, laboratory, immunological, histological and instrumental methods of research. AMA-M2, sVCAM, sP-selectin and HCRP were determined in the patients' blood serum by enzyme-linked immunoassay using test-system «Orgentec», «Biomerica» (Germany), «Bender MedSystems» (Austria). Statistical analysis was performed using the computer program «STATISTICA 6.0», the accuracy of the obtained values was determined by Student t-test.

Results: Among the 22 patients with PBC, the level of AMA-M2 averaged 113.6 ± 11.3 IU/ml (normal <20U/ml). As the results of this research showed in PBC in active stage the levels of sVCAM and sP-selectin in the blood serum averaged 40.0 ± 7.0 and 18.6 ± 1.2 ng/ml, respectively ($p < 0.001$). In these patients the increase of the levels of sVCAM and sP-selectin was accompanied by severe cholestasis syndrome: ALP 392.9 ± 60.7 U/l, GGTP 406.1 ± 81.3 U/l and an increase in the level of the high-sensitivity C-reactive protein to 0.110 ± 0, 01mg/L (for a minimum concentration of <0.005 mg/l).

Conclusion: Thus, in primary biliary cirrhosis in active stage the increase of the level of the molecules of intercellular adhesion (sVCAM and sP-selectin) can be marked accompanied by severe cholestasis syndrome and increase in the level of the high-sensitivity C-reactive protein. The increased level of the molecules of intercellular adhesion (sVCAM and sP-selectin) and HCRP reflects the severity of the autoimmune process and the severity of the PBC.

Disclosure of Interest: None declared

P1284 CLINICAL IMPLICATION OF THE GLOBE SCORE – AN ACCURATE RISK STRATIFICATION TOOL IN URSODEOXYCHOLIC ACID TREATED PATIENTS WITH PRIMARY BILIARY CIRRHOSIS (PBC) – THE GLOBAL PBC STUDY GROUP

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Introduction: Early identification of ursodeoxycholic acid (UDCA) treated patients with primary biliary cirrhosis (PBC) is important, since new therapies are under active evaluation.

Aims & Methods: To assess the association between alkaline phosphatase (ALP), bilirubin and transplant-free survival in terms of absolute risk (AR) for 5- and 10-year all-cause mortality or liver transplant using the recently proposed GLOBE score, in patients with PBC.

For current analysis the GLOBE score (www.globalpbc.com) was used, a risk score comprising age, bilirubin, ALP, albumin and platelet count after one year therapy of UDCA therapy to calculate the risk of liver transplantation/death. Various scenarios were run predicting this risk at 5- and 10-year, using static values for age (55 years), platelets (250 per 10^9/L) and albumin (1.0xULN). ALP and bilirubin levels were varied from 1 time to 4 times the upper limit of normal (ULN). Change in absolute risk was calculated for increases in bilirubin and ALP, holding the other variable constant.

Results: Table 1 shows AR at 4 levels of bilirubin and ALP, and absolute change in risk when bilirubin and ALP are increased from 1x to 2x, 2x to 3x and 3x to 4x the ULN.

Conclusion: The greatest increase in risk for death/transplant was when bilirubin increased from 1x to 2x the ULN. Similarly, the highest increase in risk resulted when ALP increased from 1x to 2x the ULN. These data indicate that early treatment, reducing and maintaining ALP and bilirubin at ULN, would have the greatest benefit in terms of absolute increased transplant-free survival in PBC patients.

Disclosure of Interest: None declared

Abstract number: P1284

Absolute risk of developing a clinical endpoint (liver transplantation or death)after 5- / 10-year UDCA treatment

Alkaline phosphatase levels (xULN)	Bilirubin levels (xULN)			
	1xULN	**2xULN**	**3xULN**	**4xULN**
1xULN	12.5% / 30.3%	22.6% / 49.9%	31.3% / 63.6%	38.9% / 73.4%
2xULN	15.5% / 36.5%	27.7% / 58.2%	37.8% / 72.1%	46.3% / 81.2%
3xULN	17.6% / 40.6%	31.0% / 63.2%	41.9% / 76.8%	50.9% / 85.3%
4xULN	19.2% / 43.7%	33.6% / 66.7%	45.0% / 80.0%	54.3% / 87.9%
Absolute difference between	**1x – 2x ULN**	**2x – 3x ULN**	**3x – 4x ULN**	
1xULN	10.1% / 19.6%	8.7% / 13.7%	7.6% / 9.8%	
2xULN	12.2% / 21.7%	10.1% / 13.9%	8.5% / 9.1%	
3xULN	13.4% / 22.6%	10.9 – 13.6%	9.0% / 8.5%	
4xULN	14.4% / 23.0%	11.4 – 13.3%	9.3% / 7.9%	
Absolute difference between	**1xULN**	**2xULN**	**3xULN**	**4xULN**
1x – 2x ULN	3.0% / 6.2%	5.1% / 8.3%	6.5% / 8.5%	7.4% / 7.8%
2x – 3x ULN	2.1% / 4.1%	3.3% / 5.0%	4.1% / 4.7%	4.6% / 4.1%
3x – 4x ULN	1.6% / 3.1%	2.6% / 3.5%	3.1% / 3.2%	3.4% / 2.6%

P1285 VIRTUAL TOUCH IMAGING QUANTIFICATION (VTIQ) ELASTOGRAPHY AS COMPARED TO LIVER BIOPSY FOR THE EVALUATION OF LIVER FIBROSIS

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Introduction: Currently, validated non-invasive methods for fibrosis assessment in chronic hepatitis are transient elastography (TE) and serological tests (FibroTest-ActiTest). Virtual Touch Imaging Quantification (VTIQ) Elastography became available in the last years.

Aims & Methods: The aim of this study is to find the relevance of VTIQ for the evaluation of liver fibrosis as compared to the reference method, liver biopsy (LB).

Our retrospective study included 281 subjects (147 women and 134 men, mean age 46.3 ± 13.1); 109 with chronic hepatitis B and 172 with chronic hepatitis C, evaluated during a 4 years period. All subjects were evaluated in the same session by LB and VTIQ. LBs were assessed according to the Metavir score. Ten VTIQ measurements were made in each patient (using a Siemens Acuson S2000™ ultrasound system), and a median value was calculated, measured in meters/second. Only measurements with IQR < 30% were considered reliable (Bota et al.2013)

Results: According to the Metavir score, 2.8%(8) pts were F0; 21.7%(61) were F1; 43.4%(122) were F2; 22.4%(63) were F3 and 9.6%(27) were F4.

From the 281 subjects, VTIQ valid measurements were obtained in 278 subjects (invalid determinations in 1.2%).

A significant correlation (Spearman rho = 0.401) was found between VTIQ measurements and fibrosis ($p < 0.0001$).

The mean values of VTIQ according to fibrosis groups were: F0 1.1 ± 0.2m/s; F1 1.3 ± 0.6m/s; F2 1.5 ± 0.6m/s; F3 1.7 ± 0.7m/s; F4 2.4 ± 0.7m/s.

The performance of VTIQ for fibrosis assessment are presented in the table.

	Cut-off (m/s)	AUROC	Sensitivity (%)	Specificity (%)	+LR	-LR	PPV (%)	NPV (%)
F1	**1.14**	0.759	71,85	87,50	5,75	0,32	**99,5**	8,4
F2	1.22	0.683	67,94	63,77	1,88	0,50	85,0	39,6
F3	1.71	0.729	51,14	86,32	3,74	0,57	63,4	79,2
F4	**1.77**	0.855	80,77	82,54	4,63	0,23	32,3	**97,7**

For the calculated optimal cut-off, VTIQ had very good positive predictive value for the presence of any fibrosis (F1-F4), even if a high overlap rate was observed in pts with F0, F1 and F2. VTIQ also had a good negative predictive value for cirrhosis (table).

Conclusion: Liver stiffness evaluation by means of VTIQ can be performed in the vast majority of patients (98.8%). ARFI is an accurate method for predicting any fibrosis (PPV 99.5% for a cut-off of 1.14 m/s), and also to exclude cirrhosis (NPV 97.7% for a cut-off of 1.77 m/s).

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P1286 INTRA AND INTEROBSERVER REPRODUCIBILITY OF POINT SHEAR WAVE ELASTOGRAPHY USING ARFI TECHNIQUE - ELASTPQ

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Introduction: Non-invasive evaluation of liver fibrosis by using ultrasound based-elastographic techniques is increasingly used in the last years. Non-invasive evaluation of liver fibrosis by using ultrasound based-elastographic techniques is increasinglyused in the last years.

Aims & Methods: The aim of the present study was to assess the reproducibility of a new point shear wave elastography which uses ARFI technique – ElastPQ, as a non-invasive method for liver fibrosis evaluation.

The study included 74 consecutive subjects, with or without chronic hepathopaties and healthy volunteers. Out of 74 subjects, in 33 subjects liver stiffness was assessed by a single operator, while in 50 subjects liver stiffness was assessed by two operators in the same session.

Two operators, with experience in liver elastography, performed 10 consecutive valid elastographic measurements in the liver parenchyma, avoiding large vessels with the ElastPQ (Philips, Affinity) technique. Reliable LS measurements were defined as the median value of 10 LS measurements expressed in kPa. The intra and interobserver reproducibility of ElastPQ technology was analyzed with intraclass correlation (ICC) coefficient.

Results: The overall intraobserver agreement was better than the interobserver one: ICC 0.92 vs. ICC 0.85. A strong correlation was obtained between measurements assessed by both operators ($r = 0.86$, $p < 0.0001$) and also between measurements assed by a single operator 0.76 ($p < 0.0001$). For both intra- and interobserver reproducibility, the ICCs were similar in patients with high body mass index (BMI) ≥25 kg/m^2 vs. <25 kg/m^2 (0.90 vs. 0.93 and 0.89 vs. 0.82, respectively).

Conclusion: ElastPQ is a highly reproducible method for assessing liver fibrosis with excellent intra and interobserver agreement.

Disclosure of Interest: None declared

P1287 DOES STEATOSIS AFFECT THE PERFORMANCE OF DIFFUSION MRI VALUE FOR FIBROSIS EVALUATION IN PATIENTS WITH CHRONIC HEPATITIS C GENOTYPE 4?

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Introduction: Diffusion-weighted magnetic resonance imaging (DWI) was new non–invasive method measures the freedom of water proton diffusion in tissues which can be described by the apparent diffusion coefficient (ADC) and was recently facilitated to be used for abdominal imaging. The impact of liver fat ADC is currently unclear.

Aims & Methods: The aim of this study was to assess the impact of liver steatosis, detected by histology on ADC value of diffusion MRI for fibrosis diagnosis in patients with chronic hepatitis C (CHC) genotype 4. Three hundreds CHC patients (186 males and 114 females), aged 43.8 ± 10.1years were histologically staged for liver fibrosis by Metavir score: Activity (A0-A3), fibrosis stage (F0-F4) and steatosis stages were assessed in liver specimens. DWI of the liver was performed within 15 to 60 days after biopsy, to avoid artifacts related to early post biopsy changes using a 1.5 Tesla (T) scanner. Following coronal localizer of the abdomen, all patients underwent axial T1 weighted images (TR/TE = 600/20 ms) and axial true FISP (TR/TE = 4.3/2.1 ms) of the liver with field of view (FOV) of 25- 25 cm , section thickness of 7 mm , interslice gap of 1mm, and acquisition matrix of 256x224. ADCs were correlated with fibrosis stage, steatosis grade, using linear regression.

Results: Mean ADC value was 1.5 ± 0.3 (range 1.0-2.09). Diffusion MRI values (ADC) decreased significantly the advance of fibrosis stage from 1.95 ± 0.02 in F0; to 1.55 ± 0.02 in F1; 1.55 ± 0.02 in F2; 1.47 ± 0.02 in F3; and 1.36 ± 0.10 in F4; $p \leq 0.001$). Similar results were obtained after exclusion patients with steatosis ≥5% ($p \leq 0.001$). There were inverse weak to moderate correlations between ADC and Age (r = -0.2), body mass index (r = -0.12), severity of necroinflammatory activity (r = -0.4), stage of fibrosis (r- = -0.6) and steatosis (r = -0.14). However the multivariate linear regression analysis revealed that fibrosis is only significant independent predictor of ADC with a coefficient of determination (R^2) = 0.23.

Conclusion: The presence of steatosis detected by histology in patients with CHC G4, has no impact on ADC value of diffusion MRI for fibrosis assessment. Therefore it is unlikely to confuse the performance of diffusion MRI to evaluate hepatic fibrosis in suspected patients with steatosis.

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P1288 ADVANCED TECHNIQUE OF LASER DOPPLER IMAGING FOR DIAGNOSIS MICROCIRCULATION CHANGES IN PATIENTS WITH MICROCIRCULATION DIFFUSE LIVER DISEASES

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Introduction: It is known that changes in patients with diffuse liver diseases at the vascular level are systemic in nature.

Aims & Methods: To unvestigate the state of the microcirculation in various forms of diffuse liver diseases by noninvasive laser Doppler imaging (LDI) with functional tests. 79 patients were divided into 3 group. The 1st group - patients with alcoholic liver cirrhosis (n = 45) among them 14 patients with class A, 18 patients with class B and 13 patients with class C; The 2nd group -patients with alcoholic steatohepatitis (ASH) and nonalcoholic steatohepatitis (NASH) (n = 21) ; the 3rd group - patients with viral hepatitis "C" (n = 13). The control group - 40 patients with diseases of digestive tract without liver diseases. Perfusion (P) c.u; concentration (C) – c.u , blood flow velocity (υ) mm\s in area of thenar and hypothenar were estimated by LDI. As a provocative test

was applied extended cold test. Difference between initial perfusion and after cold test (ΔP) was analyzed (%) afterwards.
Results: A significant increase in blood flow values (P -240.15 ± 1.8c.u; C-32 ,78 ± 3.3 c.u; υ -10.57 ± 5.0 mm\ s) in comparison with the control group (P -127 , 2 ± 5.6 c.u , C -64.8 ± 6.2 c.u , υ -2, 55 ± 2.5 mm\s) was observed in all cases of cirrhosis class C and 6 (33 %) patients of cirrhosis class B ($p < 0.05$). Cold test in these patients was negative (ΔP < 10%). For one year follow-up we established that in all these patients increased microcirculation parameters. 6 of them died. In all patients with liver cirrhosis class A and in 5(28%) patients with liver cirrhosis class B , in all patients with hepatitis C high degree of activity (more 400 000 ribonucleic acid (RNA) ME\ml) and in patients with NASH and ASH high degree of activity moderate increased of blood flow in the studied areas were observed (P – 188.64 ± 4.2c.u , C - 48, 67 ± 3.3 c.u , υ - 6.02 ± 5.2 mm\s). Microcirculation in patients with low viral load (RNA less 400 000 ME\ml) and patients NASH in low activity levels were comparable to the control group. Cold tests in these patients were primarily positive (ΔP > 15%). These data pointed out at conservation of microcirculation in these patient. We didn't reveal decompensation of liver disease in this case during follow-up period. In 7 (39%) patients with liver cirrhosis class B moderate increased of blood flow were observed too, but the cold test in these group was ΔP = 10-15%(intermediate value). Among these patients 3 became class A, 3 patients remained class B and 1 patient became class C while on treatment during follow-up period. The more the changes in liver were (by biopsy), the more significant changes were identified in microcirculatory blood flow ($r = 0.76$)
Conclusion: Changes in perfusion > 135 c.u; concentration < 58 c.u, speed > 5 mm/s in patients with diffuse liver diseases characterize the clinical significance of microcirculation disturbances in this pathological process. ΔP < 10% we estimated as disturbance of reversibility of tissue microcirculation functional resources, that served as the basis for unfavourable forecasting with high possibility of decompensation development; ΔP > 15%, pointed out at lower possibility of decompensation of disease during 12 month. ΔP = 10-15% - questionable forecasting. It takes futher medical observation.
Disclosure of Interest: None declared

P1289 EFFECTIVENESS AND SAFETY OF TRANSARTERIAL EMBOLIZATION IN PATIENTS WITH LIVER METASTASES OF A NEUROENDOCRINE TUMOUR

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Introduction: Transarterial embolization (TAE) is an effective treatment for liver metastases from neuroendocrine tumour (NET). It reduces arterial blood flow to the tumour resulting in ischemia and necrosis. In this single centre study the effectiveness and safety of TAE was evaluated.
Aims & Methods: Patients with histological confirmed gastro-entero-pancreatic NET with liver dominant metastases were retrospectively investigated. Adverse events, tumour response, decline in symptomatic carcinoid syndrome and overall survival were evaluated.
Results: A total of 30 patients (15 male, median age 61.5 years), underwent 47 TAE procedures between 2009 and 2014. The primary NET site was ileum (n = 16; 53.3%), colon (n = 6; 20%), pancreas (n = 1; 3.3%), lung (n = 1; 3.3 %) and unknown (6; 20%). Almost all patients (97%) received octreotide treatment for symptomatic NET, prior to TAE. Twenty two patients (73.3%) were also diagnosed with extrahepatic metastases. The median time from primary metastatic NET diagnosis to first TAE was 36.5 months. After TAE procedures a transient elevated level of bilirubin, gamma GT, ASAT, ALAT and LDH was seen in all patients. Two patients had major TAE related complications. No TAE related death occurred. CT scan was performed 1 and 3 month after TAE; 80.9% of the patients had a decrease of neuroendocrine liver metastases volume. This decrease was significantly higher when liver metastatic involvement before TAE was < 50%. There was a significant decrease in chromogranin A both 1 and 3 months after TAE ($p = 0.001$ and $p = 0.017$, resp.). Of the 30 patients who had a carcinoid syndrome before TAE, 88% had a decrease in clinical symptoms at 1 month follow up and 69.6% at 3 months follow up. Sixteen patients underwent 2 or 3 TAE procedures for progression of carcinoid symptoms. The overall survival at 1-year follow up was 86.7%.
Conclusion: TAE is a relative safe treatment for liver metastasized NET which can be done multiple times within 1 patient. It reduces carcinoid syndrome in the majority of patients and shows a significant reduction in tumour marker. Radiological decrease rate is significantly higher in patients who have < 50 % liver involvement.
Disclosure of Interest: None declared

P1290 THE AUTOPHAGY-RELATED MARKER BECLIN-1 IS SIGNIFICANTLY ASSOCIATED WITH CLINICAL PROGNOSIS IN HUMAN HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocellular carcinoma (HCC) is one of the most common malignancies, with an increasing incidence and is the third leading cause of cancer-related mortality in the world [1]. Most HCC patients are diagnosed at an advanced stage and have very poor prognosis and low survival. The effective biomarkers need to predict the clinical outcome of patients with HCC. Autophagy is a process through which long-lived proteins and damaged organelles are conveyed to the lysosome for removal by degradation and recycling [2,3]. Some studies have shown that autophagy plays a key role in the progression and development of cancer. But, the role of autophagy in the prognosis and metastasis of human HCC is not well unknown.
Aims & Methods
Aims: The study aims to explore the expression of markers of autophagy genes and cell proliferation using immunohistochemistry (IHC) in human HCC tissues. We also investigate the autophagy markers associated with clinicopathological characteristics and prognosis.
Methods: We retrospectively analyzed 210 patients diagnosed with HCC by histology after surgical resection at E-DA hospital/ I-Shou University, Kaohsiung, Taiwan, from 2009 to 2013. The demographic data, recurrence, and survival were collected until April 2015. The expression of autophagy-related markers (LC3, Beclin-1, Atg5, Atg7, and p62) were analyzed by IHC staining using HCC tissues and non-tumor tissues.
Results: Two hundred and ten HCC patients were collected. The average age is 59.5 years old and the rate of male is 80.9%. The rate of HBV, HCV, and Non-HBVHCV is 62%, 24%, and 14%, respectively. Median survival was 38.3 months (range 1.3-64.1 months). The positive rate of Beclin-1 was significantly lower in HCC tissues than adjacent tissues (70.5 vs. 88.5%, $P = 0.01$). In HCC, Beclin-1 expression was negatively correlated with cirrhosis background ($P = 0.04$) and Edmondson grade ($P = 0.03$). The strong positive of Beclin-1 is significantly associated with increasing the 5-year survival rates ($P = 0.02$). Univariate and multivariate Cox regression analysis revealed that Beclin-1 expression was an independent indicator for overall survival in HCC patients ($P < 0.05$).
Conclusion: Our results demonstrate that the expression of autophagy marker, Beclin-1, might be a strong prognostic factor of HCC, especially in patients underwent liver resection.

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P1291 THE EFFECT OF PROLYL HYDROXYLASE DOMAIN-2 HAPLODEFICIENCY ON LIVER PROGENITOR CELL MARKERS IN EARLY HEPATOCARCINOGENESIS

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Introduction: Prolyl hydroxylase domain (PHD) deletion results in the stabilization of hypoxia inducible factor (HIF), a key compound in the cellular response following hypoxia which has been linked to cancer development. We previously showed that PHD inhibition results in an increased expression of liver progenitor cells (LPCs) which coincided with a phenotypic switch from hepatocellular carcinoma (HCC) to hepato-cholangiocarcinoma in diethylnitrosamine (DEN)-induced hepatocarcinogenesis[1,2].
Aims & Methods: In this study, we investigated if the effect of PHD2 inhibition on the expression of markers for hypoxia and LPCs occurs during the initiation and development of HCC following DEN treatment. PHD2 haplodeficient ($PHD_2^{+/-}$) and wild type (WT) mice were weekly injected with 35mg/kg DEN and euthanized after 5, 10, 15 and 17.5 weeks of DEN induction, before tumor nodules could form[1]. Livers were prelevated and analyzed for the expression of downstream targets of HIF (Vascular endothelial growth factor alpha, Vegfa and Glucose transporter 1, Glut1) and LPC markers (cytokeratin 7, CK7; cytokeratin 19, CK19; prominin1, Prom1 and epithelial cell adhesion molecule, Epcam) using qPCR and immunohistochemistry. The results were linked to neoplastic transformation of hepatocytes determined by reticulin staining. Results were significant at $p < 0.05$.
Results: Vegfa and Glut1 RNA expression were significantly upregulated after 17.5 weeks of DEN induction in WT and $PHD_2^{+/-}$ mice with a significantly higher increase for Glut1 in $PHD_2^{+/-}$ mice. Prom1 and CK19 expression followed these results with a significant increase after 17.5 weeks of DEN induction, however without differences between $PHD_2^{+/-}$ and WT mice. For CK7 and Epcam, the RNA expression did not change during early hepatocarcinogenesis. Immunohistochemistry revealed an increased CK19 immunoreactivity after 15 weeks of DEN induction compared to earlier time points in $PHD_2^{+/-}$ mice which was mostly caused by increased cytoplasmic expression in hepatocytes rather than ductular expansion. The intracellular domain of Epcam was significantly more expressed after 17.5 weeks of DEN in $PHD_2^{+/-}$ mice compared to WT mice. Neoplastic transformation was limited to some reticulin free cells after 15 and 17.5 weeks of DEN in both $PHD_2^{+/-}$ and WT mice.
Conclusion: These results show an increased expression of LPC characteristics, coinciding with augmented expression of hypoxic markers during early HCC

development. However, the effects of PHD2 haplodeficiency were limited to non-existing. Based on this and our previous reports[1,2] we conclude that induction of the hypoxic response affects the expression of LPC characteristics and tumor phenotype not in an early event but coincides with the occurrence of neoplasticity.

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P1292 DIRECT TARGETING OF SPERM-ASSOCIATED ANTIGEN 9 (SPAG9) BY MIR-141 INFLUENCES THE GROWTH AND METASTASIS OF HEPATOCELLULAR CARCINOMA CELLS

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Introduction: Sperm-associated antigen 9 (SPAG9), a member of cancer testis (CT) antigen family, has been reported to be involved in the development of hepatocellular carcinoma (HCC), however, its post-transcriptional regulatory mechanisms have not been well understood. Since microRNAs (miRNAs) are powerful post-transcriptional regulators of gene expression. We focused on the miRNAs-mediated regulation of SPAG9. By using three publicly available algorithms (TargetScan, miRanda and PicTar), miR-141 was identified as a candidate miRNA that could target 3'-UTR of SPAG9.
Aims & Methods: The present study was aimed to investigate the role of miR-141-mediated SPAG9 regulation in the development and progression of HCC. SPAG9 and miR-141 expression levels were detected in HCC tissues and cell lines by Western blot and real-time PCR. Dual-luciferase reporter assay and Western blot were used to validate SPAG9 as a direct target gene of miR-141. Cell proliferation, apoptosis, invasion, and migration were also examined to figure out whether miR-141-mediated regulation of SPAG9 could impact on HCC progression.
Results: We observed an inverse correlation between SPAG9 and miR-141 expression in HCC tissues and cell lines. We also demonstrated that SPAG9 was a direct target gene of miR-141. The overexpression of miR-141 markedly attenuated the expression of SPAG9 via targeting a binding site located at 3'-UTR of SPAG9 mRNA. Finally, we showed that repression of SPAG9 by transfection with miR-141 mimics resulted in a significant reduction in cellular proliferation, invasion, migration and cellular motility of HCC cells, and imitating the SPAG9 knockdown effects on HCC cells. Furthermore, restoration of SPAG9 in miR-141-expressing cells was sufficient to alleviate the tumor suppressive effects of miR-141.
Conclusion: Our data suggested that the loss or suppression of miR-141 may cause aberrant overexpression of SPAG9 and promote the genesis of HCC.

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P1293 T-CELL FACTOR-4 ISOFORMS PARTICIPATE IN EMT THROUGH WNT5A INDUCTION IN HUMAN LIVER CANCER CELLS

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Introduction: The T-cell factor (TCF)-4 is a key transcriptional factor critically regulating Wnt/β-catenin signaling. Previously we identified 14 TCF-4 isoforms derived from human HCC cell lines (1). The TCF-4J and K pair have been characterized based on the presence (K) or absence (J) of a SxxSS motif, which was shown to decrease β-catenin-dependent transcriptional activity of TCF-4. TCF-4J-overexpressing HCC cells (J cells) exhibited high tumorigenic potential in contrast to TCF-4K-overexpressing cells (K cells) (2). In spite of the lower tumorigenic activity, K cells often showed morphological alteration, reminiscent of epithelial-mesenchymal transition (EMT), which is known to be involved in the non-canonical Wnt signaling pathway (Bo et al., *BMC Cancer* 2013). The finding suggested that the SxxSS motif had potential to regulate EMT through the non-canonical Wnt signaling pathway.
Aims & Methods: The aim of this study was to investigate whether the functional SxxSS motif modulated expression levels of EMT regulators and Wnt5a, a representative non-canonical Wnt ligand.
Methods: The human HCC cell line HAK-1A (Yano, et al., Hepatology 1993) was used. TCF-4K mutants (269A, 272A, and 273A) were constructed with conversion of serine (S) in the SxxSS motif to alanine (A) by site-directed mutagenesis. HAK-1A-derived stable clones overexpressing TCF-4J, K, and K-mutants (269A, 272A, and 273A cells, respectively) were established. Western blot analysis and real-time RT-PCR were employed to evaluate protein and mRNA expression levels, respectively. Sh-RNA was used to knockdown *wnt5a* gene expression. ChIP assay was performed by using SimpleChIP Enzymatic Chromatin IP Kit (Cell Signaling Technology) and specific qPCR primers for *wnt5a* gene promoter region (Qiagen).
Results: The 269A-mutant cells robustly expressed Wnt5a in both protein and mRNA levels, while empty vector-transfected cells (control), J cells, or K cells did not. Of note, Wnt5a expression was coupled with SLUG expression and EMT-like cellular morphological change. Snail was hardly expressed in the cells examined in this study. When the Wnt5a expression was specifically silenced by using sh-RNA, the expression level of SLUG was clearly decreased. The TCF-4K-mutant isoform 269A showed high affinity to the *wnt5a* promoter region.
Conclusion: The findings in this study suggest that the SxxSS motif of TCF-4 directly regulates transcription of Wnt5a, thereby modulating the expression level of the EMT-regulator SLUG in a human HCC cell line.

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P1294 MICRORNA-207 CONTROLS PRP19 EXPRESSION IN HEPATOCELLULAR CARCINOMA

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Introduction: microRNAs (miRNAs) are small non-coding RNA molecules of 21-24 nt that regulate the expression of numerous target genes by transcriptional inhibition or translational repression. Multiple lines of evidence suggest that miRNAs play important roles in tumor (such as, hepatocellular carcinoma (HCC)) development, progression, invasion, metastasis and prognosis. Our previous unpublished work suggested that microRNA-207 (miR-207) upregulates in HCC tissues than in normal liver tissues. Unfortunately, our understanding of the molecular mechanisms that governs its role in development, progression, invasion, metastasis and prognosis remains fragmentary.
Aims & Methods: In this study, a genome-wide miRNA microarray was used to identify differentially expressed miRNAs in HCCs patients. Next, miR-207 expression in normal liver tissues, HCC tissues and adjacent non-tumor tissues was validated, and the predictive values of miR-207 for the prognosis of HCC patients were explored using $\chi 2$ test, Student's t test, paired t test, and Mann-Whitney test. The biological roles of miR-207 and its underlying roles in HCC were also investigated in the Huh7, MHCC-97H, SMMC-7721, L02 and Hep3B cell lines.
Results: Forty-two miRNAs were differentially expressed in HCCs. Several of these miRNAs were previously found deregulated in other cancers. Additionally, the miR-207 was found upregulated in ~80% of HCCs and in all HCC-derived cell lines. Overexpressed intratumoral miR-207 was associated with poor survival rate ($P < 0.001$), and was an independent prognostic factor for overall survival rate ($P < 0.001$) in the patients with HCC. Overexpression of miR-207 in L02 cell line remarkably enhanced cell proliferation, migration, and invasion; while inhibition of miR-207 in Hep3B cell line caused the opposite effects. Further study found that miR-207 suppressed the expression of pre-Mrna processing factor 19 (Prp19) by directly binding to its 3'-untranslated region, and sensitized Hep3B cell to CDDP-induced apoptosis. Moreover, miR-207 expression levels correlated positively with Prp19 in human HCC tissues. Western blot showed that overexpression of miR-207 in L02 cell upregulates the expression of Prp19, while inhibition of miR-207 in Hep3B cell downregulates the expression of Prp19, suggesting that Prp19 might play as a oncogene in HCC.
Conclusion: Taken together, our findings suggest that miR-207 could play a role in the development of HCC, at least in part, by modulating Prp19. These findings establish a basis toward the development of therapeutic strategies aimed at blocking miR-207 in HCC.
Disclosure of Interest: None declared

P1295 ARE THERE ANY NEW BIOMARKERS AS A PREDICTOR OF SURVIVAL IN HEPATOCELLULAR CARCINOMA?

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Introduction: Hepatocellular carcinoma (HCC) is a worldwide increasing problem. Identification of prognosis is important for the management of HCC. We aimed to investigate the impact of interleukin (IL)-29, galectin-3, leptin, fibronectin and protease activated receptor-1 (PAR-1) on the prognosis of patients with HCC.
Aims & Methods: Sixty HCC patients (75% male) and 20 healthy volunteers (70% male) were enrolled in this prospective study. All demographic and clinical data were analyzed. Serum samples were obtained on the first admission before any adjuvant and metastatic treatment was given. Serum IL-29, galectin-3, leptin, fibronectin and PAR-1 were determined by using ELISA kits.
Results: All patients had cirrhosis and Child-Pugh stage were as follows: 61.5% Child A, 35.9% Child B and 2.6% Child C (61.7% HBV, 11.7% HCV, 6.7% HBV + HCV, 11.7% alcohol and 8.3% cryptogenic). Fifty-three percent of HCC patients were died in median 7.5 months. The mean age of the patients was 59.2 ± 10.2 years and 53.4 ± 8.2 years for the controls. Mean serum level of IL-29 was higher in patients with HCC than controls (32.55 ± 31 vs 11.46 ± 5.4 pg/mL, $p < 0.015$). Galectin-3 was significantly higher in HCC group (6.7 ± 4.2 vs 1.38 ± 0.79 ng/mL, $p < 0.001$). Fibronectin levels were higher in controls than HCC patients (260635 ± 60735 vs 257353 ± 63986 ng/mL, $p > 0.015$). But, mean PAR-1 and leptin levels were similar in two groups ($p > 0.05$). Total lesion diameter was related to worse survival ($p = 0.018$). Lesion diameter was positively correlated with PAR-1 levels ($p = 0.018$, $R = 0.332$). AFP levels was positively correlated with extrahepatic metastasis ($p = 0.005$, $R = 0.366$). Biomarkers were divided in 2 groups according to median levels. In log rank analysis, they don't have any effect on survival ($p > 0.05$).
Conclusion: IL-29 and galectin-3 were significantly higher in HCC patients. Although, they can be a diagnostic marker for HCC, they had no prognostic value in HCC patients.
Disclosure of Interest: None declared

P1296 PREDICTORS OF LONGER SURVIVAL IN UNILOBAR VERSUS BILOBAR ADVANCED HEPATOCELLULAR CARCINOMA AFTER RADIOEMBOLIZATION WITH YTTRIUM-90 MICROSPHERES

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Introduction: Hepatocellular carcinoma (HCC) is a common cancer that typically occurs in the presence of liver cirrhosis. It is considered a global problem because of its dramatically increasing incidence. More than 90% of patients have non resectable tumor at first diagnosis. While sorafenib is the currents treatment standard for advanced stage hepatocellular carcinoma (HCC), radioembolization with Yttrium-90 microspheres (Y90-TARE) is a novel transarterial approach for patients with advanced HCC. Because there are multiple patient and treatment related variables within advanced stage HCCs that should be considered for treatment selection, we aimed to analyse a number of clinical and biochemical parameter in relation to survival after TARE which are currently not part of the guidelines (for example aspartate amino transferase, AST and C-reactive protein, CRP).
Aims & Methods: Between 11/2010 and 3/2014, 202 patients with unresectable hepatocellular carcinoma were included in this prospective study. Yttrium-90 glass microspheres radiotherapy was performed in a lobar fashion via the right or left hepatic artery. In bilobar HCC, right and left liver lobe were treated within 4-6 weeks intervals. The mean radiation dose was 118 (+/-23) Gy per single treatment. Median survival time was considered as primary endpoint with further subgroup analysis within unilobar and bilobar HCCs.
Results: Among 202 patients with advanced HCC treated by 334 sessions of Y-90-TARE (mean 1.5 sessions/patient), unilobar advanced HCC was present in 85(42%) patients and bilobar advanced HCC in 117 (58%). In unilobar HCC, baseline serum AST level and CRP in combination were found to be important predictors for survival. In normal AST & CRP (found in 36/85 patients; 42%) median survival was 20.1 months (95CI:14.5-25.6); in high AST & normal CRP (3/85; 4%) was 15.3 months (95CI:10.5-19.8); in normal AST and high CRP (38/85; 45%) was 9.0 months (95CI:5.2-12.7); and in high both AST & CRP (8/85; 9%) was 1.9 months (95CI:0.0-5.2) which showed significantly reduced survival probability ($p < 0.0001$).
In bilobar HCC, multivariant analysis showed that BCLC stage and abdominal ascites had significant impact on long term survival. Median survival time in bilobar HCC in Child A patients without ascites (71/117; 60%) was 18.4 months (95CI:13.4-23.3) in BCLC-B with normal CRP (24/117; 21%) compared to 11.1 months (95CI:4.7-13.7) in patients with elevated CRP (11/117; 10%); and was 8.5 months (95CI:5.4-11.7) in BCLC-C with normal CRP (17/117; 15%) versus 5.8 months (95CI:3.8-7.7) in patients with elevated CRP (19/117; 16%), ($p < 0.01$).
Conclusion: It seems that unilobar and bilobar HCC distribution is valuable predictor for survival in advanced HCC, which is not part of current HCC staging systems. Also serum AST and CRP could have a significant role as biochemical predictors for longer survival time.
Disclosure of Interest: None declared

P1297 GEOEPIDEMIOLOGY OF HEPATOCELLULAR CARCINOMA (HCC) IN THE ISLAND OF CRETE. A POSSIBLE ROLE OF PESTICIDES

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Introduction: Geoepidemiological data of HCC are lacking in Greece. The island of Crete has a genetically homogeneous population with minimal immigration and therefore is suitable for such studies attempting to identify a possible contribution of environmental factors in HCC.
Aims & Methods: We used a data base of HCC patients constructed over the past 20 years in our Unit, the reference center for liver disease in the island. Similar data bases for chronic HCV and HBV were also used. All patients had a histological confirmation of diagnosis. Recorded data included gender, date and place of birth and place of residence for the last 15 years. The geographic area of the study comprised the four prefectures of the island of Crete. Population statistics from 1980-2010 were obtained from the Hellenic Statistical Authority. 316 HCC patients , 633 HCV and 392 HBV patients were included in the study. Time-spatial methods were applied in Gis – ArcMap 10 software. A spatial statistical test that measures spatial autocorrelation (Moran's index) was applied at a confidence level of 95%, in order to detect any possible significant difference between the spatial distribution to place of residence. Density maps with the spatial clusters configuring the prevalence of the disease of all provinces in the island were created. Kriging Interpolation method was applied, to produce a prediction map of HCC in Crete.
Results: HCV is present in pockets of high prevalence while HBV is more uniformly distributed. HCC is more prevalent in Eastern Crete. A significant spatial autocorrelation between HCC and either HCV (Moran' $I = 0.78$, $p < 0.001$) or HBV (Moran' $I = 0.87$, $p < 0.001$) was found as expected. However there is a discrepancy in the South East of Crete, where a higher prevalence of HCC than expected from the dispersion of HCV and HBV was observed. Prediction maps also identified this area as the main source of future HCC cases. This is an area where extensive use of pesticides in large green houses is widely practiced.
Conclusion: 1) HCC is mostly found in Eastern Crete and is broadly associated with the dispersion of chronic HCV and more so with Chronic HBV.
2) In an area with widespread use of pesticides a higher than expected spatial distribution of HCC was detected.
Disclosure of Interest: None declared

P1298 MEANINGFUL REDUCTION OF HEPATOCELLULAR CARCINOMA RISK IN PATIENTS WITH CHRONIC HEPATITIS C WHO RECEIVED PEGILE INTERFERON PLUS RIBAVIRIN THERAPY: TWO TERTIARY CENTER EXPERIENCE

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Introduction: Antiviral therapy may eradicate hepatitis C viral replication, but its long-term effect on the reduction of hepatocellular carcinoma (HCC) still ambiguous.
Aims & Methods: We aimed to evaluate the predictors of sustained virological response (SVR) and appraise the efficacy in decreasing HCC in chronic hepatitis C patients.
We enrolled 312 anti-HCV-positive patients who were treated with pegile interferon plus ribavirin (PR) for 12 months who admitted to Kocaeli University and Derince Education and Research Hospital. All of the patients were older than 18 years old and seronegative for HBs Ag. These patients were followed after dual therapy to the date of HCC diagnosis, death, or the end of 2014, whichever came first. The Cox's proportional hazards model was utilized to estimate the adjusted hazard ratio and 95% confidence interval associated with HCC by comparing patients with SVR or non-SVR.
Results: The mean age of the patients was 58.2 years, 162 (51.9%) were males, 298 (95.5%) were infected by HCV genotype 1, and 45 (14.4%) had cirrhosis at start of the study. There were 194 (62.2%) patients experienced SVR after received treatment. Lower HCV viral load, serum levels of total bilirubin and high platelet count were independent predictors of achieving SVR. During the 5 years of post-treatment follow-up period, 14 newly-diagnosed HCC cases (5 with SVR and 9 with non-SVR) were observed. The estimated 5-year HCC risk was 2.57% for patients with SVR and 7.6% for those with non-SVR, respectively. The cumulative risk of HCC was significantly higher for the non-SVR patients than the SVR patients ($p < 0.001$). Patients with old ages, male gender, and low levels of albumin had an increased incidence of HCC. After adjustment for the potential confounders, the patients who did not achieve SVR had 3.2 folds (95% confidence interval: 1.40-6.24) risk of developing HCC during the follow-up period.
Conclusion: Patients with chronic hepatitis C who received pegile interferon plus ribavirin therapy who achieved SVR is associated with a substantial reduction of HCC risk. Therefore chronic hepatitis C patients should be encouraged to receive antiviral therapy as early as possible and even as in young age as possible.
Disclosure of Interest: None declared

P1299 TRANSARTERIAL CHEMOEMBOLISATION IN THE TREATMENT OF INTERMEDIATE-STAGE HEPATOCELLULAR CARCINOMA; STUDY OF FACTORS PREDICTIVE OF SURVIVAL. CLINICAL EXPERIENCE IN A SINGLE CENTRE IN SPAIN

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Introduction: Transarterial chemoembolisation (TACE) is currently the treatment of choice for hepatocellular carcinoma (HCC) in the Barcelona-Clinic Liver Cancer (BCLC) classification intermediate stage. Although it is the most widely used therapy, many aspects remain to be clarified, primary among them being identifying the best candidates within the broad and heterogeneous group of patients the intermediate stage covers. The aim of this study was to determine overall survival after TACE and identify the factors predictive of survival.
Aims & Methods: From May 2002 to June 2010, all patients diagnosed with intermediate-stage HCC were included prospectively to receive treatment with conventional TACE plus adriamycin and lipiodol. Further treatment sessions were given if persistence of the tumour was detected on radiological follow-up with dynamic imaging tests (''on-demand strategy''). In each case, TACE was indicated after assessment by a multidisciplinary committee. The treatment was discontinued if tumour progression, vascular invasion, extrahepatic spread or worsening of liver function were observed during follow-up. Clinical, analytical and radiological variables were obtained for all cases. Survival was estimated using the KaplanMeyer method and prognostic factors analysed using the Cox regression model.
Results: A total of 123 patients were included. Mean age was 70.58 years. Objective response was obtained in 35.7% of the cases. The most common complication was post-embolisation syndrome (33.3%). Treatment-related mortality was 3.3%. Median overall survival was 29.2 months. In the multivariate analysis using the Cox regression model, age over 65 ($p = 0.02$), functional status 0 ($p < 0.001$), tumour size less than 5 cm ($p = 0.016$), objective response ($p = 0.003$) and re-embolisation ($p = 0.001$) were significant independent prognostic factors associated with longer survival. The actuarial survival at 1, 2, 3 and 4 years was 81%, 59%, 42% and 26% respectively.

Prognostic factors	**HR (IC95%)**	p
Age	0.963 (0.933 – 0.994)	0.020
Functional status	2,24 (1.45 – 3.44)	<0.001
Tumour size	1.76 (1.11 – 2.79)	0.016
Objective response	2.18 (1.30 – 3.64)	0.003
Re-embolisation	0.51 (0.33 – 0.77)	0.001

Conclusion: The patients surviving longest were aged over 65, with good performance status and HCC less than 5 cm in diameter, who had radiological objective response after therapy and underwent at least two sessions of TACE through the ''on-demand'' strategy. The results of this study may help improve selection of the patients with intermediate-stage HCC who will obtain greater benefit in terms of survival.
Disclosure of Interest: None declared

P1300 LONG-TERM SURVIVAL RESULT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA TREATED WITH TRANS-ARTERIAL CHEMOEMBOLIZATION USING DRUG- LOADED MICROSPHERES

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Introduction: Trans-arterial chemoembolization with drug-loaded microspheres (drug-eluting bead TACE) is a modified chemoembolization technique that has been reported in many clinical trials giving better tumour control and less side effects than conventional TACE. However, its advantage in term of long-term survival for HCC patients is still needed more evaluation. This is the first report in Vietnam on long-term results of DEB-TACE for HCC patients.
Aims & Methods
Aims: to evaluate the long-term result of HCC patients treated with TACE using doxorubicin-loaded micropheres, and to identify some prognostic factors predicting post-procedural survival.
Methods: A prospective non-randomized controlled study was done on 105 HCC patients (mean tumor size: 7.8 ±2.5mm) undergoing TACE with drug-loaded beads at 108 Military Central Hospital, from June 2011 to February 2015. We used 1 or 2 from 3 different sizes of DC-Beads (100-300μm, 300-500μm and 500-700μm) loaded with 50-150mg doxorubicin in a procedural session. Patients were followed-up for every 2-3 months after treatment. In cases of HCC remain or recurrence, patients would be treated with additional DEB-TACE or RFA/PEIT according to tumour characteristics (based on CT or MR imaging) and patient condition. Survival was canculated from the date of first TACE, using Kaplan Meier estimations. *Log-rank test* was used to analyse the differences in the mean survival time and the 1-year, 2-year and 3-year overall survival rates of subgroups according to prognostic factors.
Results: 105 HCC patients underwent totally 198 TACE procedures. The mean time of follow-up was 19.8 months. The mean overall survival time of all patients was 28 months (95%CI:24-31). The cumulative survival rates at 1-year, 2-year and 3-year follow-up were 72.4%; 55.2% and 41.3% respectively. Predictors for long-term survival were: Serum AFP, tumour morphology (single nodule or multinodules, mass or diffuse type), tumor size (smaller or larger than 8cm), grade of tumour cell differentiation, vascular invasion, Child Pugh class, Okuda and Barcelona Clinic Liver Cancer staging.
Conclusion: DC-Bead TACE is an effective treatment for HCC. However, the clinical outcome still depends on several prognostic factors.
Disclosure of Interest: None declared

P1301 CIRCULATING SCCA-IGM COMPLEX IS A USEFUL BIOMARKER TO PREDICT THE OUTCOME OF THERAPY IN HCC PATIENTS

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Introduction: Every year hepatocellular carcinoma (HCC) develops in about 3–4% of cirrhotic patients. The squamous cell carcinoma antigen (SCCA) has been found elevated in liver cancer specimens by immunohistochemistry, and detected in complex with IgM (SCCA-IgM) in serum of patients with HCC. The aim of this study was to evaluate the ability of serological SCCA-IgM levels to predict the efficacy of HCC therapy.
Aims & Methods: From April 2012 to April 2014, 216 patients with a new diagnosis of HCC were enrolled in a prospective study. The diagnosis of HCC was made according to the AASLD 2010 guidelines. The patients were staged and treated according to BCLC Staging System; in particular, BCLC stage A and B were treated with loco-regional therapy, and BCLC stage C were treated with Sorafenib. Response to therapy was evaluated with imaging techniques, according to the mRECIST criteria. Serum SCCA-IgM levels were determined by the Elisa Hepa-IC kit (Xeptagen SpA, Venezia, Italy) at basal time (T_0) and after one month of treatment (T_1). The quantization of the complex SCCA-IgM was expressed in Arbitrary Units (AU/mL).
Results: At the time of diagnosis, SCCA-IgM was reactive in 168/216 patients (78%), mean ± SD: 274.4 ± 263.2 AU/mL. At baseline and one month into therapy, SCCA-IgM levels were significantly lower in the patients that responded positively to therapy, compared to those who had a negative response (median values at T_0: 125.9 AU/mL [C.I. 50-187.9] vs. 165.1 AU/mL [C.I. 117.3-209.9]; median values at T_1: 113.4 AU/mL [C.I 50-195] vs. 170.6 AU/mL [C.I. 111.7-344.2]) (Mann Whitney U Test $p < 0.05$). Also, the difference in the marker serum levels between T_1 and T_0 (T_1-T_0)(DSCCA-IgM) was significantly different between positive and negative responders (Mann Whitney U Test $p < 0.05$).
Conclusion: These results suggest that the determination of SCCA-IgM complex may be helpful in predicting the response to therapy in patients with HCC.
Disclosure of Interest: None declared

P1302 ADHERENCE TO EASL-EORTC CLINICAL GUIDELINES FOR THE MANAGEMENT OF HEPATOCELLULAR CARCINOMA IN FIELD PRACTICE: RESULTS FROM THE ITALICA DATABASE

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Introduction: Data on adherence to joint guidelines for the management of hepatocellular carcinoma (HCC) published in 2012 by the European Association for the Study of the Liver (EASL) and the European Organization for Research and Treatment of Cancer (EORTC) are lacking.
Aims & Methods: We retrospectively evaluated the adherence to EASL-EORTC guidelines in field-practice, using data from HCC patients registered in the Nation-wide Italian database ITA.LI.CA. and diagnosed from 2012. The ITA.LI.CA. database contains data of 5428 HCC patients treated at 18 Italian Centers. Patients were stratified according to Child-Pugh (CP) and and the Barcelona Clinic Liver Cancer (BCLC) classifications. We investigated the adherence to surveillance, diagnosis, and first-line treatment recommendations.
Results: In ITALICA, 600 patients were diagnosed of HCC since 2012 (466 males; mean ± SD age 67.4 ± 10.9 years; 277(46.2%) CP-A and 163(27.2%) CP-B; 44(8%) BCLC-0, 193(35.1%) BCLC-A, 93(16.9%) BCLC-B, 172(31.3%) BCLC-C, 48(8.7%) BCLC-D). Overall, 317(55.2%) were diagnosed during a surveillance program. Of them, 231(57.9%) were cirrhotic (median surveillance duration: 6 months). Four-hundred-ninety-six (85.3%, 449 cirrhotic) patients were diagnosed applying a radiological, 80(13.7%) a histological, and 6(1%) a cytological criterion. Five (9.7%) patients in BCLC stage 0 with CP A, and single nodules underwent tumour resection; 3(1.4%) patients in BCLC-A received liver transplantation, and 83(43.1%) received radiofrequency ablation or Percutaneous Ethanol Injection. Intermediate HCC-stage patients (BCLC-B) receiving TACE were 45(47.9%), and advanced-stage patients (BCLC-C) receiving sorafenib were 38(21.9%). Palliative care was provided to terminal stage patients (BCLC-D) in 31(64.3%) cases.

Conclusion: The overall adherence in a ''real-world'' practice to EASL-EORTC guidelines was low, particularly in patients with early stage HCC. Difficulties in patients staging and the high prevalence of older patients with relevant co-morbidities may partially explain these findings. Strategies to help improve adherence to international guidelines for HCC in field-practice and new scoring criteria are required.
Disclosure of Interest: None declared

P1303 EFFICACY OF SORAFENIB IN PATIENTS WITH INTERMEDIATE-STAGE HEPATOCELLULAR CARCINOMA: RESULTS FROM THE ITA.LI.CA. DATABASE

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Introduction: Sorafenib represents the elective treatment for patients affected from advanced-stage (BCLC-C according to the Barcelona Clinic of Liver Cancer classification) HCC; this molecule is also recommended in patients with intermediate-stage (BCLC-B) disease who have failed or are not eligible to transareterial chemoembolization (TACE). However, further information on the use of sorafenib in patients with BCLC-C HCC is warranted.
Aims & Methods: This study analyses the efficacy of sorafenib in patients with BCLC-B HCC, with respect to those with BCLC-C disease, in the Nation-wide Italian database ITA.LI.CA.
The ITA.LI.CA. database contains data of 5428 HCC patients treated at 18 Italian Centers. All patients with either BCLC stage B or C and who received sorafenib were considered. Overall survival (OS), time to progression (TTP), and disease control rate (DCR) were evaluated. Safety considerations were also performed.
Results: A total of 243 patients were included. Of these, 61 were in BCLC-B stage (29 received ≥1 TACE prior to sorafenib) and 182 in BCLC-C. In the overall population, median TTP was 8 months (95%CI 6-9), median OS was 13 months (95%CI 10-15.5), and DCR was 28.3% (complete response, CR = 1.6%; partial response, PR = 8.9%; stable disease, SD = 17.8%). Patients in BCLC-B stage had a median TTP of 10 months (95%CI 6-14), a median OS of 19 months (95%CI 12.5-26.5), and a DCR of 39.1% (CR = 2.4%; PR = 9.8%; SD = 26.8%), whereas patients in BCLC-C stage had a median TTP of 7 months (95%CI 6-8), a median OS of 11 months (95%CI 10-15.5), and a DCR of 25.3% (CR = 1.3%; PR = 8.7%; SD = 15.3%). The safety profile of sorafenib was similar in the two sub-populations.
Conclusion: These ''field-practice'' findings suggest that the administration of sorafenib in BCLC-B patients with HCC may be effective and is not associated with any new safety warning.
Disclosure of Interest: None declared

P1304 CHANGES IN CD4 AND CD8AFTER INTERVENTIONAL MANAGEMENT OF HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocellular carcinoma (HCC) has many curative choices which in some circumstances are equal to or even better than surgery. These strategies for treatment of HCC may induce certain local effects which trigger distinct immunological responses that may have a systemic impact on the natural history of the tumour itself. These responses are validated through the measurement of specific immune cells in the systemic circulation.
Aims & Methods: In this study, we tried to observe and analyze the immunological changes that accompany and follow HCC ablation by different procedures of radiological intervention and compare our results with the literature. This study was conducted on 50patients diagnosed with HCC who were referred to Tropical Medicine Department at Mansoura University Hospital, Egypt and 20 healthy volunteers as a control. The therapeutic strategy was selected according to the tumor stage and general condition. RFA was performed for 12 cases, PEI for 13, MWA for12 and TACE for 13 cases. All Patients were subjected to full history taking, clinical examination, liver function tests, serum alpha fetoprotein, abdominal ultrasonography, triphasic abdominal computerized tomography and lymphocyte subset assay by flow cytometry 1 day before, and 3 weeks after the treatment.
Results: In the RFA group, CD4+ cells and CD4/CD8 ratio remarkably increased after treatment ($P < 0.001$), and the CD8+cells significantly decreased ($P < 0.002$) with concomitant increase in the CD4+/CD8+ ratio ($P < 0.001$). **In the PEI group**, CD4+cells markedly increased after treatment ($P < 0.001$), but there were no significant differences in CD8+cells and CD4/CD8 ratio. **In the MWA group**, CD4+cells markedly increased after treatment ($P < 0.001$), with increase in CD4/CD8 ratio ($P < 0.007$) but there were no significant differences in CD8+cells. **In the TACE group**, the CD4+cells and CD4/CD8 ratio dramatically decreased after treatment ($P < 0.001$), and the CD8+cells increased significantly ($P < 0.001$).
Conclusion: Our study has proved the presence of a relationship between the immunity and the different modes of therapy in HCC patients and demonstrated a positive attitude towards increasing the immune cells following the ablation technique.

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P1306 VESSEL-EMBRACING RADIOFREQUENCY ABLATION RESULTS IN GOOD COMPLETE TUMOR ERADICATION AND LOW LOCAL RECURRENCE RATE FOR TREATING HEPATOCELLULAR CARCINOMA ABUTTING MAJOR VESSELS

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Introduction: In treating hepatocellular carcinoma (HCC), heat sink effect (HSE) may result in incomplete radiofrequency ablation (RFA) and increased local recurrence rate. On the other hand, the HSE may protect the vital vessels, e.g.portal veins (PV), hepatic veins (HV) or infereior vena cava, embraced within the RFA area from thrombosis destruction, therefore, the safety margin can be maximized without sacrificing the vital vessels.
Aims & Methods: To study the complete eradication efficiency and local recurrence rate of vessel-embracing RFA (VE-RFA) by multi-tined temperature-control probe.
Material and Methods: VE-RFA is defined that during RFA the probe tines embrace certain major inflow PV or outflow HV within the optimal safety margin. From Jan 2011 to Jan 2014, nine HCC cases (9 VE-RFA treated tumors) were retrospectively compared with nine BCLC stage A-matched cases (10 nonVE-RFA treated tumors) at the same interval. The monopolar multi-tined probe (AngioDynamic) was used and the heating protocol and end-point were defined according to the manufacture's guide. Safety margin indices (SMI) was defined as: (final tine extension width – maximal tumor width) / maximal tumor width). SMI was maintained > 0.5 for each RFA procedure in both groups, under the purpose to optimize the safety margin according to the tumor size. The time ratio (TR) was defined as the heating time ratio to the manufacturers' reference time for a complete RFA procedure. The higher the TR indicated the stronger the HSE. The mean RFA time ratios of both patient groups were compared , as well as the 1-year local recurrence rates. The tumor sizes are 3.02±0.65 cm and 2.89±0.58 cm in VE-RFA and RFA group, respectively ($P = 0.65$). The SMI is 0.68±0.31 vs 0.91±0.27 ($p = 0.102$) in VE-RFA and RFA group, respectively.
Results: (1) the resultant TR is 1.34± 0.47 vs 0.99 ± 0.33 ($p = 0.033 < 0.05$) in group VE-RFA and group non-VE-RFA, respectively, for a complete heating procedure with a complete eradication defined by 2-week post-RFA CT. The data indicates marked HSE in VE-RFA group than in nonVE-RFA group (2) A positive correlation exists between the vessel diameter and the HSE. That is, the slopes of the diameter-TR regression lines are positive for both HVs and PVs. (0.115 and 0.042 , respectively) (3) The HSE (increase of TR) from increase of outflow HV diameter is 2.7 times that from increase of the inflow PV diameter. (4) Provided SMI at the value > 0.5, the local recurrence rate are low in both groups, 0/9 vs 2/ 10 ($p = 0.17$) in group VE-RFA and group non-VE-RFA, respectively, at the end of 1-year follow up, with no statistical significance.
Conclusion: Given pre-conditions of SMI > 0.5 , VE-RFA by multitined monopolar probe overcome HSE , yields good complete tumor eradication and low local recurrence rate for HCC encasing or abutting major hepatic veins or portal veins. The HSE is influenced at least by two factors, i.e. the type of veins and the diameter of veins. Presumably, the HVs yield more HSE than the PVs.
Disclosure of Interest: None declared

P1307 TUMOR VASCULARITY ON IMAGES WELL REPRESENTS THE BIOLOGICAL MALIGNANCY OF INTRAHEPATIC CHOLANGIOCARCINOMA INCLUDING THE NODAL STATUS COMPARED WITH THE TUMOR SIZE

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Introduction: Recently, several authors [1] advocated that lymph node (LN) dissection is not necessary in patients with intrahepatic cholangiocarcinoma (ICC) without nodal metastases. However, preoperative imaging studies do not indicate the exact nodal status in cases of hepatobiliary cancers. Surgeons sometimes utilize the tumor size as an absolute determinant of the indication for LN dissection of ICC. On the other hand, some authors have recently emphasized that the vascularity of ICC is strongly associated with the incidence of LN metastasis or survival. However, the relationships between the tumor size or vascularity of ICC and various histopathological factors have not yet been clearly investigated.

Aims & Methods: Seventy patients with mass-forming dominant ICC underwent hepatectomy between 2003 and 2013 were included in the subsequent analysis. Using the late arterial phase CT, we calculated the CT ratio as the CT value of the tumor divided by the CT value of the non-tumorous liver parenchyma. We examined the relationships between clinicopathological and immunohistological factors of ICC and the tumor size or vascularity. A hepatic progenitor cell and biliary marker (neural cell adhesion molecule (NCAM)) and large bile duct marker (S100P) were examined as immunohistochemical marker.
Results: The cumulative 5-year overall survival rate and median survival time were 43.3% and 44.3 months, respectively. Lymph node (LN) metastasis was found in 19 patients. A receiver operating characteristics (ROC) analysis revealed that there were no correlations between the tumor size and lymphatic invasion (AUC = 0.499, p = 0.986), perineural invasion (AUC = 0.435, p = 0.419), LN metastasis (AUC = 0.658, p = 0.658), reactivity for NCAM (AUC = 0.394, p = 0.128) or S100P (AUC = 0.439, p = 0.372) or mucin secretion (AUC = 0.605, p = 0.162), whereas there were significant correlations between the tumor vascularity of ICC and lymphatic invasion (AUC = 0.768, $p < 0.001$), perineural invasion (AUC = 0.668, p = 0.038), LN metastasis (AUC = 0.748, p = 0.001), reactivity for NCAM (AUC = 0.674, p = 0.012) or S100P (AUC = 0.713, p = 0.003) or mucin secretion (AUC = 0.743, $p < 0.001$). A Cox proportional hazards analysis identified LN metastasis (p = 0.012) and perineural invasion (p = 0.017) as independent predictors of survival. Logistic regression analysis revealed that CT ratio of < 0.94 and macroscopic mass-forming and periductal infiltration were independently associated with the incidence of LN metastasis.
Conclusion: Important prognostic factors of ICC, such as LN metastasis or perineural invasion, are not associated with the tumor size, but rather the vascularity of the tumor. Even for small tumors, surgeons should presume of the risk of LN metastasis and/or lymphatic or perineural invasion in patients with hypovascular ICC. In order to properly assess the presence of LN metastasis, it is important to consider the vascularity of the ICC lesion and the presence of macroscopic periductal infiltration with mass-forming ICC.

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Disclosure of Interest: None declared

P1308 RISK FACTORS ASSOCIATED WITH CAVERNOUS TRANSFORMATION OF THE PORTAL VEIN: A CASE-CONTROL STUDY

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Introduction: Cavernous transformation of the portal vein (CTPV) may develop as a consequence of portal vein thrombosis (PVT). Both systemic and local factors have an influence on the process of thrombogenesis. In Russia, no case-control studies aimed to assess CTPV development risk factors were conducted so far.
Aims & Methods: To evaluate the association between the development of CTPV and PVT risk factors.
Study design: Case-control study. 38 patients (16 males and 22 females, mean age 44.8 ± 14.8) with the diagnosis of CTPV on contrast-enhanced MSCT and/or Doppler ultrasonography were included in the "CTPV" group. The "Controls" group was composed of 49 age and sex-matched healthy individuals who had no CTPV. Systemic and local factors were assessed in both groups. Systemic factors included: hyperhomocysteinemia (HHcy); protein S (PS), protein C (PC) and antithrombin III (ATIII) deficiency; antiphospholipid syndrome (APS); myeloproliferative diseases (MPDs); polymorphisms in genes related to coagulation: prothrombin [FII G20210A], factor V Leiden [FVL], coagulation factor VII [FVII Arg353Gln G > A], methylenetetrahydrofolate reductase [MTHFR C677T], beta-fibrinogen [FGB beta G455A], glycoprotein Ib (platelet) alpha polypeptide [GP1BA c. -5T > C], integrin alpha-2 [ITGA2 C807T], platelet glycoprotein [ITGB3 (GPIIIa) Leu59Pro T > C], methionine synthase reductase [MTRR A66G], plasminogen activator inhibitor [PAI-1 4G/5G], P-selectin glycoprotein ligand-1 [SELPLG Met62Iso G > A], Janus kinase-2 [JAK2 V617F G > T].
Results: Local factors were found in 14 (37%) patients. A statistically significant association was established between CTPV and omphalitis and umbilical sepsis (p = 0.01), while no significant results were obtained for other local factors (abdominal infections, liver cirrhosis, abdominal surgery). Significant differences between "CTPV" and "Controls" were found for MPDs (p = 0.001), JAK2 V617F (p = 0.02), PS and PC deficiency (p = 0.02), No significant differences were established for APS, ATIII deficiency and HHcy.
No significant differences between two groups were found when studying allele distribution of the following genes related to coagulation: FII G20210A (Odds Ratio [OR] 3.4; 95% Confidence Interval [CI] 0.3 to 39.6), FVL (p = 0.4), FGB beta G455A (OR 0.7; CI 0.3 to 2.1), FVII Arg353Gln (OR 0.6; CI 0.2 to 2.1), MTHFR C677T (OR 0.7; CI 0.3 to 1.8), MTRR A66G (OR 1.4; CI 0.3 to 6.1), GP1BA c. -5T > C (OR 0.9; CI 0.3 to 2.6), ITGB3 (GPIIIa) Leu59Pro (OR 1.3; CI 0.4 to 4.0), SELPLG Met62Iso (OR 0.4; CI 0.1 to 2.3), ITGA2 C807T (OR 0.8; CI 0.3 to 2.2).
The differences between the patients and controls in the frequency of 4G allele carriers, and 5G/5G homozygotes of PAI-1 lay close to the border of statistical significance (p = 0.07; OR 3.9; CI 0.8 to 18.9).
Conclusion: This study established an association between CTPV and following risk factors: omphalitis and umbilical sepsis; MPDs, PS and PC deficiency, JAK2 V617F. No significant differences were found for abdominal infections, liver cirrhosis, abdominal surgery, APS, ATIII deficiency, HHcy and polymorphisms in genes related to coagulation. The obtained results for PAI-1 gene lie in close proximity to statistical significance. Investigations with a larger group of participants are required to specify the role of genes related to coagulation in the development of CTPV.
Disclosure of Interest: None declared

P1309 USEFULNESS OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING FOR DIFFERENTIATION BETWEEN BENIGN AND MALIGNANT ELEVATED LESIONS OF THE GALLBLADDER

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Introduction: The usefulness of diffusion-weighted magnetic resonance imaging (MRI) in gastrointestinal cancer has been reported. In this study, we examined the true positive rate of differentiation between benign and malignant elevated lesions of the gallbladder on diffusion-weighted MRI compared with pathological diagnosis, and assessed the usefulness.
Aims & Methods: The subjects were 59 patients who underwent diffusion-weighted MRI for gallbladder polyps or gallbladder cancer and who underwent resection from October 2009 to December 2013. We defined high intensity at high b values with low intensity on ADC maps as diffusion suppression, and an indication of cancer on diffusion-weighted MRI. We compared the findings with those of pathological diagnosis in all 59 cases. Then we classified the cases into the following 3 groups: (1) suspected gallbladder polyp group, 16 cases, (2) suspected early gallbladder cancer group, 22 cases, (3) suspected advanced cancer group, 21 cases. We examined the true positive rate of diffusion-weighted MRI for each group.
Results: The true positive rate, sensitivity, and specificity were 88.1%, 93.5%, and 82.1%, respectively, overall, (1) 87.5%, x%, and 87.5%, respectively, in the suspected gallbladder polyp group, (2) 86.4%, 86.7%, and 85.7%, respectively, in the suspected early cancer group, and (3) 90.5%, 60.0%, and 100%, respectively, in the suspected advanced cancer group.
Diffusion-weighted MRI showed high true positive rates. There were two false-negative cases in group (2), both consisting of intramucosal cancer in part of the lesion 20 mm or less in diameter. There were four false-positive cases; two cases in group (2), both consisting of adenoma 10 mm in diameter, and two cases in group (3), both consisting of xanthogranuloma.
Conclusion: Diffusion-weighted MRI was useful for differentiation between benign and malignant elevated lesions of the gallbladder.

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Disclosure of Interest: None declared

P1310 ENDOSCOPIC PAPILLECTOMY OF AMPULLARY NEOPLASMS: A SINGLE-CENTER EXPERIENCE

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Introduction: Endoscopic papillectomy (EP) offers a minimally invasive method for lesions of the ampulla of Vater as an alternative option to surgery. This study aimed to evaluate the results of EP performed for ampullary neoplasms at a single center.
Aims & Methods: From January 2005 to October 2014, 19 patients diagnosed with ampullary tumor were treated with EP. The cases were analysed retrospectively. At least 4 biopsies were taken in all patients before EP procedure. Histologic diagnosis was adenoma in all cases. EP was performed for ampullary lesions without endoscopic or histopathological findings of malignancy. Duodenoscope and hot snare were used for papillectomy. After EP, we placed a pancreatic stent randomly in 5 of 19 patients (26%).
Results: 19 patients (13 men and 6 women; median age 65.1 years, range 28-82) were enrolled. The median follow-up period was 36 months (range 14-68 months). Out of 19 patient, 18 were non-familial adenomatous polyposis (FAP) cases and one patient was with FAP. The papillary lesions ranged from 9 to 32 mm in size. Histopathological examination of the resected specimens revealed nonspecific changes in 1 patient (5%), low-grade dysplasia in 9 (48%), high-grade dysplasia in 5 (26%) and carcinoma in 4 (21%). Pancreatitis occurred in one of the patients (20%) with pancreatic stent. Pancreatitis developed in 3 cases of the group without pancreatic stent (21%) ($p > 0.05$). No mortality was seen and morbidity occured in 31.5 % of the patients, including pancreatitis in 4 (21.5%), bleeding in 1 (5%), biliary complications in 1 (5%). No perforation and papillary stenosis were observed. The mean hospital stay was 2.7 days (range 1-15 days). The resection was en bloc in 11 patients (58%) and the piecemeal technique was carried out in 8 cases (42%). Treatment was accepted inadequate in 4 patients diagnosed with adenocarcinoma (11%) because of submucosal invasion. These patients were undergone pancreatoduodenectomy. During the follow-up, these 4 patients died due to complications of

adenocarcinoma or surgery within 1 year. No recurrence of tumor was observed in the other 15 cases. Eventually, EP was considered to be curative in 78.9% of all patients.
Conclusion: EP has lower morbidity and mortality rates than surgical procedures. EP is also an important staging approach and a safe, effective and technically applicable treatment option for lesions of the ampulla of Vater as well. It should be taken into consideration as the first-line treatment option for tumors of the ampulla of Vater without intraductal invasion. Further studies including much more patients are needed to decide whether pancreatic stenting is necessary.
Disclosure of Interest: None declared

P1311 RECURRENCE OF AMPULLARY ADENOMAS AFTER ENDOSCOPIC PAPILLECTOMY

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Introduction: Endoscopic papillectomy has been regarded as a safe and effective treatment for ampullary tumors. However, recurrence after complete resection was frequently observed.
Aims & Methods: The aim of the present study was to analyze the recurrence rate and management after endoscopic papillectomy. Twenty patients with papillary mass who had undergone endoscopic papillectomy over a 10-year period were reviewed (16 male, 4 female; mean age 63 years). Endoscopic papillectomy was performed for both benign and premalignant ampullary tumors. Surveillance after the procedure was performed at 3 and 9 months and then each year afterwards with lateral scopy. The mean duration of the follow-up was 26 months (range: 6-79 months). Pathological diagnosis, follow-up, long-term outcomes were reviewed.
Results: Pathologic diagnoses were low-grade dysplasia (n = 11), high-grade dysplasia (n = 3), adenomyoma (n = 3), inflammatory lesion (n = 2), and paraganglioma (n = 1). Complete resection was achieved in 18 cases (90%); two cases with incomplete resection were treated with surgical ampullectomy in the case with high-grade dysplasia and endoscopic ablation with electrocautery in the other patient with low-grade dysplasia. Three sporadic cases and one familial colonic polyposis recurred during the follow-up at 16, 18, 24, and 36 months. All cases revealed low-grade dysplasia by surveillance biopsies and they were treated with electrocautery. During the follow-up period (mean 14 months; range, 6-26 months) after the 2nd treatment, recurrence was not observed.
Conclusion: Recurrence occurred frequently in ampullary adenomas after complete resection. However, these cases can be safely treated with electrocautery. Careful surveillance is needed after endoscopic treatment for ampullary adenomas.
Disclosure of Interest: None declared

P1312 ENDOSCOPIC METALLIC STENT PLACEMENT FOR UNRESECTABLE MALIGNANT BILIARY STRICTURE USING A BALLOON ENTEROSCOPE IN PATIENTS WITH SURGICALLY ALTERED GASTROINTESTINAL ANATOMY

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Introduction: Recently, reports on endoscopic retrograde cholangiography using a single- (SBE) or double-balloon enteroscope (DBE) in patients with surgically altered gastrointestinal anatomy have been increasing. However, there have been few studies on endoscopic metallic stent (MS) placement in patients with surgically altered gastrointestinal anatomy.
Aims & Methods: The aim of this study was to investigate the efficacy and safety of endoscopic MS placement for unresectable malignant biliary stricture using a short SBE or DBE in patients with surgically altered gastrointestinal anatomy. Between July 2010 and July 2014, 11 patients with unresectable malignant biliary stricture and surgically altered gastrointestinal anatomy (mean age, 76 yrs.; 5 males, 6 females) in whom endoscopic MS placement using a short SBE (1520 mm working length, 3.2 mm working channel) or a DBE (1520 mm working length, 2.8 mm working channel) had been attempted were included in this study. Main outcome measurements were technical success, clinical success, early complications (within three days after MS placement), late complications, and stent patency. Clinical success was defined as a decrease of total bilirubin level to a normal level or less than half of the initial bilirubin level. Complications were according to consensus criteria.
Results: Five patients had lymph node metastasis from gastric cancer, 4 had pancreatic cancer, 1 had bile duct cancer, and 1 had gallbladder cancer. The gastrointestinal reconstruction methods which had been performed were Roux-en Y reconstruction in 6 patients, hepaticojejunostomy in 4 (pancreatoduodenectomy in 2, total pancreatectomy in 1, and choledochectomy in 1), and BillrothIIreconstruction in 1. Reaching the papilla or the choledochojejunostomy site was successful in 91% (10/11). Endoscopic MS placement was successful in all patients except in one in whom the papilla could not be reached. Clinical success was obtained in all patients (10/10). Mean procedure time was 76 minutes. Early complication occurred in one patient (mild pancreatitis). In a mean follow-up period of 113 days, late complication occurred in one patient (stent occlusion). Mean stent patency was 252 days.
Conclusion: Endoscopic MS placement for unresectable malignant biliary stricture using a short SBE or DBE in patients with surgically altered gastrointestinal anatomy had high technical and clinical success rates with an acceptable complication rate.
Disclosure of Interest: None declared

P1313 MICRORNAS IN SERUM AND BILE OF PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS AND/OR CHOLANGIOCARCINOMA

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Introduction: Patients with primary sclerosing cholangitis (PSC) are at high risk for the development of cholangiocarcinoma (CC). Analysis of micro ribonucleic acid (MiRNA) patterns is an evolving research field in biliary pathophysiology with potential value in diagnosis and therapy.
Aims & Methods: Our aim was to evaluate miRNA patterns in serum and bile of patients with PSC and/or CC. Serum and bile from consecutive patients with PSC (n = 40 (serum), n = 52 (bile)), CC (n = 31 (serum), n = 19 (bile)) and patients with CC complicating PSC (PSC/CC) (n = 12 (bile)) were analyzed in a cross-sectional study between 2009 and 2012. The miRNA levels in serum and bile were determined with global miRNA profiling and subsequent miRNA-specific polymerase chain reaction-mediated validation.
Results: Serum analysis revealed significant differences for miR-1281 ($p = 0.001$), miR-126 ($p = 0.001$), miR-26a ($p = 0.001$), miR-30b ($p = 0.001$) and miR-122 ($p = 0.034$) between patients with PSC and patients with CC. MiR-412 ($p = 0.001$), miR-640 ($p = 0.001$), miR-1537 ($p = 0.003$) and miR-3189 ($p = 0.001$) were significantly different between patients with PSC and PSC/CC in bile.
Conclusion: Patients with PSC and/or CC have distinct miRNA profiles in serum and bile. Furthermore, miRNA concentrations are different in bile of patients with CC on top of PSC indicating the potential diagnostic value of these miRNAs.
Disclosure of Interest: None declared

P1314 THE IMPLICATION OF ANOMALOUS UNION OF PANCREATICOBILIARY DUCT IN PATIENTS WITH BILIARY TRACT CANCERS: COMMUNITY-BASED, SINGLE-CENTER EXPERIENCE IN KOREA

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Introduction: Anomalous union of pancreaticobiliary duct (AUPBD) is characterized as long common channel of the pancreaticobiliary junction. AUPBD is well known as pathogenesis of choledochal cyst, and is associated with various biliary tract cancers. The aim of this study was to see the incidence of AUPBD in Korean patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) and to elucidate its association with biliary tract cancers.
Aims & Methods: Seven hundred twenty eight patients underwent ERCP according to indications between March 2010 and May 2014 at Inje University Haeundae Paik Hospital, secondary, community-based medical center. ERCP was performed by one experienced endoscopist. Four hundred forty two biliary tract cancer patients were retrospectively reviewed during same period at the hospital.
Results: During that period, AUPBD was detected in 11 patients. Ten (1.37%) patients were via ERCP, and 1 case was additionally from the review of imaging in biliary tract cancers. The mean length of the common channel was 14.9 mm with a range of 6 to 20 mm. There are 7 patients of biliary tract cancer with AUPBD. Four patients are gallbladder (GB) cancer and 3 patients are bile duct cancer. The incidence of malignancy in APBDU was 63.6%. Bile duct dilatation was found in one case of GB cancer group and 1 bile duct cancer. Higher incidence of cancer was observed in bile duct dilatation group (100%, 1 GB cancer and 1 CBD cancer), compared to no dilatation group (56%). Four cases showed AUPBD on ERCP but no biliary tract cancer. On review of 442 biliary tract cancer patients, there were 127 patients with GB cancer (28.3%) and bile duct cancer 315 (72.1%). In 442 biliary tract cancers, only 7 patients were associated with AUPBD (1.6%). Patients of GB cancer with AUPBD were 3 patients. The lesions were located at fundus in 2 patients and one was in body. Patients of bile duct cancer with AUPBD were four. The location of bile duct cancer were 1 proximal, 1 middle, 1 distal portion and 1 cystic duct. In four patients with AUPBD without biliary tract cancer, these patients were diagnosed with computed tomography, ERCP and magnetic resonance cholangiopancreatography. Three patients were diagnosed as acute cholecystitis and one patient was diagnosed only as AUPBD without biliary disease by regular check-up.
Conclusion: AUPBD is a rare congenital anomaly which is related to biliary tract cancers. The rate of biliary malignancies is extremely high in AUPBD patients of Korea, especially in dilated bile duct cases. In terms of biliary tract cancers, the incidence of AUPBD is still low, but we are careful to delineate it.
Disclosure of Interest: None declared

P1315 IS EXTENDED RESECTION FOR ADVANCED GALLBLADDER CANCER JUSTIFIED?

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Introduction: The clinical impact of extended resection for advanced gallbladder cancer remains unclear.
Aims & Methods: A total of 96 patients underwent resection for Stage II, III, or IV gallbladder cancer between 2003 and 2012. Of these, 29 patients who underwent major hepatectomy (major Hx group; resecting two or more sections) were enrolled in this study. Moreover, resection was not undertaken after laparotomy in 15 patients (unresectable group) between 2003 and 2012 because they had unsuspected distant metastasis. Of these, 12 patients underwent non-surgical treatments: three patient received chemotherapy with gemcitabine, three patients received S-1 + cisplatin, five patients received gemcitabine + cisplatin, and one patient received irinotecan + cisplatin. Surgical results of the major Hx group were examined, and overall survival (OS) between the major Hx group and the unresectable group were compared in this study.
Results: In the major Hx group, 23 patients underwent right hemihepatectomy, two patients underwent central bisectionectomy, three patients underwent right hepatic trisectionectomy, and one patient underwent left hepatic trisectionectomy. Twenty-five patients underwent extrahepatic bile duct resection, nine patients underwent portal vein resection and reconstruction (PVR group) and nine patients underwent combined pancreatoduodenectomy (major HPD group). There was no in-hospital mortality in the major Hx group. The OS in the major Hx group was significantly better than that in the unresectable group (median survival time (MST) 17.7 vs. 11.4 months, 5-year OS; 26.3% vs. 0.0%, $p = 0.004$). Especially, the OS in patients with Stage III ($n = 15$, MST 29.8 months, 5-year OS 31.6%) and Stage IVa ($n = 9$, MST 17.6 months, 5-year OS 29.6%) were significantly better than that in the unresectable group ($p = 0.008$, 0.025), however, the OS in patients with Stage IVb ($n = 4$, MST 13.6 months, 5-year OS 0.0%) was comparable with that in the unresectable group ($p = 0.995$). Cox proportional hazard analysis revealed that only lymph node metastasis ($p = 0.032$) was independent prognostic factor of survival in the major Hx group, however, the OS in patients with lymph node metastasis ($n = 20$, MST 16.3 months, 5-year OS 10.0%) was better than that in the unresectable group ($p = 0.062$). The OS in the PVR group ($n = 9$, MST 17.6 months, 5-year OS 33.3%) was comparable with that in the non-PVR group ($n = 20$, MST 21.5 months, 5-year OS 26.2%, $p = 0.817$), and the OS in the PVR group was better than that in the unresectable group ($p = 0.054$). Overall morbidity in the major HPD group ($n = 9$) was significantly higher than that in non-PD group ($n = 20$, 89% vs. 40%, $p = 0.014$) The OS was comparable between the major HPD group and non-PD group (5-year OS; 34.6% vs. 21.1%, MST; 29.8 months vs. 17.2 months, $p = 0.565$), and the OS in the major HPD group was significantly better than that in the unresectable group ($p = 0.017$).
Conclusion: In the patients with Stage III or IVA gallbladder cancer, aggressive major Hx, including major HPD or combined PVR, may be justified for otherwise unresectable tumors. However, the surgical indications for major Hx in the patients with bulky lymph node metastasis should be carefully evaluated due to the poor prognosis after surgery. On the other hand, Stage IVB gallbladder cancer should be treated as systemic disease.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 09:00–14:00
PANCREAS III – HALL 7

P1316 PLATELET SECRETION OF CXCL4 REGULATES NEUTROPHIL RECRUITMENT AND TISSUE INJURY IN ACUTE SEVERE PANCREATITIS

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Introduction: Platelets are known to play an important role in acute pancreatitis via promotion of neutrophil accumulation although mechanisms behind platelet-dependent accumulation of neutrophils in the pancreas remain elusive. Platelets contain a wide-spectrum of different pro-inflammatory compounds, such as chemokines. CXCL4 (platelet factor 4) is one of the most abundant chemokine in platelets and we hypothesized that CXCL4 might be involved in platelet-dependent accumulation of neutrophils in the pancreas.
Aims & Methods: The aim of this study was to examine the role of CXCL4 in acute pancreatitis. Pancreatitis was provoked by infusion of taurocholate into the pancreatic duct in C57BL/6 mice. Animals were treated with an antibody against CXCL4 or platelets prior to induction of pancreatitis. Plasma and lung levels of CXCL4, CXCL2 and IL-6 were determined by use of ELISA. Flow cytometry was used to examine surface expression of Mac-1 on neutrophils. Plasma was obtained from healthy individuals (controls) and patients with severe acute pancreatitis.
Results: Challenge with taurocholate increased plasma levels of CXCL4 and depletion of platelets markedly reduced plasma levels of CXCL4, indicating that circulating levels of CXCL4 are mainly derived from platelets in acute pancreatitis. Inhibition of CXCL4 reduced taurocholate-induced neutrophil recruitment, IL-6 secretion, edema formation, amylase release and tissue damage in the pancreas. However, immunoneutralization of CXCL4 had no effect on CXCL2-evoked neutrophil expression of Mac-1 or chemotaxis in vitro, suggesting an indirect effect of CXCL4 on neutrophil recruitment in acute pancreatitis. Targeting CXCL4 significantly attenuated plasma and lung levels of CXCL2, which is a potent neutrophil chemoattractant and inhibition of the CXCL2 receptor attenuated neutrophil infiltration and tissue damage in the inflamed pancreas. Patients with severe acute pancreatitis had significantly increased plasma levels of CXCL4 compared to healthy controls.
Conclusion: These results suggest that platelet-derived CXCL4 is a potent stimulator of neutrophil accumulation in acute pancreatitis and that this is mediated via generation of CXCL2 in the inflamed pancreas. We conclude that CXCL4 plays an important role pancreatic inflammation and that targeting CXCL4 might be a useful way to ameliorate pathological inflammation and tissue damage in acute pancreatitis.
Disclosure of Interest: None declared

P1317 AFMK, METABOLITE OF MELATONIN, ATTENUATES ACUTE PANCREATITIS BY ACTIVATION OF CELLULAR ANTIOXIDATIVE MECHANISMS

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Introduction: Melatonin is well known as antioxidant and pancreatic protector, but the effect of melatonin metabolite: N^1-acetyl-N^2-formyl-^{5}methoxykynuramine (AFMK) on acute pancreatitis was unknown.
Aims & Methods: To assess the effects of AFMK on caerulein-induced pancreatitis (AP) in the rats and on the level of an antioxidant enzyme glutathione peroxidase (GPx) and tumor necrosis factor alpha (TNF alpha) in AR42J pancreatic acinar cells.
AP was induced by subcutaneous caerulein infusion (25 microgr/kg). AFMK (5, 10 or 20 mg/kg) was given intraperitonealy to the rats 30 min prior to the induction of AP. Lipid peroxidation products (MDA + 4HNE) and the activity of GPx were measured in pancreatic tissue. Blood samples were taken for evaluation of amylase and TNF alpha concentrations. GPx, and TNF alpha were determined by Western blot in AR42J cells subjected to AFMK (10^{-12}, 10^{-10}, 10^{-8} M) without or with addition of caerulein (10^{-8}M).
Results: AP was confirmed by histological examination and by increases of amylase and TNF alpha blood levels (by 800% and 300%, respectively). Pancreatic MDA + 4HNE was increased by 300%, whereas GPx activity was reduced by 50% in AP rats. AFMK significantly diminished histological manifestations of AP, decreased amylase and TNFalpha blood concentrations, reduced MDA + 4HNE and augmented GPx in the pancreas of AP rats. In AR42J cells AFMK alone or combined with caerulein markedly increased protein signals for GPx, and reduced that for TNFalpha.
Conclusion: AFMK significantly attenuated acute pancreatitis. This could be related to antioxidative effect of this substance and possibly, to the modulation of TNF alpha production.
Disclosure of Interest: None declared

P1318 REGULATOR OF CALCINEURIN 1 IS HIGHLY OVEREXPRESSED IN CERULEIN INDUCED ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) ranges from a mild localized inflammation to a severe systemic disease with high mortality. Inflammation leads to production of free radicals, which in turn contributes to worsening of the inflammatory response. Repeated injections of the cholecystokinin analogue cerulein, which induces oxidative stress and AP, is one of the most frequently used *in vivo* models of AP. Numerous diagnostic and prognostic markers of acute pancreatitis have been evaluated over the years, but there is still a lack of specific markers of AP and an early marker which can reliably predict mortality.
Aims & Methods: The overall aim of this study was to identify and evaluate potential diagnostic and prognostic markers of AP.
AP was induced through 9 hourly injections of cerulein in C57/Bl6J-mice. Control mice were injected with sodium chloride. RNA from pancreatic tissue collected one hour post the last injection, was analyzed by microarray. Altered expression of selected genes was confirmed by real-time PCR from two separate experiments.
AR42J-cells (as a substitute for primary acinar cells) were stimulated with cerulein and the expression of selected genes was evaluated by real-time PCR. In order to investigate the role of oxidative stress, we treated the cells with the antioxidant N-acetylcystein (NAC) at the time of cerulein-stimulation. Blood from AP and control mice collected one hour post the last injection was processed and serum protein levels of the most promising gene, regulator of calcineurin 1 (Rcan1), was measured by ELISA.
Results: 2038 genes out of more than 16000 genes were identified as differentially expressed between mice with cerulein-induced AP and control mice. Altered expression of Rcan1, Lcn2, Srxn1, Rtn4, Sesn2, Plaur and Epha2 in murine pancreatic tissue was confirmed.
The stress regulated genes Rcan1 and Sesn2 were further studied. Their expression was significantly increased in cerulein-stimulated AR42J-cells, but this was

blocked by NAC. Rcan1 serum levels was significantly higher in mice with AP mice compared to controls.
Conclusion: Rcan1 expression is highly increased in a well-established mouse model of AP. Rcan1 is regulated by oxidative stress. Clinical studies are warranted to determine whether RCAN1 can serve as a prognostic marker in patients with AP.
Disclosure of Interest: None declared

P1319 LESIONS OF PANCREATITIS IN OBESE RATS DECREASE AFTER BARIATRIC SURGERY

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Introduction: Obesity is a well-known risk factor for pancreatitis. Mechanisms involved are multiple: pro-inflammatory cytokines induced by the adipose tissue, insulin resistance and hyperinsulinism, especially. Pancreatic stellate cells are activated and increase the extra cellular matrix synthesis. Bariatric surgery is one of the more efficient treatments of morbid obesity.
Aims & Methods
Aim: To assess pancreatic endocrine and exocrine lesions in obese rats (high-fat diet, HFD) and to analyze consequences of bariatric surgery on these lesions.
Methods: 30 male Wistar rats were included: obese (after 4 months HFD) or non obese (ND, normal diet). A part of HFD rats underwent bariatric surgery: by pass (BP) or sleeve gastrectomy (SG). Four groups were constituted: Gr1, HFD (n = 8); Gr2, HFD-BP (n = 11); Gr3 HFD-SG (n = 5); Gr4, ND (n = 8). After rat sacrifice (J14 or J40 after surgery), weight, % of weight loss and glycoregulation were analyzed. Each entire pancreas specimen was analyzed by pathological exam: number of adipocytes islets, fibrosis, acino-ductal metaplasia, abnormality of Langerhans islets (HHF: hypertrophy, hypervascularisation, fibrosis), and hemosiderin deposition in intra acinar or endocrine location.
Results: A first comparison between HFD and ND rats showed an increase of HHF and hemosiderin deposition in HFD rats ($p = 0.0012$ and $p = 0.0078$, respectively). The increase of the weight in HFD rats was associated with abnormalities of the glycoregulation ($r = 0.44$, $p = 0.08$).
In the all-4 groups, HHF lesions were associated with hemosiderin deposition ($r = 0.88$, $p < 0.0001$).
A second analyze was performed in HFD rats after bariatric surgery. In operated rats, it was observed a decrease of 1/ number of HHF lesions ($p = 0.001$), 2/ hemosiderin deposition ($p = 0.0006$) and 3/ amount of adipocytes ($p = 0.01$). This decrease was more important in HFD-By Pass compared to HFD-Sleeve Gastrectomy. In HFD-BP rats, HHF lesions and hemosiderin deposition were associated with acino-ductal metaplasia lesions ($p = 0.08$ et $p = 0.02$). The number of acino-ductal metaplasia lesions was higher in rats with higher weight before sacrifice ($p = 0.03$). Moreover, number of HHF lesions was associated with a decreased glycemia after by-pass procedure ($r = -0.76$, $p = 0.02$) but with an increased glycemia after sleeve gastrectomy ($r = 0.95$, $p = 0.05$).
Conclusion: Pancreas specimens of obese rats show pancreatitis lesions (acino-ductal metaplasia, fibrosis) in acinar location and in the endocrine-exocrine interface. Abundant hemosiderin deposition confirmed the angiogenesis process and the vascular lesions associated with the activation of the pancreatic stellate cells and the fibrogenesis.
Bariatric surgery, and the by pass procedure especially, allows decreasing pathological pancreatic lesions in obese rats and reversing the pancreatitis process in an early manner.
Disclosure of Interest: None declared

P1320 KYNURENIC ACID AND ITS NOVEL ANALOGUE SZR-72 DIMINISH THE SEVERITY OF EXPERIMENTAL ACUTE NECROTIZING PANCREATITIS IN RATS

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Introduction: The pathogenesis of acute pancreatitis (AP) is not well understood and the disease has no specific therapy. There is evidence that the blood brain barrier (BBB) permeable L-kynurenic acid (KYN) analogue SZR-72 has immune modulatory roles in several inflammatory diseases.
Aims & Methods: We investigated the effects of KYN and SZR-72 on experimental AP.
In the AP groups, male SPRD rats were injected intraperitoneally (i.p.) with 3 g/kg L-ornithine 1 hour after the administration of physiological saline (PS) (n = 6-8) or 30-300 mg/kg SZR-72 (n = 6-8) or KYN (n = 6-8). Control animals were injected i.p. with PS instead of L-ornithine or 30-300 mg/kg SZR-72 or KYN (n = 6-8). Animals were sacrificed at 24 hours. Laboratory [serum amylase-, pancreatic myeloperoxidase activity, pancreatic dry/wet weight ratio] and histological parameters were measured to evaluate disease severity.
Results: The injection of rats with L-ornithine significantly increased the measured laboratory and histological parameters vs. the control groups. The administration of 30-300 mg/kg SZR-72 or KYN did not influence the examined parameters in the control groups. Pre-treatment of AP rats with 30 mg/kg SZR-72 or KYN did not have affect on disease severity. However, all measured laboratory and histological parameters were significantly reduced in AP animals in response to treatment with 300 mg/kg SZR-72 or KYN.
Conclusion: Our experiments demonstrated that SZR-72 and KYN have a dose-dependent protective effect on L-ornithine-induced AP. Since KYN is non BBB permeable and both KYN and SZR-72 exerted a beneficial effect on AP severity, this beneficial effect seems to peripheral. Further investigations are needed to determine the mechanism of SZR-72 action.
This study was supported by OTKA, TÁMOP and MTA.
Disclosure of Interest: None declared

P1321 PREVENTING POST-ERCP PANCREATITIS (PEP): THE ROLE OF PROPHYLACTIC PANCREATIC DUCT STENTING IN THE RECTAL NSAID ERA

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Introduction: Pancreatitis is an important complication following ERCP. Rectal NSAIDs at ERCP is now the standard of care to reduce the risk of PEP. They are particularly effective in those patients where prophylactic pancreatic stenting has failed. Pancreatic duct (PD) stenting also reduces the risk of PEP in high risk patients but failed PD stenting carries reported PEP rates (up to 35%).
Aims & Methods: To assess whether prophylactic pancreatic stenting is still justified in the rectal NSAID era.
We retrospectively evaluated the use of pancreatic stents in a UK tertiary referral centre between January 2013 & December 2014 in whom rectal NSAIDs were used universally. Prophylactic PD stenting was attempted in those patients with predicted high risk of PEP (e.g. SOD, multiple pancreatic cannulation).
Electronic records were reviewed for indication of pancreatic stenting, successful placement and complications. Patients were contacted by telephone where hospital records were insufficient.
Results: A total of 1361 ERCPs were conducted during the study period. Pancreatic stenting was attempted in 250 cases (18%) and was successful in 235 patients (94%). Prophylactic pancreatic stenting failed in 14 patients (5.6%). Only one patient from this group (1/14 = 7%) developed PEP, and had both sphincter of Oddi dysfunction (SOD) and a contra-indication to NSAIDs. Sixty-one per cent (153/250), of successfully placed pancreatic stents were inserted prophylactically, in whom 12% (19/153) developed PEP. The majority (79%, 15/19) of these patients had SOD, where pancreatic sphincterotomy was also performed in 40% (6/15). The relative risk for PEP between those successfully stented and those where stenting failed was 0.5 (p = ns). NSAID use was contraindicated in 22 patients (9%, 22/250) due to allergy or renal impairment, of whom two (9%) developed PEP.
Conclusion: The rate of PEP in high-risk patients receiving PD stents was similar to previous studies. Of note, PEP rates in failed stenting were surprisingly low (7%). This might reflect NSAID use, and questions the necessity of PD stenting in the NSAID era.
Disclosure of Interest: None declared

P1322 THE USE OF ALLOPURINOL AS A PROPHYLAXIS FOR POST ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) PANCREATITIS

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Introduction: Pancreatitis is the most serious ERCP complication. Many trials were conducted to reduce the frequency and severity of post ERCP pancreatitis. The efficacy of allopurinol and other antioxidants were studied in prevention of post ERCP pancreatitis.
Aims & Methods: The aim of this study was to prospectively evaluate the use of allopurinol in the prevention of post – ERCP pancreatitis. One hundred consecutive patients of both sexes, their age ranged from 20-70 years, who were indicated for ERCP, whatever the etiology, in Ain Shams Specialized Hospital during the period from January 2011 to December 2014 were recruited. The subjects were divided into **Group 1:** 50 patients who received allopurinol tablets before the ERCP procedure (300 mg 15 hours before the procedure and another dose of 300mg of allopurinol 3 hours before the procedure) **(Study group). Group 2:** 50 patients who were subjected to ERCP without allopurinol prophylaxis **(Control group).** Both groups were matched together as regards age, sex, clinical picture before ERCP, comorbidities, ERCP procedures and ERCP findings. The patients were followed up for the 24 hours after the procedure clinically for detection of abdominal pain and manifestations of any other complications. Laboratory investigations including CBC, ALT, AST, serum amylase and serum lipase were evaluated. Radiological confirmation of cases suspected to have pancreatitis was done.
Results: Pancreatitis was diagnosed in 4 patients (4%) who belonged to the control group. However, there was no statistically significant difference between both groups. Post-ERCP Elevation of ALT was statistically significantly higher in group2 than in group 1 (94 vs. 127 U, $p < \mathbf{0.001}$). Asymptomatic elevation of serum amylase was present in 19 patients (38%) from group 1 and 46 patients (92%) from group 2 with statisticaly significant difference between both groups (median 102 vs .610U $p < \mathbf{0.001}$). Female gender, younger age, precut needle sphincterotomy, unintended pancreatic duct cannulation and injection appeared to be significant risk factors for post-ERCP pancreatitis.
Conclusion: Allopurinol tablets 300mg orally (15 hours, and 3 hours before ERCP) reduced post-ERCP pancreatitis, asymptomatic hyperamylesemia, vomiting, hospitalization, and elevation of ALT.
Disclosure of Interest: None declared

P1323 GALLSTONE AND ALCOHOLIC PANCREATITIS – EVALUATION OF ATLANTA AND DETERMINANT-BASED CLASSIFICATION SCORES

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Introduction: Gallstones and alcohol represent the most common causes of acute pancreatitis. Classification scores have not been evaluated separately for these two entities.
Aims & Methods: To evaluate the performance of 1992 Atlanta (AT1992), Revised Atlanta (AT2012) and Determinant-based-classification (DBC) in several outcomes in patients with gallstone and alcoholic pancreatitis. Retrospective study including admissions between January 2003 and September 2014 in a single tertiary referral center. Demographics, mortality, admission to intensive care unit (ICU) and need for interventional procedures were considered outcomes. Statistical analysis was performed using SPSS v21.0.
Results: 358 patients (59.2% male) were included, 59.2% with gallstone pancreatitis. Age at admission was lower in alcoholic pancreatitis (47.1 ± 12.8 versus 72.6 ± 14.1 years, $p < 0.001$). Persistent organ failure (16.5% versus 6.6%, $p = 0.007$), ICU admission (43.0% versus 22.6%, $p < 0.001$) and mortality (8.5% versus 2.2%, $p = 0.016$) were higher in gallstone pancreatitis. There was no difference in the need for interventions or duration of hospitalization. DBC showed higher accuracy in predicting mortality in both alcoholic and gallstone pancreatitis (AUC 0.90 and 0.87, $p < 0.001$), while AT2012 was significant only for gallstone pancreatitis (AUC 0.761 and 0.873, $p > 0.05$ and $p < 0.001$). AT1992 could not predict mortality in either situation. DBC fared better in predicting ICU admission (AUC 0.80 and 0.84 versus 0.76 and 0.77 versus 0.68 and 0.7, $p < 0.001$) and in the need of interventions (0.85 and 0.90 versus 0.73 and 0.76 versus 0.62 and 0.69, $p < 0.001$).
Conclusion: Alcoholic and gallstone pancreatitis are separate entities. DBC was superior in predicting all clinical outcomes especially in patients with alcoholic pancreatitis.
Disclosure of Interest: None declared

P1324 ATLANTA, REVISED ATLANTA AND DETERMINANT-BASED CLASSIFICATION – APPLICATION IN A COHORT OF PORTUGUESE PATIENTS WITH ACUTE PANCREATITIS

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Introduction: Acute pancreatitis represents a complex and potential fatal disease whose clinical course may be highly variable. Over the years, several classification systems have been developed in order to predict disease severity. These scores have not been previously validated for the Portuguese population.
Aims & Methods: To evaluate the accuracy of 1992 Atlanta (AT1992), Revised Atlanta (AT2012) and Determinant-based-classification (DBC) scores in predicting severe clinical outcomes in Portuguese patients with acute pancreatitis. Retrospective study including admissions between January 2003 and September 2014 in a tertiary referral center. Clinical outcomes included mortality, admission to intensive care unit (ICU), need for interventional procedure and total and ICU length of stay. Statistical analysis was performed with STATA v13.0 and SPSS v21.0.
Results: 525 patients (59% male) were included. Mean age at admission was 56.4 ± 19.1 years. Most common etiologies included gallstones (38.7%), alcohol (26.1%) and idiopathic (17.9%). During hospitalization 23.0% developed organ failure (in 46.3% persistent) and 5.9% were deceased. In all classification scores higher grades of severity were associated with worse outcomes. Overall, DBC was superior to AT2012 and AT1992 in predicting need for interventions (AUC 0.88 versus 0.78 versus 0.70, $p < 0.001$), admission to ICU (AUC 0.81 versus 0.80 versus 0.75, $p < 0.001$) and mortality (AUC 0.91 versus 0.89 versus 0.69, $p < 0.001$). All scores performed similarly in evaluating total and ICU length of stay.
Conclusion: Recent classification scores performed better in all clinical outcomes and showed higher accuracy in predicting severe acute pancreatitis. Our data supports their use for Portuguese patients with acute pancreatitis.
Disclosure of Interest: None declared

P1325 TRENDS OF HOSPITALIZATION FOR ACUTE AND CHRONIC PANCREATITIS IN A PORTUGUESE MAJOR REFERRAL CENTER

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Introduction: The incidence of acute and chronic pancreatitis has risen over the last decades. No study has specifically addressed hospitalization and mortality in Portuguese patients with acute and chronic pancreatitis.
Aims & Methods: To evaluate the trends in hospitalization and mortality in acute and chronic pancreatitis in a Portuguese tertiary referral center. Retrospective study including hospital admissions between 6/1988 and 3/2014 in a single center. Statistical analysis was performed using SPSSv21.0.
Results: During the study period, there were 4699 and 1338 admissions respectively for acute and chronic pancreatitis corresponding to 3807 and 831 patients. There was an annual growth in hospitalizations in both acute (25.1%) and chronic pancreatitis (23.1%). Women were more commonly admitted with acute pancreatitis (2462 versus 2237) the reverse being true for chronic pancreatitis (326 versus 1012). Age was similar between patients with acute and chronic pancreatitis (67.9 ± 19.0 and 64.9 ± 15.2). 7.3% with acute and 4.9% with chronic pancreatitis required admission to intensive care units (ICUs). Overall, mortality was higher in chronic pancreatitis (8.8% versus 14.2%, $p < 0.05$) and in patients admitted to ICUs (43.4% and 22.9% respectively for acute and chronic pancreatitis). There was a trend towards decreased mortality in acute pancreatitis (15.2% versus 5.1%, $p < 0.05$). Older age at admission but not the number of hospitalizations predicted in-hospital mortality ($p < 0.001$).
Conclusion: Admissions for acute and chronic pancreatitis have increased over the last 25 years. Although mortality remains high it has decreased over time. Age remains an important predictor of mortality.
Disclosure of Interest: None declared

P1326 WHAT IS THE NATURAL HISTORY OF FLUID COLLECTIONS IN ACUTE PANCREATITIS?

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Introduction: The recently revised Atlanta criteria changed the perspective on the fluid collection (FC) in the context of acute pancreatitis (AP) and the natural history of these reclassified collections is not yet defined.
Aims & Methods
Aim: Evaluate the natural history of fluid collections in acute pancreatitis.
We retrospectively evaluated all patients admitted to a Gastroenterology department of a tertiary hospital between January-2012 and December-2014 with the diagnosis of AP complicated by FC.
Results: Of the 491 patients admitted with AP (466 interstitial edematous AP - IEP, 27 necrotizing AP - NP), 55 (12%) developed FC. This subgroup: male sex-67%; mean age-59 years; mean number of days with symptoms prior to admission 1.83; etiology lithiasic-26% / ethanolic-26% / hypertriglyceridemia-3.7% / post-ERCP-9.3% / idiopathic-35%; moderately severe-59%.
Thirty IEP developed peripancreatic fluid collections (PPFC), 13 (43%) evolved to pseudocysts, 3 of which were infected. Regarding NP, 25 complicated: 11 acute necrotic collections acute (ANC), 54% evolving into walled-off necrosis (WON); 14 FC without evidence of necrosis. Two ANC and the WON became infected.
During follow-up, there was spontaneous resolution in: 40% > pseudocysts (minimum detected time of resolution- 57 days) and 46% > ANC. Fifteen patients required drainage, mostly because of FC infection: percutaneous-10 (success-30%), endoscopic necrosectomy-4 CNA/WON (success-25%), surgical-9 (4 in PPFC/pseudocysts infected; 5 with infected CNA/WON previously submitted to necrosectomy in, including the cases of radiological and/or endoscopic failure; success-33%). A patient suspected of having a pseudocyst underwent cephalic duodenopancreatectomy, revealing a intraductal mucinous papillary neoplasm. We documented 10 deaths: 40% with infected necrotic collections, 60% submitted to surgery, 80% during the AP hospitalization.
Conclusion: The FC following AP are relatively frequent events in our clinical practice. The PPFC evolved, in about half the cases, into pseudocysts that, in a considerable percentage of the cases, were resolved. In the context of a NP, most developed FC. The ANC solved in nearly 50% of cases. However, evolving into WON, the prognosis becomes reserved, for the high morbidity and mortality rates that are associated, despite the interventions performed.
Disclosure of Interest: None declared

P1327 SELECTIVE UTILIZATION OF ERCP AND ENDOSCOPIC ULTRASOUND FOR GALLSTONE PANCREATITIS WITH THE ABSENCE OF CHOLEDOCHOLITHIASIS ON MULTIDETECTOR COMPUTED TOMOGRAPHY

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Introduction: Endoscopic ultrasound (EUS) is an accurate diagnostic tool to detect common bile duct (CBD) stones that could not be otherwise detected by multidetector computed tomography.
Aims & Methods: This study aimed to evaluate the necessity for performing endoscopic retrograde cholangiopancreatography (ERCP) in the patients with gallstone pancreatitis when sludge was revealed in the CBD by EUS. Consecutive forty-one patients (M:F, mean age, 57 ± 18 years) with the suspicion of gallstone pancreatitis and no evidence of CBD stones by MDCT underwent EUS within 24 hours after admission. Early ERCP (within 72 hours after EUS) was performed in the patients with CBD stones or sludge by EUS findings, as well as the patients showing clinical deterioration. The patients' medical records were retrospectively analyzed based on clinical symptoms, biochemical data, and hospital courses.
Results: EUS revealed CBD stones, sludge, and none in 13 (31.0%), 7(17%), and 25 (51.3%) patients, respectively. ERCP was performed in 20 patients with CBD stones or sludge and 3 patients with clinical deterioration. CBD stones were revealed by ERCP in 11 out of 13 cases. However, sludge was revealed in 3 out of 7 and 3 patients with aggravated cases. All patients were improved and hospital days did not differ between the two conditions (with or without ERCP). However, 2 patients showed major complications including perforation and bleeding and improved after conservative management.
Conclusion: Fifty percent of the patients with sludge by EUS showed no evidence of CBD lesions by ERCP. Therefore, ERCP in the patients with sludge

and stable clinical course are not necessary. Further studies are needed to determine proper timing of EUS in gallstone pancreatitis.
Disclosure of Interest: None declared

P1328 CLINICAL OUTCOMES OF ENDOSCOPIC PANCREATIC SPHINCTEROTOMY COMBINED PANCREATIC DUCT STENT IN PATIENTS WITH ACUTE RECURRENT PANCREATITIS CAUSED BY BILIARY MICROLITHIASIS

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Introduction: To investigate the feasibility of EPS combined pancreatic duct stent for acute recurrent pancreatitis caused by biliary microlithiasis.
Aims & Methods: The 52 patients of ARP (2 or more attacks of AP) from 2005 to 2014 were diagnosed biliary microlithiasis by ERCP, bile microscopy or IDUS and all underwent EST or EPS. All the patients were under follow-up after endoscopic therapy to observe the recurrence and incidence of complication. Compare the rate of recurrence, incidence of the early and late complication, the time of hospitalized and costs between two groups. Compare the known risk factors of post EST late complication such as the diameter of the CBD, papillary diverticulum, and history of the gallbladder surgery between patients with long-term complication and without.
Results: 52 patients (male 28, female 24) suffered from frequent episodes of acute pancreatitis from 2 to more than 20 times. All the patients were non-randomly divided into 2 groups according to the endoscopic therapy: 28 cases in EST group (with or without EPBD or ENBD) and 24 cases in EPS group (with or without pancreatic stent). There were 9 cases PEP after the endoscopic therapy (3 in EST group, 6 in EPS group, $P = 0.322$). The mean time of hospitalization in EST group was 7 days, while it was 5 days in EPS group ($P = 0.040$). The mean costs was 18648.20 yuan each patient in EST group and 15642.65 yuan in EPS group ($P = 0.013$). During the follow up (mean 64 months, range 3-118 months), there were 5 patients occurred pancreatitis recurrence, 3 in EST group, 2 in EPS group, the treatment efficiency in EST group and EPS group is 89.3% and 91.7% respectively ($P = 1.000$ with chi-square test and $P = 0.888$ with Log-rank test). The incidence of long-term complication is 32.1% in EST group and 8.3% in EPS group ($P = 0.046$ with chi-square test and $P = 0.388$ with Log-rank test). The P value of the diameter of the CBD, papillary diverticulum, and history of the gallbladder surgery to the incidence of long-term complication is 0.929, 0.838, 0.921 respectively.
Conclusion: EPS has equivalent treatment efficiency to EST through blocking the pathophysiology progress of microlithiasis inducing pancreatitis episodes. At the same time, EPS save the function of biliary sphincter so that decrease the risk of long-term complication, and pancreatic stent is efficient to prevent PEP. In summary, EPS combined with pancreatic stent is more suitable to the treatment of acute recurrent pancreatitis caused by biliary microlithiasis.
Disclosure of Interest: None declared

P1329 CHRONIC PANCREATITIS IN PATIENTS WITHOUT AN ADEQUATE FOLLOW-UP: NUTRITIONAL CONSEQUENCES AND QUALITY OF LIFE, PRELIMINARY RESULTS OF THE PANCREVOL STUDY

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Introduction: Chronic pancreatitis (CP) can lead to development of pancreatic exocrine insufficiency (PEI).
Some CP patients are not adequately monitored. Consequently diagnosis of complications such as PEI may be delayed, resulting in postponement of specific treatment.
Aims & Methods: To evaluate nutritional status, quality of life(QoL) and PEI in CP patients without adequate follow-up.
Cross-sectional multicenter study involving 11 hospitals. CP patients without follow-up by gastroenterologist in the last two years were included. A complete medical exam including laboratory and EORTC-QoL-c30 questionnaire were performed to evaluate CP and complications. PEI status was determined by fecal elastase-1 concentration in stools (FE).
Results: 56% smokers, 52% regular alcohol consumers). Mean time (95%CI) from diagnosis to the inclusion in the study was 7.2(5.3-9.3) years.
25.5% of the patients indicated their overall health and their QoL was 1-2 (7 points scales, 1-very poor, 7-excellent).
FE analysis was available in 37 patients: 20(54.0%) had FE < 200 mcg/g, and 17(45.9 %) were considered to suffer from severe PEI (FE < 100mcg//g).
Analytical parameters out of range and clinically significant were: albumin, RBP, lipids, glucose, HbA1C, LDL, magnesium, vitamins K, A, D, E, B12; and prothrombin time.
Statistical significant differences between nonePEI (n = 17) PEI patients (n = 20) were observed at (median [Q1, Q3]): glucose (102.0 [90.0,116.0]177.5 [113.0,224.5]), HbA1C (5.5 [5.4,6.0] 7.0 [6.4,8.0]) and Vitamin E (14.3 [13.0,15.6] 10.1 [6.6,13.0]).
Conclusion: Unmonitored CP-patients suffering from PEI have impaired nutritional status and low QoL. Closer monitoring is needed for these patients.
Disclosure of Interest: C. Marra-Lopez Valenciano: None declared, E. Marín Serrano: None declared, J. Millastre Bocos: None declared, E. Martínez Moneo: None declared, F. Bolado: None declared, M. Francisco Gonzalez: None declared, A. Hernandez Martin: None declared, A. Del Pozo-García: None declared, E. Perez Rodriguez: None declared, E. Labrador Conflict with: Mylan employee, L. Orera Peña: None declared, E. De-Madaria: None declared

P1330 PANCREATIC MANIFESTATIONS OF VON HIPPEL LINDAU SYNDROME - A CASE SERIES

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Introduction: Von Hippel Lindau (VHL) syndrome is an autosomal dominant genetic disorder that has a high penetrance and wide phenotypic expression. Close to 60 percent of patients with VHL show pancreatic involvement. An animal study has shown that the VHL gene can regulate endocrine function but this phenomenon has not been described in humans. There are only a few case reports that describe the relationship between VHL and exocrine pancreatic insufficiency. The aim of our study is to describe pancreatic findings (by imaging) and to correlate with the presence of exocrine and / or endocrine function in a group of patients with this genetic disorder.
Aims & Methods: We performed a retrospective electronic medical record review of patients with VHL seen in our Pancreatic Disease Center. We collected the following information: age, sex, gender, genetic mutation, characteristics of organ involvement, pancreatic imaging findings and degree of cyst involvement, clinical evidence of exocrine pancreatic insufficiency (EPI) (the frequency of bowel movements, weight loss, steatorrhea, gas, post prandial abdominal distention), fecal elastase-1 measurement and evidence of endocrine insufficiency (HbA1c).
Results: A total of 13 patients were identified. Nine patients were women and four were men. The median age of our patient group was 37 (19-70). Of these 13 patients, eleven had a documented genetic mutation. Eleven patients had a strong family history of VHL. One was a sporadic mutation. Simple pancreatic cystic lesions were present in eight. In this group, six patients had complete cystic replacement of the pancreas, the median age was 46.5 (23-56), two patients had significant duodenal compression causing gastric outlet obstruction requiring laparoscopic gastrojejunostomy. Three had symptoms suggestive of EPI (all with complete cystic replacement of the pancreas) and two had a fecal elastase measured consistent with severe pancreatic exocrine insufficiency (less than 50 and 88 with normal being > 200). One patient provided an inadequate sample. Pancreatic enzyme replacement therapy was started with marked improvement in symptoms including weight gain. In addition, three patients with complete cystic replacement of the pancreas were screened for EPI, two had a normal fecal elastase and one provided an inadequate sample. Among the three patients with symptomatic EPI, all had a HbA1c measured and two were newly diagnosed with type 3c diabetes (HbA1c 6.8 and 8.1). Four patients had lesions in the pancreas highly suggestive of pancreatic neuroendocrine tumors (PNETs) and one had a lesion suggestive of a serous cystadenoma.
Conclusion: Complete cystic replacement of the pancreas is common in patients with VHL. Particular attention must be made for the early diagnosis of exocrine and endocrine pancreatic insufficiency, both of which were newly diagnosed in our small cohort. Guidelines for screening and management of pancreatic involvement in patients with VHL are needed to improve and standardize quality of care.
Disclosure of Interest: None declared

P1331 OBSERVATIONAL, PROSPECTIVE, SINGLE-CENTER STUDY TO EVALUATE THE DIAGNOSTIC YIELD OF THE DYNAMIC EUS, EUS-ELASTOGRAPHY AND ENDOSCOPIC PANCREATIC FUNCTION TEST (EPFT) FOR THE DIAGNOSIS OF EARLY CHRONIC PANCREATITIS (CP)

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Introduction: Early diagnosis of CP is hindered by the limited accuracy of diagnostic methods. EUS and the endoscopic pancreatic function test (ePFT) are the most sensitive morphological and functional method respectively in this setting. EUS-elastography allows for evaluating the degree of pancreatic fibrosis in CP, and the dynamic evaluation of the main pancreatic duct (MPD) after i.v. secretin provides with additional dynamic information. We developed a multimodal EUS-based approach for pancreatic evaluation by integrating these four methods.
Aims & Methods: Aim of our study was to evaluate the concordance among the different data obtained by this EUS-based multimodal test in patients with suspected early CP.
Methods: A prospective, observational study was designed. Patients with clinically suspected CP and 3-4 EUS criteria of the disease at EUS were included after informed consent. For the multimodal test, EUS was performed under deep

sedation with the Pentax EG-3270UK linear scope, attached to the HI-VISION Ascendus. Quantitative elastography was performed in the head, body and tail of the pancreas and the mean strain ratio (SR) was considered as the final result (normal SR < 2.25). After that, secretin (0.2 μg/kg) was given intravenously and duodenal fluid was collected at 15, 30 and 45 minutes thereafter for bicarbonate quantification (normal peak > 80 mEq/L). Diameter of the MPD was measured by EUS at 5, 10, 25 and 40 min after secretin stimulation. A maximal dilatation of the MPD of at least 50% from basal was considered as normal. A descriptive analysis was performed.
Results: 29 patients (mean age 39.8 years, range 18-65, 16 male) were included. The EUS-based multimodal procedure was feasible in 28 cases (19 with 3 EUS criteria and 9 with 4 EUS criteria of CP respectively). Elastography (SR) was abnormally high in all 28 patients. Peak bicarbonate concentration was abnormally low in 24 (85.7%) patients. Dynamic dilatation of the MPD after secretin was reduced in 21 (75%) cases. In addition to showing 3-4 criteria of CP at EUS, 20 patients (71.4%) had all three additional parameters abnormal (elastography, bicarbonate concentration and dynamic dilatation of the MPD) and strongly supported the diagnosis of CP. Five patients (17.9%) had two parameters abnormal (elastography and bicarbonate in one, and elastography and MPD distensibility in 4) and three patients (10.7%) had only the elastography abnormal. There were 2 complications related to the procedure: Mild acute pancreatitis and pulmonary aspiration related to deep sedation.
Conclusion: The multimodal EUS-based pancreatic evaluation including B-mode EUS, elastography, ePFT and dynamic evaluation of the MPD after secretin stimulation provides with relevant dynamic morphological and functional information of the pancreas supporting the diagnosis of early CP.
Disclosure of Interest: None declared

P1332 IMPACT OF PANCREATIC EXOCRINE INSUFFICIENCY (PEI) ON THE MORTALITY RATE OF CHRONIC PANCREATITIS (CP): A RETROSPECTIVE EVALUATION OF A SINGLE-CENTER PROSPECTIVE DATABASE

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Introduction: Prevalence of CP is increasing in last years mainly due to the improvement of diagnosing technologies. EPI, defined as the inability of the exocrine pancreas to perform a normal digestive function, is the leading consequence of CP. Little is known about the mortality in patients with CP, and there is no data about the mortality in patients with CP and EPI.
Aims & Methods: We aimed to assess the risk of death in patients with CP with and without EPI.
Methods: We performed a retrospective analysis of a prospectively collected database of patients with CP under follow-up in our Pancreas Unit. Diagnosis of CP and EPI was based on EUS and C13-MTG breath test respectively. Mortality rate and causes of death were compared between patients with and without EPI. Statical analysis was performed using the chi-square test and T-student test.
Results: A total of 480 patients were analyzed (77.5% men), with a median age of 53 years (range 15-88) during a median follow-up of 5.3 years (IC95% 4.2-6.4). Prevalence of EPI was 21.8% (105 patients), 82.7% men, with a median age of 54 years (range 15-83). Patients without EPI (375, 78.2%), had a median age of 53 years (range 19-88), and 75.7% were men. The main etiology was alcohol and/or smoking (63.3%). There were a total of 41 deaths (17.1‰ /year). The main cause of death was cancer (n = 16) of lung (n = 4), pharynx or larynx origin (n = 3), cholangiocarcinoma (n = 2), prostate (n = 2), and others. Six patients developed pancreatic cancer during follow-up, but only 1 patient died for this reason. Pancreatic cancer was diagnosed at early stage in the remaining 5 patients and are considered to be cured. Other causes of death were infectious disease (10 cases, 5 from biliary origin), liver cirrhosis (n = 4), cardiovacular disease (n = 4), and others (n = 7). The number of deaths among the EPI group was 18 (34.3 ‰/year), in contrast with the non-EPI group (23 cases, 12.3‰/year, $p < 0.001$), with median ages of 57 (IC95% 52-65) and 63 years (IC95% 58-66), respectively ($p < 0.05$). Causes of death were similar in patients with and without EPI. Median time between diagnosis of CP and death was (5.1 [IC95% 3.3-5.3] and 6.2 years [IC95% 4.8-8.4] in patients with and without EPI). Etiology of CP in patients who died was alcohol and/or tobacco in all cases except one (CFTR mutation).
Conclusion: Annual mortality rate in patients with CP in our cohort was 17.1‰ /year. Patients with CP die at a young age. Mortality rate is markedly higher in patients with CP and EPI than in those without EPI. Most deaths are related to alcohol and/or tobacco abuse. Surveillance of these patients may be a good strategy to prevent death from pancreatic cancer.
Disclosure of Interest: None declared

P1333 LONG-TERM FOLLOW-UP AND NATURAL HISTORY OF TROPICAL PANCREATITIS

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Introduction: Tropical pancreatitis has high morbidity and long-term complications. To study the natural history and occurance of malignancy, we followed a prospective cohort in S India.
Aims & Methods
Aims: To evaluate the long-term sequele and complications in Tropical pancreatitis and to estimate the survival in associated malignancy.
Methods: In this prospective study, we studied 1480 subjects with tropical pancreatitits in a tertiary referral centre attached to Trivandrum Medical college in S India recruited between January 1980 and March 2006 and followed up till March 2015. At each follow up visit, data were collected for any complications. C T scan, MRI and MRCP were carried out and mortality and morbidity were assessed. Univariate analysis, Cox Proportional Hazard regression and Kaplan Meir Survival curves were plotted and analysed.
Results: Of the 1480 sujects, 96% had cacific pancreatitis. Mean follow up was 9.3 years and median was 5-3 (range 1-33 years). 164 subjects developed pancreatic malignancy. Age in those with malignacy was 45 ± 12.4 years and 34.2 ± 12.08 in those without malignancy. 12 had pancreatic ascites and 8 had pancreatic absess. 38 percent in the malignancy group had hepatic/ distant metastasis and were inoperable. The relative risk of mortality for: age over 50 was 4.97 (95% CI 3.7-6.67); for smoking 1.39 (95% CI 1.01-1.89). KM survival probability were 0.55 (95% CI 0.42-0.66) at 3 months; 0.24 at 6 months and 0.13 at 9 months. Duration of diabetes and abdominal pain didnot affect survival.
Conclusion: Pancreatic malignacy developed in 11% of subjects with tropical pancreatitis on long-term follow-up and has increase chance of metastatsis and high mortality.
Disclosure of Interest: None declared

P1334 EVALUATION OF VITAMIN D STATUS IN PATIENTS WITH CHRONIC PANCREATITIS, RECURRENT PANCREATITIS AND AFTER PANCREATIC SURGERY

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Introduction: Deficiency of fat-soluble vitamins such as vitamin D (VD) is present in chronic pancreatitis (CP), reccurent pancreatitis (RP) and after pancreatic surgery (PS) but little is known for it extent.
Aims & Methods: To determine the prevalence of VD deficiency in patients with CP, RP and after PS and to assess its relationship to the severity of morphological imaging data. Study encompassed 78 patients (40 male, 38 female), mean aged 52 years (range 20-84y), who consented to participate; 49 patients suffered from CP, 21 patients – from RP, 8 patients underwent PS. Alcohol abuse was the most common aetiology (40 patients), 19 patients had chole- or choledoholithiasis, and 19 patients were with other etiology. Patients were divided into four groups (gr.) according to imaging morphological data based on Cambridge classification for CT/MRCP (grade I-IV): 18 in gr. I, 20 in gr.II; 21 in gr.III , and 19 in gr.IV; 39 patients were with proven pancreatic exocrine insufficiency (PEI). Exocrine function was evaluated using the secretin-enhanced MRCP, with ^{13}C mixed triglycerides breath test (cut-off at 29%) and faecal elastase-1 (normal > 200 μg/g). Determination of 25-hydroxyvitamin D (25OHD, sum of $25OHD_3$ and $25OHD_2$) was performed by a validated, DEQAS certified ID-LC-MS/MS method with accuracy and precision within 7.5% and linearity range 3.0-300.0 nmol/L. VD status was assessed as deficiency (25OHD < 25 nmol/L), severe insufficiency (25–50 nmol/L), mild insufficiency (50–80 nmol/L), and sufficiency (> 80 nmol/L). Statistical analysis was performed with SPSS v15 package.
Results: Total 25OHD for all patients was 38.9 ± 25.7 nmol/L (range 3.8–105.7 nmol/L); 30 patients (38.5%) had deficiency; profound insufficiency was found in 28.2% of patients; another 26.9 % were with mild insufficiency, and only 5 patients (6.4%) were in sufficiency status. Mean 25OHD in the morphological groups was as follows: gr.I: 58.0 ± 22.0 nmol/L, gr.II 49.6 ± 21.2 nmol/L, gr.III 30.0 ± 24.4 nmol/L and gr.IV 23.4 ± 20.0 nmol/L. VD status worsened with severity of morphological changes - deficiency, severe insufficiency, and mild insufficiency being respectively 11%, 22% and 67% (gr. I), 10%, 50% and 40% (gr.II), 62%, 24% and 14% (gr.III), and 68%, 16% and 16% (gr.IV). There was a statistically significant difference in VD status between gr.I and III, $p < 0.01$; gr.I and IV, $p < 0.001$; gr.II and III, $p < 0.05$; and gr.II and IV, $p < 0.01$. Lowest 25OHD levels (14.7 ± 6.1 nmol/L) were registered in patients with most severe imaging data (Cambridge III and IV) regardless of season or cause. VD status was lower in patients with proven PEI compared to without PEI, $p < 0.05$. VD status was lower in patients with alcohol aetiology, in females and in older patients > 50y but this is not statistically significant. There was no significant seasonal difference in VD status within groups.

Conclusion: Most of our patients with or without PEI were with vitamin D deficiency and insufficiency and there was a strong relationship between 25OHD levels and severity of morphological imaging changes.
Disclosure of Interest: S. Siminkovitch Financial support for research: Medical University Sofia- Research Project 5C/2014, M. Kovacheva-Slavova: None declared, B. Vladimirov Financial support for research: Medical University Sofia- Research Project 5C/2014, J. Genov: None declared, R. Mitova: None declared, P. Gecov: None declared, D. Svinarov Financial support for research: Medical University Sofia- Research Project 5C/2014, B. Golemanov: None declared

P1335 CHANGES OF IMMUNE SYSTEM AND CYTOKINE LEVELS IN PATIENTS WITH CHRONIC PANCREATITIS

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Introduction: According to the present point of view, there is an important complex of exogenous and endogenous etiological factors in development of chronic pancreatitis (CP): toxic-metabolic, immune, genetic, nutritional and many others, and that's why this disease is considered polyetiological.
Aims & Methods: To examine the state of the immune system and cytokine levels in patients with various forms of CP. There were examined of 210 patients with various forms of CP - I group - obstructive (26 patients), II - calculous (56) III – chronic inflammatory pancreatitis (78), IV - CP complicated by pseudocyst (50). Subpopulations of lymphocytes was determined using monoclonal antibodies (standard method NIH USA). Changes of levels of immunoglobulin classes IgA, IgM, IgG in the serum was determined by radial immunodiffusion Mancini. Study of proinflammatory and profibrotic cytokines TNF-α, IL-10, REG-1 α, TGF- β1, the concentration of lactoferrin was carried out by ELISA.
Results: Chronic inflammation with CP is accompanied by dysfunction of immune system: reduction of T-lymphocytes (CD3+), T-helper cells (CD4+), increase of level of citotoxic T-cels (CD8+), the phagocytic activity of neutrophils, activation of humoral immunity in all patients by the level of the CIC and B-cell markers (CD19+). The level of immune disorders increases with prolonged duration of disease. At the same time cytokine regulation of immune cells is disturbed, that is manifested by increased levels Lithostathine-1-alpha (REG-1α) 8.7 times (much more than in patients of III and IV groups ($p < 0.001$), and lactoferrin 18.7 times (much more than in patients of I and II groups ($p < 0.001$). The level of proinflammatory cytokines (TNF-α) was significantly higher in patients of II and IV groups ($p < 0.001$), the content of TGF-β1 - in patients of II and III ($p < 0.001$). For all patients it was characteristical decrease in the level of apoptosis protein receptor CD95 ($p < 0.01$).
In determining the relationship between markers of stone formation it was found that calcification of duct / pancreatic of parenchyma detected at the level of the coefficient of calcification (REG 1 α / lactoferrin) of less than 0.5. At the level of the coefficient of 0.5-1.0 - high probability of stone formation, and a value of 1.5 and above it - is low.
Identified markers of progression CP: coefficient calcification (REG 1α / lactoferrin) 0.5-1.0; translocation DNAase I from the cytoplasm to the nucleus of acinar cells; activation of collagen (reduction ratio oxyproline/ Glucuronic acid 0.5 below), increase in fibrosis activators (TGF-β1, TNF-a), intensification of lipid peroxidation (MDA).
Conclusion: All patients with CP were had violation of regulatory, proliferation and activation functions of the immune system, which leads to frustration in the cytokine level of immunity and, consequently, the deepening of the inflammatory and fibrotic process.
Disclosure of Interest: None declared

P1336 HIGH PREVALENCE OF EXOCRINE PANCREATIC INSUFFICIENCY IN 1105 SWEDISH PATIENTS WITH GASTROINTESTINAL SYMPTOMS

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Introduction: With age, there is a physiological decline of organ function. For the pancreas this could be demonstrated histologically in a autopsy study[1] and also in an epidemiological study[2]. The aim of this study was to determine the exocrine pancreatic function in a cohort of patients with clinical symptoms of pancreatic insufficiency (eg, abdominal pain, diarrhea, bloating) which, however, had no previously diagnosed pancreatic pathology.
Aims & Methods: District physicians and gastroenterologists were offered to perform a fecal elastase-1 test in those patients who had gastrointestinal symptoms that could indicate exocrine pancreatic insufficiency (EPI) (abdominal pain, bloating, diarrhea). Patients had no known pancreatic disorders.
Results: 1105 F-elastase (FE-1) tests were performed by a standard ELISA (ScheBo Biotech®). The referring doctors received the test result and were offered counseling by phone. The results showed that 208/1105 (18.4%) had exocrine pancreatic insufficiency (EPI) (<200 μg/g) and 8.3% had even FE 1 <100 μg/g. The EPI-frequency increased with age: 8.3% for less than 30 years and 29% in the group older than 80 years. The results confirmed our interim analysis from 2014. In a separate group of patients with diabetes mellitus (n = 89; 80% IDDM), which was tested regardless of clinical manifestation, the frequency of EPI has also been significantly higher and 7.9% showed an FE-1 < 100 μg/g.
Conclusion: Consistent with previous studies, we were able to identify a high EPI frequency in patients who have some type of gastrointestinal symptoms. The prevalence of EPI was markedly increasing with age.

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Disclosure of Interest: None declared

P1337 EVALUATION OF PREALBUMIN AND RETINOL BINDING PROTEIN AS SCREENING TOOLS FOR MALNUTRITION IN PATIENTS WITH CHRONIC PANCREATITIS, RECURRENT PANCREATITIS AND AFTER PANCREATIC SURGERY – PRELIMINARY RESULTS

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Introduction: Malnutrition is one of the most important consequences in chronic pancreatitis and it correlates with risk of complications and mortality. Its early assessment with serum nutritional markers together with imaging and anthropometric data provide better decisions regard to enzym replacement therapy.
Aims & Methods: Evaluation of the potential role of prealbumin (preAlb) and retinol binding protein (RBP) as screening tools for malnutrition in patients with chronic pancreatitis (CP), recurrent pancreatitis and after pancreatic surgery and their correlation with morphological changes based on CT/MRCP data. Serum samples of 80 patients (41 male, 39 female) at mean age 52 (20-84) were collected in our centre for the period February 2014 – April 2015. 49 patients had CP, 22 patients – recurrent pancreatitis, 9 patients underwent pancreatic surgery. Alcohol was the most common aetiology being the cause in 41 patients (51.3%), 19 patients had chole- and choledoholithiasis and 20 patients were with other etiology. Exocrine function was evaluated using the secretin-enhanced MRCP, ^{13}C mixed triglycerides breath test (cut-off 29%) and faecal elastase-1 (normal >200 μg/g). 39 patients were with pancreatic exocrine insufficiency (PEI) and 41 without. We divided patients according to imaging morphological data based on Cambridge classification for CT/MRCP (grade I–IV) in group (gr.) I-19, II-20; III-22; IV-19 patients. Serum preAlb and RBP levels were measured by immunonephelometry assay. In addition to clinical information, BMI, imaging data, preAlb and RBP were assessed and other proteins: albumin and CRP. The statistical analysis was performed via SPSS version 15.
Results: Mean ± SD in common group: PreAlb for all patients was 0.2001 ±0.1016g/L, and RBP- 0.0384 ±0.0289; 40% of patients (7% of Cambridge grade I) had both preAlb and RBP below reference limits; 52% of patients were with preAlb under 0.2 g/L (mean 0.1309) with following distribution in Cambridge groups: I- 26%; II- 50%; III- 62% and IV- 75%. RBP under 0.03 g/L was found in 46.25% of patients (mean 0.0286) with following distribution in Cambridge gr. I- 26%; II- 50%; III- 52% and IV- 50%. PreAlb mean for patients with proven PEI was 0.1875 vs. 0.2120 in those without PEI, and for RBP 0.0368 vs. 0.0401. Based on clinical data and BMI the estimated sensitivity and specificity for malnutrition detection of preAlb are 68.85% (95% CI 55.71% to 80.10%) and 73.68 with positive predictive value 89.36%. The sensitivity and specificity of RBP in the group are 57.14% and 79.17% respectively with a positive predictive value of 86.49%. When comparing the data for prealbumin and RBP with imaging morphological data we found statistically significant correlation. It is for preAlb between gr. I and gr. III, $p < 0.05$; between gr. I and gr. IV, $p < 0.01$; as well between groups with mild imaging changes (both I and II) and groups with severe imaging changes (III and IV), $p < 0.05$. Similar were data regard to the RBP ($p < 0.001$).
Conclusion: Prealbumin and RBP tests are easy to perform and reliable tools in combination with imaging data and BMI for screening of malnutrition in patients with CP.
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P1338 IMAGING MODALITIES IN CHRONIC PANCREATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Chronic pancreatitis (CP) is an inflammatory disease of the pancreas, which often is accompanied with severe pain and impaired endocrine and exocrine pancreatic function. Imaging modalities are indispensable for the diagnosis and the treatment of CP. The most frequent used imaging modalities are endoscopic retrograde cholangiopancreatography (ERCP), abdominal ultrasonography (US), endoscopic ultrasonography (EUS), magnetic resonance imaging (MRI) or computed tomography (CT). Aim of this study was to give diagnostic accuracy summary estimates for imaging modalities for CP.

Aims & Methods: A broad systematic search was performed in Cochrane Library, MEDLINE, EMBASE and CINAHL databases for studies evaluating imaging modalities for CP. The search included terms for chronic pancreatitis, MRI, CT, EUS, ERCP and US. The inclusion criteria were: one or more imaging modality was evaluated in patients with CP (≥5 patients), the imaging technique was compared with a reference standard, and enough data was reported to extract the number of true-positive, true-negative, false-positive, and false-negative results. We excluded studies that reported other imaging techniques than mentioned above, or imaging techniques used for treatment, reviews, case-reports, and book chapters. All search hits were evaluated for eligibility by two reviewers. The Quality Assessment of Diagnostic Accuracy Studies - 2 (QUADAS-2) tool was used to assess the methodological quality of the included studies. Bivariate random-effects modeling was used to obtain summary estimates of sensitivity and specificity (I2 > 25%).
Results: A total of 7641 titles and abstracts were screened for eligibility. For 220 studies, the full text was retrieved, of which 45 studies fulfilled the inclusion criteria, with evaluation of 3629 patients. Sensitivity of ERCP 82% (95% CI: 76% > 87%) was significant higher than the sensitivity of US 67% (95% CI: 53% > 78%) (p = 0.018). The sensitivity of EUS 82% (95% CI: 71% > 90%), MRI 78% (95% CI: 69% > 85%) and CT 75% (95% CI: 66% > 83%) did not differ significantly. There were also no significant differences in specificity for the CT 91% (95% CI: 81% > 96%), MRI 96% (95% CI: 90% > 98%), EUS 91% (95% CI: 83% > 95%), ERCP 94% (95% CI: 87% > 98%) and US 98% (95% CI: 89% > 100%).
Conclusion: The ERCP and EUS have the highest diagnostic accuracy of all the imaging modalities in detection of CP, followed by the CT and MRI. The US had the lowest diagnostic accuracy.
Disclosure of Interest: None declared

P1339 COMPARISON OF DIFFERENT CLASSIFICATION TOOLS FOR THE DIAGNOSIS OF CHRONIC PANCREATITIS

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Introduction: Several classification tools for the diagnosis of chronic pancreatitis (CP) are used in daily practice and in clinical research. There are, however, no studies describing and comparing the differences between the classification tools. The aim of this study was to compare the Mannheim, Büchler and Luneburg classification tools for CP.
Aims & Methods: A retrospective analysis of a prospectively collected multicentre patient cohort including 669 patients with a first episode of acute pancreatitis was performed. The patients were retrospectively followed-up for a median period of 5 years, through medical records and patient's questionnaires. We evaluated and compared the Mannheim, Büchler and Lüneburg classification tools for 1) the diagnosis of CP; 2) the influence of each criteria (subtracting or adding) within the classification tool on the total number of diagnosed patients; 3) the agreement (Kappa) of the different classification tools; 4) the estimated sensitivity, specificity, positive predictive value and negative predictive values for each classification tool with Bayesian latent-class analysis.
Results: The median follow-up period of the patients was 57 months (IQR 42-70). 1) CP was diagnosed in 50 (7%), 60 (9%), 59 (9%), 61 (9%) and 46 (7%) of 669 patients by the Mannheim definite, Mannheim propable, Lüneburg, Büchler and the treating physician, respectively. 2) Adding or subtracting of the following criteria led to significant changes in the total number of diagnosis of CP: abdominal pain, recurrent pancreatitis, moderate to marked ductal lesions, endocrine and exocrine insufficiency, pancreatic calcifications and pancreatic pseudocysts. 3) The overall agreement between the Mannheim, Büchler and Lüneburg was substantial (Kappa 0.75, ranging 0.69 – 0.79). The agreement between the different classification tools and the diagnosis made by the physician was moderate (Kappa 0.60, ranging 0.52 – 0.71). 4) The Büchler score had the highest sensitivity (94%), followed by the Mannheim (87%) and the Lüneburg tool (81%). The specificity ranged from 97% to 99%, with the positive predictive value ranging from 72% (Lüneburg) to 92% (Mannheim).
Conclusion: Differences between the total number of diagnosis of CP by the classification tools can be mainly attributed to whether abdominal pain or recurrent pancreatitis, exocrine and endocrine pancreatic insufficiency, pancreatic calcifications, moderate to marked ductal lesions and pancreatic pseudocysts are included in the classification tools. A combination of these criteria in a modified classification tool may lead to a higher diagnostic accuracy for the diagnosis of CP. The overall agreement between the classification tools was substantial.
Disclosure of Interest: None declared

P1340 CHRONIC PANCREATITIS: WHERE DO WE STAND? AN INTERNATIONAL MULTIDISCIPLINARY SURVEY AND CASE VIGNETTE STUDY

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Introduction: There is very little insight into factors associated with the decision making of surgeons and gastroenterologist in different aspects of diagnoses and treatment of chronic pancreatitis (CP). The aim of the study was to gain more insight into the current opinion and clinical decision making of international expert pancreatologists regarding the diagnosis and treatment of CP.
Aims & Methods: An online survey and clinical case vignettes regarding the diagnosis and treatment of CP was send by e-mail to members of the International Hepato-Pancreato-Biliary Association, American Pancreatic Association, European Pancreatic Club, European Society of Gastrointestinal Endoscopy and the Dutch Pancreatitis Study Group. The survey consisted of several short questions regarding the use of imaging modalities and classification tools in the diagnosis of CP. Furthermore, the use of surgery, endoscopy and extracorporeal shock wave lithotripsy (ESWL) in the treatment of CP. This survey was proceeded by questions and statements regarding several controversial and clinical cases of CP.
Results: A total of 288 pancreatologists, 56% surgeons and 44% gastroenterologists, participated with the survey. The majority (54%) was registered as a specialist for over 10 years and 77% worked at an academic center in Europe (59%), North-America (16%) or Asia (15%). 52% of the specialists did not use any classification tool for the diagnosis of CP, the rest used either the Mayo Clinic (28%), Mannheim (25%), or Büchler (25%) tools. Overall, computed tomography was the most preferred imaging modality to asses an enlarged pancreatic head (59%), pancreatic pseudocyst (55%), pancreatic calcifications (75%) and peripancreatic fat infiltration (68%). Magnetic resonance imaging was preferred when evaluating main pancreatic duct abnormalities (60%). The majority (59%) of the gastroenterologists indicated to use ESWL the treatment of CP. Total pancreatectomy with auto-island transplantation (TP-AIT) was significantly more often performed in North-America, compared to other continents (p < 0.001). TP-AIT was most preferred treatment in patients with parenchymal calcifications, without dilatation of the main pancreatic duct (PD) (27%) and in patients with refractory pain despite maximal medical, endoscopic and surgical treatment (21%). Distal pancreatectomy (57%) or endoscopic + ESWL (39%) were the preferred treatments of a solitary stone in the PD of the pancreatic tail. In patients with casting stones over the entire PD, 59% preferred an operation (Frey) versus 41% endoscopic + ESWL, as was the case in patients with an enlarged pancreatic head, 58% preferred an operative treatment (PPPD) versus 42% endoscopy.
Conclusion: In most clinical cases there was no consensus regarding the preferred treatment, with variance between surgery or endoscopy/ESWL. The diversity of clinical and morphological presentation of CP and lack of evidence based guidelines and studies, demonstrate that the clinical decision making is for most part still based on local expertise, beliefs and disbeliefs. The treatment should be performed in a multidisciplinary team in an expert center.
Disclosure of Interest: None declared

P1341 ADVANCES IN HIGH RESOLUTION CROSS SECTIONAL IMAGING AND THE RISING PREVALENCE OF PANCREATIC CYSTS OVER THE PAST DECADE

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Introduction: Increasingly, pancreatic cystic lesions (PCLs) are being discovered incidentally in patients who undergo cross-sectional imaging. It has been suggested that this increase is a direct result of the development of more sophisticated imaging techniques, but only limited data are available on the real prevalence of PCLs.
Aims & Methods: To determine the PCL prevalence in patients undergoing magnetic resonance imaging (MRI) for non-pancreatic indications on successive MR systems. Also, to compare prevalence based on the demographic and comorbidity features of the patients.
All consecutive abdominal MRIs performed between January and February from 2005 to 2014 were listed. Clinical charts were chronologically reviewed to identify the first 50 suitable candidates of each year. Exclusion criteria were: positive history of pancreatic disease including cysts, pancreatic symptoms, pancreatic indication of the study or previous abdominal MRIs. Once selected, each study was reviewed by an expert pancreatic MRI radiologist.
Results: 1962 patients were reviewed to find 500 suitable candidates. Overall, 208 patients(41.6%) had a non-reported incidental cyst. The proposed diagnosis was uncertain in 128 cases(62%), followed by an IPMN in 72 patients(35%). Extrapancreatic cysts were found in 70% of the patients and were strongly associated with PCLs. The univariate logistic regression showed a strong relationship between PCLs and age (p < 0.0001), diabetes mellitus (DM) (p = 0.001) and personal history of a previous cancer (p = 0.01) (specifically, non-melanoma skin cancer [p = 0.03] and hepatocellular carcinoma [p = 0.02]). The multivariable model showed a strong association between the type of hardware and software and PCLs (p < 0.0001) with newer versions corresponding with increased numbers of detected PCLs. Although PCLs occurred with greater frequency in the higher field strength MRIs, it was not significantly associated (p = 0.10). However, the small number of 3T MRIs limited the ability to test with sufficient power.
Table 1: Association between MRI technical features and diagnosis of PCLs

		Univariate analysis		Multivariate analysis	
Variable	% with PCL	OR (95% CI)	P value	OR (95% CI)	P value
Hardware platform*		Overall test 0.0002		Overall test <0.0001	
Symphony (2001)	30.3	1.00	–	1.00	–

(continued)

Table 1: Continued

Variable	% with PCL	Univariate analysis OR (95% CI)	P value	Multivariate analysis OR (95% CI)	P value
Sonata (2001)	23.1	0.7 (0.3-1.6)	0.37	1.0 (0.4-2.5)	0.98
Espree (2004)	48.4	2.2 (1.2-3.9)	0.012	2.7 (1.3-5.4)	0.005
Avanto (2006)/ Aera (2013)¤	49.0	2.2 (1.4-3.4)	0.0004	3.0 (1.8-5.0)	<0.0001
Skyra (2010)	56.3	3.0 (1.4-6.4)	0.006	3.9 (1.6-9.2)	0.002
Software		Overall test <0.0001		Overall test <0.0001	
VA	29.0	1.00	–	1.00	–
VB	49.1	2.4 (1.6-3.5)	<0.0001	3.0 (1.9-4.7)	<0.0001
VD	51.4	2.6 (1.3-5.3)	0.009	3.1 (1.4-6.8)	0.006

*Install date included with platform model. Skyra is 3T other platforms are 1.5T¤These 2 versions, technically similar, were merged due to small sample size

Conclusion: Our study demonstrates the relationship between the higher trend of incidental PCLs observed in recent years and the improvements in the technical features of MRIs. Also, we confirmed the association between older age, DM and PCLs. In addition, we postulate that a history of non-pancreatic neoplasms and extrapancreatic cysts may have an influence on the presence of PCLs
Disclosure of Interest: None declared

P1342 INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM INTERNATIONAL REGISTRY: LONG-TERM ANALYSIS

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Introduction: Intraductal papillary mucinous neoplasms (IPMNs) are increasingly diagnosed with a variable natural history. Given their malignant potential, intensive surveillance programs are recommended. However, it is unclear whether all patients benefit from this strategy
Aims & Methods: To calculate the frequency of malignant transformation in an long-term observational IPMN cohort. Also, to describe the demographic, clinical and imaging features associated with malignancy.
A longitudinal IPMN registry was created involving five centers in Europe and the United States. Patients with a clinical suspicion of IPMN were included. Data regarding demographics, symptoms, imaging tests and surgical procedures were collected. Only patients with a follow-up greater than 1 year and with incident malignant cases (diagnosed 3 months after the initial visit) were analyzed. Malignancy was defined as surgically-confirmed high-grade dysplasia or invasive cancer. The demographic, clinical and imaging features of the malignant group were compared with the rest of the cohort in both the initial and the last visit
Results: A total of 495 patients seen between 1999 and 2014 were included, with a median follow-up of 3 years. The median age was 67 with a female predominance (65%). 89% of the cohort had a branch duct involvement. There was a median number of 1 cyst per patient (median size of 15mm). Overall, 19 patients were diagnosed with malignancy with a time until diagnosis ranging from 3 months to 11 years. The incidence of malignancy was 7 cases per 1000-persons-year with a bimodal distribution corresponding to the intervals 3-36 and 54-66 months. An isolated case was diagnosed after 11years of follow-up. No differences between groups were seen regarding age, gender or BMI. Cyst size, main/mixed duct involvement and the presence of symptoms, concretely steatorrhea and diabetes mellitus, were significantly associated with malignancy during the entire follow-up.
Table 1: Study variables significantly associated with malignancy

VARIABLE	INITIAL VISIT			FINAL VISIT		
Malignancy (%)	Control (%)	P value	Malignancy (%)	Control (%)	P value	
Cyst size	16	451	0.003*	13	344	<0.001*
Mean (mm) ± SD	27.7 ± 16.0	17.5 ± 12.4	32.2 ± 10.1	17.2 ± 10.4		
Duct involvement	19	469	<0.001¥	15	370	0.001¤
Main/Mixed duct	9 (47.4%)	43 (9.2%)	6 (40.0%)	30 (8.2%)		
Branch duct	10 (52.6%)	426 (90.8%)	9 (60.0%)	340 (91.9%)		
Mass-nodule	19	472	0.14¤	16	429	<0.001¥
Yes	3 (15.8%)	31 (6.6%)	5 (31.3%)	14 (3.2%)		
Symptoms	19	473	<0.001¤	17	463	<0.001¥
Yes	15 (79.0%)	167 (35.3%)	8 (47.1%)	45 (9.7%)		
Steatorrhea	19	476	0.03¤	19	476	0.04¤
Yes	17 (89.5%)	470 (98.7%)	1 (5.3%)	0 (0%)		
Diabetes mellitus	19	476	<0.001¥	19	476	<0.001¥
Yes	7 (36.8%)	50 (10.5%)	6 (31.6%)	33 (6.9%)		

*Wilcoxon rank-sum test, ¥Chi-square test, ¤Fisher's exact test

Conclusion: Malignant transformation of IPMNs tends to occur in the first 6 years since diagnosis. Late malignant transformations are rare, although the risk is still present. The cyst size, main/mixed duct involvement and pancreas-specific symptoms are good predictors of malignancy.
Disclosure of Interest: None declared

P1343 MODELLING OF SUSPICIOUS AND HIGH RISK ENDOSONOGRAPHIC MORPHOLOGY, CYTOPATHOLOGY AND CYST BIOCHEMISTRY HIGHLIGHTS THE ACCURACY OF ENDOSONOGRAPHY TO PREDICT OPERATIVE HISTOLOGICAL OUTCOME IN PANCREATIC CYSTIC TUMOURS

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Introduction: Distinguishing benign from potentially malignant pancreatic cystic lesions has important prognostic and therapeutic implications. Diagnosis is achieved through a combination of history, imaging, biochemical, endoultrasonographic (EUS) and cyst aspirate (CA) analysis. We evaluated the accuracy of suspicious and high risk variables identified at EUS and CA analysis to predict premalignant or malignant histopathology confirmed at surgery.
Aims & Methods: Patients who underwent EUS prior to surgery were selected. Data on age, sex, cyst location, suspicious (S) or high risk (HR) EUS or CA features, diagnosis (grouped as benign vs premalignant/malignant) at EUS (EUS-D), post CA analysis (CA-D) and combined EUS and CA analysis (EUS&CA-D) were collected. These were compared with final histological diagnosis (H-D) from surgery. High-risk (HR) variables were defined as C4/C5 diagnosis or carcinoma embryonic antigen (CEA) >192ng/ml on CA, and cyst size >30mm, PD dilatation >10mm, mural nodules or mixed solid/cystic components at EUS Suspicious (S) variables included HR features or mucin, C3 diagnosis or amylase >1000 U/L on CA, and pancreatic duct (PD) dilatation or cyst wall thickening on EUS. Variables were assigned a score of 1 when present, and combined with either EUS-D (EUS-D-S or EUS-D-HR) or CA-D (CA-DS or CS-D-HR). A single positive variable defined positivity in groups. EUS and CA outcomes were then evaluated to identify the sensitivity, specificity, area under the ROC curve (AUC) and likelihood ratio (LR) to predict H-D.
Results: 38 patients were identified (mean age 60.4 years, range 19-81; 52.6% female). Histology identified benign (18.5%; retention cysts, accessory spleen, chronic pancreatitis, hydatid, serous cystic neoplasm), premalignant (60.5%; intraductal papillary mucinous neoplasm (IPMN), mucinous cystadenoma, solid pseudopapillary tumour) or malignant disease (21.1%; adenocarcinoma, adenosquamous carcinoma, neuroendocrine tumour). Analysis (AUC and LR) ranked by AUC confirmed EUS-D-S significantly predicted H-D (0.81, p = 0.022; 5.87) with a sensitivity and specificity of 83.7% and 85.7% respectively. This was followed by EUS-D-HR (0.68; 4.29; p = 0.187), CS-D-HR (0.64; 1.83; p = 0.306), EUS&CA-D-HR (0.62; 1.81; p = 0.374) and CS-D-S (0.52; 1.04; p = 0.89). EUS&CA-D-S did not predict H-D (0.5; 1.16; p = 1.0).
Conclusion: EUS can accurately predict final H-D in patients cystic pancreatic lesions with excellent sensitivity and specificity when modelled appropriately. Interestingly, the accuracy of this method diminished when combined with CA variables.
Disclosure of Interest: None declared

P1344 BIOMARKER RESEARCH IN PANCREATIC NEUROENDOCRINE NEOPLASIAS: CUX1 AND DRUG METABOLISM MARKERS AS MODULATORS OF RESPONSE TO CYTOTOXIC CHEMOTHERAPY

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Introduction: Previously, we presented an association between the expression of the transcription factor CUX1, metastatic behaviour and poor differentiation in human insulinomas. CUX1 mediated tumor-promoting functions via enhancing proliferation, resistance to apoptosis and angiogenesis *in-vitro*. In patients with non-functioning pancreatic neuroendocrine tumors (PNETs), the role of CUX1 has to be elucidated. In these patients, chemotherapy is recommended as first-line therapy in metastatic disease. However, biomarkers in this setting are still lacking. Therefore we assessed the role of CUX1 and proteins involved in the metabolism of cytotoxic chemotherapy in patients with metastatic PNETs.
Aims & Methods: We analysed expression of CUX1, O6-methylguanine-DNA methyltransferase (MGMT), thymidylate synthase (TS) and dihydropyrimidine dehydrogenase (DPD) via immunohistochemistry in 34 out of 93 PNET patients treated with streptozocin (STZ)-based regimens and dacarbacine (DTIC). To further assess the functional role of CUX1, profiling of DNA damage-, proliferation- and apoptosis-associated genes was performed in CUX1-modulated BON1 cells. Genes regulated on mRNA level were validated via immunoblotting. Statistical evaluation was performed with cox regression, log-rank test and Fisher's exact test.

Results: The mPFS (progression-free survival) in this cohort receiving chemotherapy was 11 months. 80% of the patients progressed within 24 months. A predefined CUX1 immunoreactivity score (IRS) higher than 8 was significantly associated with shorter PFS in this patient cohort. Functionally, CUX1 affects caspases and DAPK1 as mediators of resistance mechanisms to cytotoxic drugs. In contrast, established drug metabolism markers such as MGMT and DPD had no predictive value. Interestingly, decreased TS expression was linked to reduced PFS in patients receiving cytotoxic chemotherapy.
Conclusion: We identified the transcription factor CUX1 and TS as modulator of responsiveness to chemotherapy and potential novel biomarker in patients with PNETs.
Disclosure of Interest: None declared

P1345 ACCURACY OF PREOPERATIVE DIAGNOSIS AND SURGICAL MANAGEMENT OF PATIENTS WITH PANCREATIC CYSTS

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Introduction: Optimal preoperative diagnosis of pancreatic cysts improves decision making. In premalignant pancreatic cysts, surgery prevents malignant progression. However, the natural history of pancreatic cysts is not well characterized and cysts with dysplasia do not always develop invasive malignancy. Therefore, it is unclear in which patients the benefits of surgery outweigh the risks.
Aims & Methods: We aimed to determine the accuracy of the preoperative diagnosis in patients with pancreatic cysts who underwent resection and to evaluate the proportion of patients in whom surgery was retrospectively justified. From our prospective database (2006-present) of patients with pancreatic cysts, we extracted patients who underwent pancreatic surgery. The decision for surgical treatment was made in our multidisciplinary pancreatic and hepatobiliary meeting based on the international guidelines (Tanaka et. al 2012 and Del Chiaro et al. 2013). Surgery was considered justified for malignancy and symptomatic pancreatic cysts (i.e. recurrent pancreatitis, weight loss or abdominal pain likely caused by the cyst). Cysts with high-grade (HG) dysplasia or invasive malignancy were considered malignant.
Results: From the 113 patients who underwent resection, data were incomplete for 3 patients. Therefore 110 patients were included in our analysis (median age 62.5 years (IQR 48.75-71), 58% female). Patients underwent surgery median 3 months (IQR 2-6) after identification of the cyst. Only 11 patients (10%) were referred for surgery during initial follow-up because of suspicion of malignancy (8%) or symptoms (2%). Preoperative classification of the type of cyst was correct in 71% of patients and in 86% of patients the correct differentiation between benign and (pre)malignant was made.
In hindsight, surgery was justified in 46% of patients: resection of a neoplastic pancreatic cyst with invasive malignancy (22%) or HG dysplasia (5%), pancreatic malignancy (7%), solid pseudopapillary neoplasm (4%), neuroendocrine tumour (2%), acinar cell carcinoma (1%), sarcoma of the stomach (1%) or a symptomatic cyst (5%). In the remaining 54% of patients surgery could be seen as overtreatment: resection of a premalignant cyst without HG dysplasia or invasive malignancy in 42% and of a pancreatic cyst with no malignant potential in 13%.
Conclusion: In most patients with pancreatic cysts preoperative differentiation between benign and (pre)malignant is correct. Nevertheless, when following the current guidelines, overtreatment is inevitable.
Disclosure of Interest: S. Lekkerkerker: None declared, M. Besselink: None declared, O. Busch: None declared, E. Rauws: None declared, P. Fockens Consultancy: Olympus, Fujifilm, Covidien, J. van Hooft Consultancy: Cook, Boston Scientific, Covidien

P1346 WINDOW OF OPPORTUNITY IN RESECTABLE PANCREATIC CANCER

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Introduction: The diagnostic dilemma of imaging-based resectability assessment in pancreatic cancer is illustrated by the facts that 1) a tumor that has been considered resectable still carries the risk of understaged disease due to diagnostic inaccuracy, 2) determining the resectability of a tumor cannot rule out rapid tumor progress or incipient dissemination once the diagnosis has been made. Comprising a significant fraction of the patients' overall survival, a prolonged delay from onset of symptoms to diagnosis and treatment may even imply an increased risk for unanticipated progression from resectable to unresectable disease at laparotomy (UDP). In contrast to tumor size (TS) and vascular involvement (VI) at diagnostic imaging, the ''window of opportunity'', i.e. time interval from imaging to resection (IR) represents a risk factor for UDP that may be may be potentially controllable.
Aims & Methods: To evaluate the IR interval together with vascular involvement (VI) and tumor size (TS) as potential risk factors for UDP. Patients with histologically confirmed PC planned for curative-intent resection from 2008-2014 were identified from a prospectively maintained database. IR, TS, and VI were recorded. Their impact on UDP was evaluated using univariate and multivariate regression. Risk estimates were approximated as hazard ratios (HR).
Results: Median IR was 43 days. Of 349 PC patients planned for resection, 82 had UDP (resectability rate 86.5%). The UDP risk increased significantly for IR $\geq$ 33 days (26.2% vs 13.5%; HR 2.270; $p = 0.021$) and TS > 30 mm (28.6% vs 10.5%; HR 2.732; $p < 0.001$). Major VI significantly increased the UDP risk in univariate (37.9% vs 20.6%, HR 2.423; $p = 0.007$) but did not contribute to the prediction model in multivariate analysis ($p = 0.411$), in contrast to IR ($p = 0.029$) and TS ($p < 0.001$), which were independent UDP risk factors. UDP confirmed <33 days after imaging was significantly associated with a prolonged disease-specific survival (15.4 vs 6.7 months, $p = 0.019$).
Conclusion: Determining a low-stage pancreatic cancer at diagnostic imaging cannot rule out rapid tumor progress to advanced-stage or incipient dissemination once the diagnosis has been made. Operation within 33 days after diagnostic imaging may halve the risk of unanticipated tumor progression at laparotomy. The results underscore the need of efficiency and streamlining in the management of pancreatic cancer at all stages of medical care.

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Disclosure of Interest: None declared

P1347 PAIN AS A PREDICTOR OF SURVIVAL IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA – A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Neuropathic, abdominal pain occurs in the majority of patients with pancreatic ductal adenocarcinoma (PCa). Serveral studies could clearly demonstrate that the severity and frequency of pain correlates with pathohistological characteristics of PCa. Nevertheless a consensus of the clinical value of pain as predictor of abdominal pain hasn't been reached yet.
Aims & Methods
Aims: Investigation of pain as a prognostic tool in patients with PCa.
Methods: For this purpose PRISMA-Guidelines were used to perform systematic review and meta-analysis. By screening the databases of Scopus, Pubmed, The Cochrane library and Google Scholar for the terms ''pain'', ''survival'', ''recurrence'', ''pancreatic ductal adenocarcinoma'' and ''pancreatic cancer relevant papers were extracted and included in systematic review.
Results: A total of 4000 studies could be identified analyzing the influence of pain in PCa. After exclusion of irrelevant paper 38 studies could be identified meeting all predefined inclusion criteria for systematic review. 7 univariate hazard ratios (HR) and 2 univariate odds ratios (OR) could be included in the meta-analysis, identifying pain as a strong prognostic factor on OS (HR 1.63, CI: 1.18-2.24, $p = 0.003$; OR 2.69, CI: 1.56-4.62; $p = 0.0004$). Furthermore, by pooling multivariate HR, pain was revealed to be also an independent factor on OS (HR 1.55, CI: 1.29-1.87, $p < 0.00001$).
Conclusion: This is the first systematic review and meta-analysis investigating the impact of pain on OS in patients with PCa.
Here, we could clearly identify pain as a negative predictor of patients' outcome. Therefore, abdominal pain in patients suffering from PCa should receive increased attention due to its high clinical relevance.
Disclosure of Interest: None declared

P1348 OUTCOME AND SURVIVAL AFTER DISTAL PANCREATECTOMY FOR PANCREATIC DUCTAL ADENOCARCINOMA: A NATIONWIDE RETROSPECTIVE ANALYSIS

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Introduction: Nationwide series on outcome and predictors of survival after distal pancreatectomy (DP) for pancreatic ductal adenocarcinoma (PDAC) are lacking.
Aims & Methods: Adults who underwent DP for PDAC in 17 Dutch pancreatic centers between January 2005 and September 2013 were analyzed retrospectively. Patients were excluded when histopathological diagnosis was not PDAC or when data was lacking. Primary outcome was survival. Predictors of survival were identified using a Cox regression model.
Results: In total, 761 consecutive patients were identified, 620 patients were excluded, because of non-PDAC histopathology (n = 616) or lack of data (n = 4). Therefore, 141 patients (45% (n = 63) male, mean age 64 years (SD10)) were included. Multivisceral resection was performed in 43 patients (30%) and laparoscopic resection in 7 patients (5%). A major (Clavien-Dindo score III or higher) complication occurred in 33% of patients. Mean tumor size was 44mm (SD23) and histopathological examination showed 70 R0 resections (50%). 90-day mortality was 6%. Overall, 63 patients (45%) received adjuvant chemotherapy. Median survival was 17.0 months (IQR 13.0-21.0) with a median follow-up of 17 months (IQR 8-29). One-, three- and five-year cumulative survival were 64%, 29% and 22%, respectively. Independent predictors of poor postoperative survival were R1/R2 resection (HR 1.63 (95% CI 1.09-2.43)), pT3/pT4 stage (HR 1.92 (95% CI 1.28-2.86)) and not receiving adjuvant chemotherapy (HR 1.59 (95% CI 1.06-2.38)).
Conclusion: This nationwide series identified several independent predictors of survival after DP for PDAC. Further studies should assess to what extent improved surgical technique, patient selection and use of adjuvant chemotherapy improve survival.
Disclosure of Interest: None declared

P1350 CONTRAST-ENHANCED ENDOSCOPIC ULTRASONOGRAPHY FOR PANCREATIC CANCER: DIFFERENTIAL DIAGNOSIS AND HISTOLOGICAL EVALUATION

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Introduction: The differential diagnosis of pancreatic solid lesions remains challenging. The aim of this study was to investigate the usefulness of contrast-enhanced endoscopic ultrasonography (CE-EUS) in differentiating pancreatic cancer (PC) from other pathological lesions. In addition, to examine what histology CE-EUS images reflected, the images were compared with histology in PC with resection.
Aims & Methods: CE-EUS was performed for patients with a pancreatic solid lesion consecutively. Tumors were classified into three vascular patterns (hypervascular, isovascular, and hypovascular) at two time phases (early phase and late images). The correlations between vascular patterns, and histology of tumors or immunostaining of resected PC tissues were examined.
Results: Total 147 patients underwent CE-EUS. The final diagnoses were PC (n = 109), inflammatory mass (n = 11), autoimmune pancreatitis (n = 9), neuroendocrine tumor (n = 8) and others. In late phase image, 104 of 109 PCs showed hypovascular pattern, which diagnosed PC with sensitivity and specificity of 94% and 71%, respectively. Of 28 PCs with surgery, 10 presented isovascular, while 18 hypovascular in early phase image. Histology of early isovascular PCs was more likely to be differentiated than that of early hypovascular PCs. (iso; 6 well- and 4 moderately-differentiated, hypo; 3 well-, 15 moderately-, and 1 poorly-differentiated) ($P = 0.028$). Immunostaining revealed that hypovascular area in early phase image reflected heterogeneous prevalence of tumor cells with fibrous tissue, necrosis, and few vessels. Therefore, in our experience of 61 EUS-FNA procedures, all 8 cases in which diagnosis was not possible from the obtained sample exhibited the early hypovascular pattern ($P = 0.02$).
Conclusion: CE-EUS could be useful for differential diagnosis in solid pancreatic lesions, histological differentiation of PCs and diagnostic value of EUS-FNA.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 09:00–14:00
ENDOSCOPY AND IMAGING III – HALL 7

P1351 SHORT-TERM RESULTS OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION IN A COUNTRY WITH LOW INCIDENCE OF GASTRIC CANCER

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Introduction: Gastric endoscopic submucosal dissection (G-ESD) has been accepted as a minimally invasive treatment modality of a defined subgroup of patients with early gastric cancer. It is less invasive than surgery and provides the same long-term survival. Nevertheless, in countries with low incidence of gastric cancer, quality of G- ESD remains an important issue. The purpose of this study is to evaluate short-term results of G-ESD in a single European institution.
Aims & Methods: All patients treated by G-ESD in our center between November 2011 and October 2014 were included. G-ESD was indicated according to expanded criteria of the Japanese Gastric Cancer Association. G-ESD was performed by using either Flush-knife, IT-knife 2 and Dual-knife. G-ESD was indicated only for lesions being considered manageable with regard to the endoscopists experience. The 30-day mortality, *En bloc* resection, R0 resection, curative resection and complications were considered as short-term results.
Results: Among 25 patients, 14 (56%) were males and 11(44%) were females. Mean age was 71.5 (range 40-90) years. The mean lesion size was 20 (range 5-66) mm. From a total of 25 lesions, the location was as follows: antrum 15(60%), angulus 3(12%), body 3(12%), subcardia 3(12%), cardia 1(4%). Lesion morphology according to Paris classification was: 0-Is 7(28%), 0-IIa 10(40%), 0-IIb 1(4%), 0II-a + IIc 5(20%) and 0II-a + III 1(4%) and 1(4%) remaining lesion was subepithelial. The final histology was neoplastic in 20(80%), of them LGIEN in 3(12%), HGIEN in 5(20%), T1m carcinoma in 5(20%), T1sm1 carcinoma in 3(12%), T1sm2 and sm3 2(8%) and neuroendocrine tumour in 2(8%). Remaining 5(20%) lesions were non- neoplastic, of them hyperplastic 3(12%), intestinal metaplasia 1(4%) and ectopic pancreas 1(4%). Results of the forceps biopsy corresponded to final histology in 14(56%) of cases. The 30-day mortality was none. In the cases of neoplastic lesions, *En bloc*, R0 and curative resection was achieved in 17(85%), 17(85%) and 16(80%) respectively. Perforation and delayed bleeding occurred in 2(8%) and 0(0%) of all cases respectively.
Conclusion: Gastric endoscopic submucosal dissection may be considered feasible and safe treatment even in a country with low incidence of gastric cancer. The curative resection was achieved in 80% and perforation occurred in 8% of the cases.
Disclosure of Interest: None declared

P1352 OVER-THE-SCOPE-CLIP FOR THE TREATMENT OF A BROAD SPECTRUM OF ENDOLUMINAL GASTROINTESTINAL DEFECTS: SINGLE CENTER EXPERIENCE WITH 116 APPLICATIONS

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Introduction: The over-the-scope clip system, OTSC (Ovesco Endoscopy, Tübingen, Germany) is an advanced clipping device developed for closure of luminal gastrointestinal (GI) defects.
Aims & Methods: The aim was to evaluate the clinical outcomes of patients treated with the OTSC.
This is an observational, open-label, retrospective, single-arm case series conducted at a tertiary care endoscopy unit. This study involved 116 clip applications in 90 patients (median age 57 years [range 25-86], 31 women) with endoluminal GI defects from fistulae and anastomotic dehiscence to peptic ulcer bleeding and stent anchoring.
Results: A total of 116 clips were applied in 90 patients. The range of indications included gastrointestinal bleeding (n = 21), gastrocutaneous fistulas (n = 17), tracheo-oesophageal and/or oesophagopleural fistulae (n = 20), gastrocutaneous fistulae (n = 24), resection of submucosal tumor (n = 16), stent fixation (n = 10), and perforation closure (n = 8). The deployment success rate for the OTSC device was 97.4% (113 out of 116 applications). The clinical success rate was 84.4% (98 of 116 applications). The clinical success was highest in gastrocutaneous fistulae (95.2%), peptic ulcer bleeding (95.2%), stent anchoring (90%), and closure of perforation (85.7%), whereas the clinical success for TE fistulae was lowest (50%). Complications related to the application of the clipping device included minor bleeding (n = 2). There were no further complications related to endoscopy or sedation.
Conclusion: To our knowledge, this is the largest single-center experience using the OTSC system. The OTSC system is a useful device in a variety primary and iatrogenically-induced endoluminal GI tract disorders including leaks, GI bleeding and stent anchoring, even in very old and frail patients. The success rates for GI bleeding, closure of gastrocutaneous fistulae, endoscopic resection and stent fixation are high (>90%), whereas the success rates for tracheoesophageal fistulae closure is lower (50%).
Disclosure of Interest: None declared

P1353 EXTREME ENDOSCOPY: A NEW PARADIGM IN INTERVENTIONAL ENDOSCOPY

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Introduction: Extreme endoscopy is a new discipline in interventional GI endoscopy. Previous data on extreme endoscopy comes from case reports.

Aims & Methods: The aim was to report on the feasibility and outcomes of extreme endoscopy.

Observational, retrospective study conducted at a tertiary care hospital during an 18-month period. All procedures were performed under general anesthesia. Extreme endoscopy comprises five key components: (i) use of multiple scopes or dual endoscope technique; (ii) use of various types of overtubes (OT), (iii) utilization of modified devices, (iv) use of fluoroscopy and, (v) necessity of utilizing a tool box with: wire cutter, glue, tape, foam (Endosponge). Single- or double balloon enteroscopy (SBE, DBE) (n = 215) and DBE or SBE ERCP (n = 85) were not defined as extreme endoscopy, unless the technique was utilized to perform a) endoscopic re-anastomosis of disrupted GI tract; b) PATENT (percutaneous assisted transprosthetic endoscopic therapy); c) SBE- or DBE-rendezvous-ERCP; d) endoluminal stenting, e) removal of migrated SEMS from the small bowel. Additional exclusions: endoscopic submucosal dissection (ESD) or peroral endoscopic myotomy (POEM) cases (n = 45) and pancreatic necrosectomies (n = 28). Success was defined as resolution of the primary luminal problem.

Results: 65 patients (29 female, 36 male, median age 62.5 years, age range 21-81) with various types of complex primary, secondary or post-surgical anatomy endoluminal GI defects that underwent 85 procedures were studied. In 23 patients (35%) previous surgical, endoscopic or radiologic attempts at solving the problem had failed. In 13 patients (20%) there were no other interventional treatment options available. Interventions performed: PATENT (n = 3), endoscopic re-anastomosis of the disrupted or perforated GI tract (n = 6), Endosponge placement for drainage of huge cavities (n = 3), OT-assisted removal of mesh (n = 2), OT-assisted removal of migrated lap bands (n = 3), OT-assisted SEMS placement of the small bowel and/or colon (n = 31), combined closure of fistula or perforation and placement of direct endoscopic jejunostomy (n = 7), SBE- or DBE ERCP with exchange of scope for slim cholangioscope to perform elecrohydraulic lithotripsy (EHL) (n = 8), rendezvous-DBE ERCP to place SEMS into the bile duct (n = 4) or to place plastic stents percutaneously under direct endoscopic view (n = 2), OT-assisted endoscopy allowing for ERCP or PEG placement in patients with esophageal stenosis (n = 4). The technical success was 87.8%. The mean procedure time was 35 minutes (range 45 min to 4 hours). There were no major adverse events associated with the procedures.

Conclusion: This is the largest study reporting on extreme endoscopy. Albeit time consuming, extreme endoscopic interventions lead to a resolution or remediation of complex endoluminal disorders in the majority of patients. It appears that extreme endoscopy may provide hope for patients in whom no other choices exist. Now multi-center studies in this topic are warranted.

Disclosure of Interest: None declared

P1354 A MULTICENTRE PROSPECTIVE STUDY OF THE REAL TIME USE OF NBI IN THE DIAGNOSIS OF PREMALIGNANT GASTRIC CONDITIONS AND LESIONS

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Introduction: In the stomach, the correlation between white light endoscopy (WLE) and histology in the diagnosis of gastric premalignant conditions is considered low. In reference centres, virtual chromoendoscopy with Narrow-Band Imaging (NBI) has been associated to the identification of these lesions with high accuracy.

Aims & Methods

Aim: To evaluate the diagnostic validity of high resolution endoscopy with and without NBI in the diagnosis of gastric premalignant conditions.

Methods: A multicentre prospective study (5 tertiary centres in 5 countries: Portugal, Italy, Romania, United Kingdom and United States of America) involving the systematic use of high-resolution scopes with imaging registry with and without NBI in a centralized informatics platform available online. All users used the same NBI classification. Endoscopic biopsies were obtained systematically and histological result was considered the diagnostic gold standard.

Results: A total of 226 patients and 1076 images and biopsies were included. The indication for endoscopy was symptoms (83%) and surveillance (17%). The final per-patient diagnoses were as follows: normal mucosa (42%), intestinal metaplasia only in the antrum or corpus (37%) and extensive intestinal metaplasia (21%) with an additional 22 lesions with dysplasia in 19 patients being diagnosed. With NBI the validity per biopsy was 11% higher than WLE (93% vs 82%, $p < 0.001$), with no difference in the identification of *Helicobacter pylori* gastritis (75% vs 74%). NBI sensitivity for dysplasia was 91% (vs 78% WLE, $p < 0.001$) with a negative likelihood ratio of 0.1. NBI specificity for intestinal metaplasia was 97% (vs 99% WLE) with a positive likelihood ratio of 34.8, with a superior sensitivity when compared to WLE (88% vs 57%, $p < 0.001$).

Conclusion: For the first time, diverse centres using a single classification show that use of NBI in real-time demonstrates a high concordance with the histological results and is superior to conventional endoscopy. The global diagnostic accuracy superior to 90% suggests that routine use of NBI may allow guided instead of random biopsy samples during gastroscopy.

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Disclosure of Interest: None declared

P1355 RGD-MODIFIED PAMAM FOR TARGETED FLUORESCENCE IMAGING OF ESOPHAGEAL NEOPLASMS

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Introduction: Despite significant advances in diagnosis and treatment, the prognosis of esophageal squamous cell carcinoma (ESCC) remains poor highlighting the importance of early detection. Although white light (WL) upper endoscopy can be used for screening of the esophagus, it has limited sensitivity for early stage disease. Thus, development of new promising near-infrared (NIR) optical imaging combined with targeted fluorescent nanoprobes to improve the diagnostic capabilities of upper GI endoscopy for early detection of ESCC is an urgent need.

Aims & Methods: The aim of this study was to develop a method for the detection of esophagus neoplasms using near-infrared imaging with a RGD-modified nanoprobes Cy5.5-PAMAM-PEG-c(RGDfk)(PC-PEG-RGD). The targeted nanoprobe PC-PEG-RGD and the control non-targeted nanoprobe Cy5.5-PAMAM-PEG (PC-PEG) were characterized by hydrogen nuclear magnetic resonance spectroscopy, fourier transform infrared spectroscopy, ultraviolet spectrometry and fluorescence spectrometry. The toxicity of nanoprobes to esophageal squamous cancer cells TE-1 were researched by MTT method. The targeting effects of PC-PEG-RGD and PC-PEG to TE-1 cells were studied by confocal microscopy imaging and flow cytometry. The 4-NQO induced esophageal cancer model was imaged for NIR signal after the injection of nanoprobes for 24 hours. Target to background ratios (TBR) were compared for both WL and NIR imaging. The paresence of tumor was confirmed by histology and the integrin-β3 expression was observed by immunohistochemical staining.

Results: The molar ratio of PAMAM/PEG/c(RGDfk) in PC-PEG-RGD was measured as 10/14/1. The presence of Cy5.5 was also confirmed by the absorption peak at 675nm and the emission peek at 700nm in the ultraviolet spectra and fluorescence spectra, respectively, for both targeted and non-targeted nanoprobes. The IC_{50} values of PAMAM, PC-PEG and PC-PEG-RGD were 2.04μM, 1.35μM and 1.70μM, respectively. The mean Cy5.5 fluorescence intensity of TE-1 cells with 0.1μM nanoprobes were 2625.00 ± 476.60 (non-targeted, 2 hours), 22485.00 ± 698.61 (targeted, 2 hours), 3670.25 ± 247.89(non-targeted, 24 hours) and 49203.75 ± 818.94 (non-targeted, 24 hours). The difference between different groups had statistical signigicance. The attachment of PC-PEG-RGD on the cell membrane when the TE-1 cells were treated with this nanoprobe for 24 hours at 37°C was demonstrated in vitro confocal fluorescence microscopic imaging. NIR imaging shows the targeted nanoprobe PC-PEG-RGD enhanced the local esophageal neoplasms fluorescence intensity significantly. And the location of tumor tissue intetrin-β expression was correspond to the place of near-infrared fluorescence in confocal fluorescence microscopic imaging.

Conclusion: The targeted RGD-modified PAMAM with novel imaging devices has the potential to improve esophageal neoplasms detection by fluorescently highlighting tumorous regions.

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Disclosure of Interest: None declared

P1356 HIGH-DEFINITION (HD) ENDOSCOPY BUT NOT I-SCAN SIGNIFICANTLY INCREASES THE DETECTION OF MARKERS OF COELIAC DISEASE: A MULTICENTRE UK STUDY

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Introduction: Coeliac disease (CD) remains underdiagnosed. Many patients with CD have undergone a previous endoscopy where the opportunity to make a diagnosis was missed. Clinicians may rely on endoscopic markers of CD to guide biopsy but they lack sensitivity. A routine duodenal biopsy approach may solve this problem but it is expensive. Methods to improve the macroscopic detection of CD at endoscopy to guide biopsy would seem advantageous. I-Scan, a digital enhancement technique, has shown promising results. However, only one, single-centre study has been performed. This was an uncontrolled, unblinded trial in high prevalence population (35% CD). We aimed to assess the utility of I-Scan in a lower prevalence population in a randomised controlled trial.
Aims & Methods: Patients from 2 UK hospitals (Royal Hallamshire Hospital, Sheffield and St. Mary's Hospital, London) were randomized into 2 groups: Group 1 standard HD white light endoscopy (WLE) and Group 2 WLE plus I-Scan. These patients were compared to a standard non-HD WLE control group, Group 3. The presence of endoscopic markers of CD, scalloping, mosaic pattern, nodularity, loss of duodenal folds or increased vascularity was noted throughout the duodenum. All patients received at least 4 duodenal biopsies. Coeliac serology was performed concurrently. Macroscopic markers of CD are compared to villous atrophy (VA) on histology as the gold standard.
Results: 700 patients (63% female, mean age 51.7) were recruited (201 into Group 1, 199 in Group 2 and 300 into Group 3). In total 130 (18.5%) new diagnoses of CD were made (19 in Group 1, 22 in Group 2 and 89 in Group 3). In new CD cases, endoscopic markers of CD were seen in 80.5% in the HD groups compared to 41.6% in Group 3 ($p < 0.0001$).
In Group 2, I-Scan appeared to enhance changes in 18% of new CD cases. However there was no significant difference in sensitivity between Group 1 (89.5%) and Group 2 (72.7%) ($p = 0.2$). Full sensitivity and specificity analysis is shown in table 1.
The severity of VA was analysed for missed cases. There was no significant difference in the distribution of VA severity across the 3 groups ($p = 0.6$). The use of HD and I-scan did not prevent total VA being missed.
Table 1: Analysis of the 3 interventions

	Sensitivity	Specificity	PPV	NPV
Group 1	89.5 (65.5 - 98.2)	92.9 (87.8 - 96.0)	56.7 (37.7 - 74.0)	98.8 (95.4 - 99.8)
Group 2	72.7 (49.6 - 88.4)	84.8 (78.5 - 89.6)	37.2 (23.4 - 53.3)	96.2 (91.5 - 98.4)
Group 3	41.6 (31.4 - 52.5)	98.1 (94.9 - 99.4)	90.2 (75.9 - 96.8)	79.9 (74.4 - 84.5)

Conclusion: HD endoscopy significantly increases the detection of the endoscopic markers of CD ($p < 0.0001$). However although I-scan appears to enhance the changes of VA it does not significantly increase the detection of markers ($p = 0.2$).

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Disclosure of Interest: None declared

P1357 NICEVIS - RESULTS OF A RANDOMISED CONTROLLED TRIAL OF SIMETICONE AND N-ACETYLCYSTEINE AS A PRE-PROCEDURE DRINK TO IMPROVE MUCOSAL VISIBILITY DURING DIAGNOSTIC GASTROSCOPY

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Introduction: Despite advances in endoscope technology there is still a significant miss rate of neoplastic lesions during gastroscopy. Mucosal views during gastroscopy are frequently impaired by residual bubbles and mucus.
Aims & Methods: We conducted a randomised controlled trial in 126 patients attending for routine outpatient gastroscopy. Trial ref: EudraCT Number 2013-001097-24. Subjects were randomised in a 1:1:1 ratio to receive a pre-procedure drink of water, Simeticone and n-acetylcysteine (Group A), water alone (Group B) or no preparation (Group C). Study endoscopists were blinded to group allocation. 4 digital images were taken at pre-defined locations during the procedure – lower oesophagus, upper body, antrum & fundus. Images were then collated and rated for mucosal visibility (MV) using a 4 point scale (1 = best, 4 = worst) by 4 separate experienced endoscopists who were also blinded to group allocation. The primary outcome measure was mean mucosal visibility score. Secondary outcome measures were total procedure duration and volume of fluid flush required during the procedure to achieve adequate mucosal views.
Results

Group	A - Simeticone/ NAC	B – Water	C – no preparation
Mean Mucosal Visibility (MV) Score (range 1-4)	1.35	2.11	2.21
Mean Procedure duration (sec)	309	352	334
Mean Volume of flush (ml)	2.0	31.5	39.2

Results are shown in table 1. There were no significant differences between groups in age, gender or indication for endoscopy. The mean MV score for group A was significantly better than for group B and group C ($p < 0.001$ for both comparisons). There was no significant difference in mean MV score between groups B and C ($p = 0.541$). Interobserver agreement of MV scores was good (mean kappa 0.464).
Mean volume of flush required during gastroscopy to achieve adequate mucosal views was significantly lower in group A than group B ($p = 0.001$) and group C ($P < 0.001$). There was no significant difference in mean flush volume between groups B & C ($p = 0.583$). Procedure duration did not differ significantly between any groups.
Subgroup analysis of MV scores at each location demonstrated significantly better mucosal visibility in group A compared to group B and group C at all locations ($p < 0.0025$ for all comparisons).
There were no adverse events related to the trial medication.
Conclusion: A pre-procedure drink containing Simeticone and n-acetylcysteine significantly improves mucosal visibility during routine gastroscopy. It also significantly reduces the need for flushes during the procedure to achieve adequate views. This may improve detection of early neoplasia and other pathology during gastroscopy. Subanalysis of separate locations demonstrates significant benefit in both the lower oesophagus as well as stomach, demonstrating potential benefit in Barrett's oesophagus surveillance procedures.
Disclosure of Interest: None declared

P1358 CLINICAL IMPACT OF ENDOSCOPIC RADIAL INCISION FOR ESOPHAGOGASTRIC ANASTOMOTIC STRICTURE: A PRELIMINARY PROSPECTIVE STUDY

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Introduction: Benign esophagogastric anastomotic stricture after surgery seriously affects the quality of life of the patients, especially for patients with refractory dysphagia symptom after several traditional dilations. However, there is little promising endoscopic techniques which is safe, effective and easy to learn. Therefore, we performed a new endoscopic therapy, endoscopic radial incision (ERI) in order to improve the prognosis of benign esophagogastric anastomotic stricture.
Aims & Methods: We performed ERI for patients suffered from esophagogastric anastomotic stricture and evaluated the safety, efficacy and operating time of this procedure. A total of 17 patients with esophagogastric anastomotic stricture after surgery, as diagnosed by esophagogastroduodenoscopy and a dysphagia score ≥ 3 were prospectively included. The primary outcome was symptom relief during follow-up. Secondary outcomes were procedure-related parameters and adverse events.
Results: Each patient was successfully received one-time ERI. The average time for ERI procedure was 10 minutes (range 4–20 minutes). Esophageal perforation occurred in one case and was successfully managed with conservative treatments. During a mean follow-up period of 9 months (range: 2-18 months), the mean dysphagia score decreased from a mean of 3.11(range 3-4) to 0.9(range 0-2) after ERI ($P < 0.001$).
Conclusion: ERI seems to be a safe and effective therapeutic method for benign esophagogastric anastomotic stricture after surgery.
Disclosure of Interest: None declared

P1359 OUT OF HOURS BLEEDER SERVICE - THE LEICESTER EXPERIENCE OVER TEN-YEARS

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Introduction: University Hospitals of Leicester (UHL) NHS Trust has been offering a comprehensive out of hour (OOH) endoscopy service for almost 10 years. Following our publication in *Frontline Gastroenterology*[1] reviewing our OOH data from inception of the service in 2006 to 2010, we felt it important to review the evolution of the service.

In the wake of rising demands we introduced a Consultant-led and Registrar supported weekday in-reach service in 2013, with a morning visit to the acute medical units and a daily in-patient emergency list. Our study looked at the effect of this on OOH endoscopy volume, call outs and therapeutic interventions.

Aims & Methods: To compare our data with our previous data set we analysed 6 month periods of OOH data from each year [2011-15]. Activity was collated by reviewing endoscopy reports [Unisoft reporting tool), separate OOH record books and daily spreadsheet activity returns. We looked at indication and timing of procedures, endoscopic findings, interventions and outcomes.

Results

"Appropriate" Indications	"Inappropriate" Indications
Haematemesis	Dysphagia
Haematemesis + Melaena	Nausea + Vomiting
Melaena	Weight loss
Liver disease + evidence of bleed	Diarrhoea
Liver disease +drop in Haemoglobin	Anaemia
Dysphagia + Haematemesis	Abdominal pain
Intermittent rectal bleeding	Constipation
Overt rectal bleeding	Dyspepsia and previous peptic ulcer
Bloody diarrhoea	IBD assessment

640 procedures were performed during the study period. The introduction of an in-reach service initially resulted in reduced daytime weekend activity but one-year later weekend activity was back to baseline. Although there was an apparent increase in 'true OOH calls', i.e. 5pm until 9 am over our 5 year period the absolute numbers remain small and are in fact not different from our previous study with approximately one emergency procedure per week. There was a 15.9% rise in appropriate referrals as per UHL criteria (see above table).

Endoscopic findings of varices and variceal bleeding increased by approximately 3.5-fold. There was also a 3.5-fold increase in the proportion of endoscopies employing combination therapy and the use of adrenaline injection mono-therapy halved, a reflection of complaince with recently published National Institute for Health and Care Excellance (NICE) guidance[2]. The number of patients requiring emergency laparotomy or arterial embolisation remained very small [2-4 cases per 6 month interval].

Conclusion: The total number of procedures has reduced compared to 2006-2010[1]. This is likely to be the result of better education, change in referral pathways and working patterns. The increase of patients presenting with variceal bleeding appears to reflect a nationwide trend. We observed a decrease in the use of adrenaline mono-therapy and concurrent increase in combination therapy for non-variceal upper gastrointestinal bleeds. Provision of an inreach service and daily in-patient endoscopy list has not affected our overall in-patient endoscopy volume in the study period intervals. Gastroenterology units need to review and re-invent their in-patient and OOH work pattern on a regular basis to address the increasing demands on inpatient endoscopy services.

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WEDNESDAY, OCTOBER 28, 2015 09:00-14:00

ENDOSCOPY AND IMAGING III - HALL 7

P1360 DIAGNOSIS OF INVASION DEPTH OF EARLY ESOPHAGEAL CANCER BY JAPANESE CLASSIFICATION OF MAGNIFYING ENDOSCOPY FOR SUPERFICIAL SQUAMOUS CELL CARCINOMA (RETROSPECTIVE SINGLE CENTER STUDY)

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Introduction: Recently, the Japan esophageal society constructed a new classification. This classification was intended to be simple and easily applicable in general clinical practice. But the true accuracy of diagnosis is under consideration.

Aims & Methods

Aim: To investigate the accuracy of diagnostic criteria based on Japanese classification of magnifying endoscopy for surficial esophageal squamous cell carcinoma (SESCC), the examination by magnifying endoscopy of each SESCC cases was reviewed according to the classifications. Furthermore, in misdiagnosis cases, the causes of misdiagnosis were investigated.

Cases and Methods: Between April 2011 and December 2012, the cases of SESCC undergone endoscopic submucosal dissection (ESD) at Department of Surgery, Keio University School of medicine were extracted and only the cases with appropriate evaluation by magnifying endoscopy before the endoscopic treatment were included and the findings of magnifying endoscopy were reviewed as detail. The endoscopic diagnoses of cancer invasion depth by diagnostic criteria based on Japanese classification of magnifying endoscopy for SESCC and the final histopathological diagnoses of resected cancer lesions were compared. The accuracy rate was calculated according to classifications of magnifying endoscopy and the causes of misdiagnoses cases were investigated.

Results: 90 cases were reviewed in detail. According to classifications of magnifying endoscopy, 71 cases are classified to B1, 16 cases B2, and 3 cases B3. Accuracy rates of diagnoses of tumor depth were 91.5% of B1 (65 cases), 56.2% of B2 (9 cases), and 100% of B3 (3 cases).The causes of misdiagnoses according to classifications of magnifying endoscopy were investigated. B1 cases: The causes of difficulty of diagnoses were considered to be surficial normal epithelia or cornification covered on cancer mucosa by endoscopic findings. Compared endoscopic findings and histopathological findings, very small deepest cancer invasion area or normal epithelia covered on deepest invasion cancer area leaded to misdiagnoses of cancer vessels. B2 cases: The causes of difficulty of diagnoses by endoscopic findings were considered as follows; to be large cancer making impossible to examine whole cancer lesions in detail which was cause of misdiagnoses of cancer vessels in deepest cancer invasion area, to have change of cancer vessels by inflammation, and to be diagnosed as more advanced lesions by the cancer form.

Conclusion: The accuracy of diagnosis of SESCC invasion depth using the diagnostic criteria based on Japanese classification of magnifying endoscopy for SESCC was over 90% of accuracy rate in B1 cases, while about 50% in B2 cases. In B1 cases, when the deepest cancer invasion area was very small or surface of cancer lesion was covered by normal epithelia, the diagnosis of cancer invasion depth was difficult, while the consistency of B1 vessels and depth of cancer invasion was high in the area that cancer vessels could be diagnosed. In B2 cases, the cancer lesion was often large which caused inadequate examination or modified surficial vessels leaded to be difficult to diagnose depth of cancer invasion. So that, the consistency of B2 vessels and histopathological cancer invasion depth was not so high in the result.

Disclosure of Interest: None declared

P1361 OUTCOMES OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN PEDIATRIC AGE WITH A PEXIES TRIANGULATION SYSTEM

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Introduction: The percutaneous endoscopic gastrostomy (PEG) is the method of choice for the establishment of gastrostomies in pediatric patients. This procedure can be performed as a direct technique or a thread pulling method. However, there are little data about gastropexy technique in children to date.

Aims & Methods: The aim of this analysis is to report the experience of PEG placements by pexias triangulation system in pediatric patients. All consecutive pediatric patients who underwent a PEG by pexies from 2010 to 2014 were reviewed. Clinical and demographic variables as age, weight, indications (emergency or deferred), complications, need for endoscopy and time tracking were collected. In 18 cases it was placed a button through the expansion system.

Results: Nineteen cases (12 female, mean age: 6.3, range: 7 months-13 yr): 18 cases of PEG and 1 case of direct jejunostomy were collected. The minimum weight was 5.7 kg (7 patients weighing less than 15 kg).

The indications for PEG were as follows: encephalopathy (n = 9, 50%), malnutrition (n = 7) (2 secondary to cystic fibrosis, 1 neurofibromatosis, 1 heart disease, 1 methylmalonic acidemia and 2 neoplasms), dysphagia due to refractory esophageal stenosis (n = 1), myopathy (n = 1) and suction-swallowing disorder prolonged in patients with distal arthrogryposis (n = 1).

There was only one (5.2%) procedure-related emergency complication (intestinal perforation) in a patient with a history of multiple abdominal surgery and surgical gastrostomy presenting with a gastric prolapse. We detected procedure-related deferred complications in 3 cases (all with encephalopathy): episodes of irritability and apnea at 18 hrs after the start of enteral nutrition (n = 1) and vomits (n = 2). All were self-limiting after stopping nutrition and subsequent restart. Direct jejunostomy as a single incident peristoma losses was resolved by replacing the probe button and managing nutrition ball 30 cms beyond the stoma. None of the patients required new endoscopy or sedation to spare because all allowed implemented a low profile device. The mean follow-up was 2 months.

Conclusion: Percutaneous endoscopic gastrostomy with a pexies triangulation system is a recently developed technique using a three-suture to pexy the stomach to the abdominal wall. This device allows direct implantation of a button during the endoscopic procedure and reasonable security rates according to our data. It may avoid the need of a second endoscopy for the PEG tube removal.

Disclosure of Interest: None declared

P1362 MANAGING BOERHAAVE'S SYNDROME USING SELF-EXPANDABLE METAL STENTS: A UNIQUE CASE SERIES

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Introduction: Boerhaave's syndrome (BS) is a rare and potentially fatal condition due to spontaneous rupture of the esophagus, usually following intense effort of vomiting or retching. Surgical repair or exclusion of the esophagus in combination with pleural drainage and broad-spectrum antibiotics is usually recommended. Despite early recognition and treatment, mortality remains high. Recently, endoscopic management has been advocated in selected cases.
Aims & Methods: We report our experience managing BS with a primarily endoscopic approach using self-expandable covered metallic stents (SEMS). Patients presenting with BS between 8/2010 and 12/2013 were studied.
Results: We included 5 male patients with BS. The mean age was 47.4 ± 19.6 years. Etiologies included food impaction with bolus of meat, retching due to alcohol withdrawal and pill impaction in distal esophageal stricture secondary to eosinophilic esophagitis. CT findings included pneumomediastinum in 4 patients and air in the hepatic parenchyma and gastric wall in 1 patient. All patients received broad spectrum antibiotics. Additionally, drainage of purulent pleural effusions was performed in 3 patients. One patient required mechanical ventilation due to type 1 respiratory failure. The median (IQR) time to emergency endoscopy was 35(3.5-516) hours. SEMS were successfully placed in all patients and effectively excluded the perforations. SEMS used included partially covered Ultraflex® 70/100 x 23/28 mm (n = 2), partially covered Hanarostent® 60/100 x 20/26 mm, fully covered Hanarostent® 100/140 x 20/26 mm and fully covered Wallflex® 120 x 18/25 mm. The median (IQR) time to resumption of oral feeding was 3.0(54-162) days. There were no complications and patients were discharged after a median (IQR) of 16(7-44.5) days. The median (IQR) time until removal of SEMS was 8(5.5-66.5) weeks.
Conclusion: Our case series included patients with 3 different etiologies of Boerhaave's syndrome. In our opinion, emergency placement of SEMS provided an effective and minimally invasive alternative to conventional surgical management. Other potential benefits of interventional endoscopy included shortened hospital stay and faster resumption of oral feeding.
Disclosure of Interest: None declared

P1363 SUBEPITHELIAL LESIONS OF THE STOMACH: MONITORING OR RESECTION

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Introduction: Gastric subepithelial tumors represent a diagnostic and therapeutic challenge, given the histologic heterogeneity and potential malignant behavior.
Aims & Methods: To evaluate the interest, efficiency and safety of endoscopic resection for subepithelial gastric lesions, especially of size < 20 mm. We realized a single-center retrospective study in a tertiary care center of 34 patients with subepithelial gastric lesions who underwent a preoperative diagnosis by EUS ± FNA and an endoscopic resection.
Results: A total of 34 lesions (4 GIST, 4 leiomyoma, 6 neuroendocrine tumors (NETs), 6 pancreatic rest, 7 focal inflammatory tissue, 2 lipoma, 1 well differentiated focal signet ring cells carcinoma, 1 schwannoma, 1 benign fibroid tumor, 1 hamartoma, 1 eosinophilic granuloma). Mean histological size was 18.5 mm. Concordance between EUS ± FNA evaluation and final histological diagnosis was 50%. 9 EMR, 19 ESD and 6 Hybrid Resection were performed. 94.1% lesions were resected in one piece. Complete histological and definitive resection, with a follow up of 6 months, was obtained in 91.2%. A vertical resection was insufficient in 4 cases. The GIST needs a complementary surgical resection and the NETs was successfully treated by a new ESD session. There were only one severe adverse event (2.9%); 1 pneumoperitoneum with ESD, 3 bleeding with 1 ESD and 2 EMR, always treated conservatively or endoscopically.
Conclusion: Endoscopic resection is safe and should be the procedure of choice for both diagnosis and definitive resection for subepithelial gastric lesions of size under 20 mm.
Disclosure of Interest: None declared

P1364 EFFICACY OF A NEW HEMOSTATIC FORCEPS (FD-Y0007) DURING GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic submucosal dissection (ESD) is widely accepted as a standard treatment for early gastric cancer. One challenging aspect of ESD is hemostasis. It is often difficult to control pulsatile bleeding from arterioles or bleeding from raw surfaces deep in the submucosal layer. We developed a new hemostatic forceps with a large cup and a rotation function (FD-Y0007) with the aim of achieving more effective hemostasis.
Aims & Methods: The objective of this study was to investigate the hemostatic ability of the FD-Y0007 during gastric ESD. This study was a prospective randomized controlled trial, which was conducted at a cancer referral center. Fifty-nine (59) patients who were scheduled to undergo ESD for a total of 66 gastric neoplasms (median tumor size of 16 mm) were enrolled and randomly assigned to either the Coagrasper or the FD-Y0007, which was used for hemostasis throughout the case. The procedures were performed by 4 endoscopists. The main outcome measure was the time required to obtain hemostasis, which was measured for the first episode of bleeding during each case.
Results: Hemostasis time for the first bleeding episode during ESD was 45 seconds (range 11 - 230) for the Coagrasper vs. 15 seconds (range 9 - 56) for the FD-Y0007 ($p < 0.001$). When all episodes of bleeding were 32 (range 7-230) second in Coagrasper vs. 14 (range 5-235) second in FD-Y0007 ($p < 0.001$). The rate of number of grasping attempts required for hemostasis was ≤ 2 in the Coagrasper was 59% and that in the FD-Y0007 was 89% ($p < 0.001$). The operation time (54 minutes vs. 45 minutes), rate of en bloc resection (96% vs. 100%), and number of adverse events (perforation; 3.2% vs. 6.9% and bleeding; 0% vs.0%) were not significantly different between the two groups. In addition, the FD-Y0007 demonstrated more effective hemostatic ability than the Coagrasper independent of tumor location or bleeding pattern.
Conclusion: Compared to the Coagrasper, the FD-Y0007 efficiently reduces the hemostatic time during gastric ESD with no increase in adverse events.
Disclosure of Interest: None declared

P1365 PER-ORAL ENDOSCOPIC PYLOROMYOTOMY ACCELERATES GASTRIC EMPTYING IN HEALTHY PIGS: A PROOF OF CONCEPT

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Introduction: Gastroparesis is defined as a syndrome of objectively delayed gastric emptying in the absence of mechanical obstruction and cardinal symptoms (early satiety, postprandial fullness, nausea, vomiting). Gastric emptying scintigraphy is considered as a standard for diagnosis of gastroparesis. Manometric studies of patients with gastroparesis show prolonged periods of increased pyloric tone and phasic contractions, a phenomenon termed as "pylorospasm". Endoscopic therapies of pylorospasm have emerged with recently the development of per-oral endoscopic pylorotomy (POP) by analogy to POEM in achalasia. We explore the effect of POP on gastric-emptying in normal pigs.
Aims & Methods: A first gastric emptying scintigraphy of a semi-solid meal labelled with 15 MBq Tc99m-DTPA was performed in 4 large white pigs (25.5 +/- 2.9 kgs) under a light sedation with intravenous propofol beginned 15 minutes after a premedication with intramuscular ketamine. The semi-solid meal

Abstract number: P1362. Table 1: Characteristics, type of stent used and outcomes of the patients

Patient	Sex/ Age	Symptoms	Etiology	Type/dimensionsof Stent (mm)	Time from onset	Pleural drainage	TT discharge	TT removal
1	M/72	Epigastric pain, hematemesis, dyspnea	Food impaction with meat bolus	Ultraflex®, partially covered metallic stent23/28 x 70/100	72hours	Yes	9 days	5 weeks
2	M/48	Thoracalgia, hematemesis	Alcohol withdrawal	Ultraflex® partiallycovered metallic stent 23/28 x 70/100	24hours	Yes	6 days	6 weeks
3	M/18	Epigastric pain, vomiting, hematemesis	Eosinophilic esophagitis	Hanarostent®, partially covered metallic stent20/26 x 60/100	<12hours	No	5 days	8 weeks
4	M/55	Epigastric pain, vomiting, dyspnea	Alcohol withdrawal	Hanarostent®, covered metallic stent20/26 x 100/140	39 days	Yes	54 days	9 weeks
5	M/44	Epigastric pain, vomiting	Alcohol withdrawal	Wallflex®, covered metallic stent 18/25x120	<12hours	No	16 days	31 mths

(M=male; TT = time to)

was administered after initiation of the sedation using a large nasogastric feeding tube.
Between 2 to 5 days after, an endoscopic pylorotomy (POP) was performed on anesthetised pigs (intravenous propofol and sufentanyl) with an hybridknife type T (Erbe Medical, Germany) according to the previous reported technique: mucosal entrance in the antrum at the greater curvature 3 to 5 cm proximal to the pyloric opening; submucosal tunnel dissection; endoscopic pyloromyotomy and closure with endoscopic hemoclips.
After 7 days of follow-up a second gastric emptying scintigraphy was performed according to the above mentionned protocol to evaluate the effect of the POP on the gastric emptying of normal pigs.
Results: POP: Mean duration of the procedure was 55 (+/- 4) minutes. All cases were completely performed under air insufflation. No bleeding occured perprocedure or post-procedure. Only one perforation for the first case occured during the myotomy phase but without any clinical significance during the 7 days of follow up before the second gastric emptying scintigraphy.
Gastric emptying scintigraphy: The post-POP gastric emptyning was 2.22 fold faster than the pre-POP gastric emptying with statistical significance: T 1/2 post-POP = 84.5 (+/-) 35.7 min vs T 1/2 pre-POP = 188.4 (+/- 87.3) min; $p = 0.029$.
Conclusion: Per-oral endoscopic pyloromyotomy is safe and accelerate gastric emptying of a factor of 2 in healthy pigs. A study is ongoing on a model of gastroparesis in pigs which have previously been treated by a troncular vagotomy and a pilot human study will begin at the end of the year to confirm this promising results. Just like POEM in achalasie, POP may become the standard treatment of gastroparesis.

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P1366 ACUTE UPPER GI BLEEDING (AUGIB) OUTCOMES IN A 24/7 TERTIARY CENTRE, MUCH NEEDED TOPICAL DISCUSSION IN AN ERA OF TOPICAL HAEMOSTATIC ENDOSCOPIC TREATMENT

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Introduction: Despite highly successful endoscopic treatment[1], acute upper gastrointestinal bleeding (AUGIB) rebleeding rate of 13% and mortality of 10% remains a key concern[2]. Topical haemostatic therapy is evolving in Non variceal Gastrointestinal bleed (NVGIB) management and registry data[3] suggest that it is non inferior to current standard endoscopic treatment.
Aims & Methods: Our hospital is a tertiary centre with 24/7 endoscopy/interventional radiology/surgery facilities but falls in most deprived quintile of deprivation. We reviewed our 24/7 AUGIB services to look at NVGIB rebleeding/mortality outcomes and to evaluate the service need for topical haemostatic therapy. We performed a retrospective study over a 12 month period from September 2012 to August 2013. We searched Hospitals Episode Statistics (HES) for haematemesis, melaena or unspecified gastrointestinal haemorrhage codes and collected demographics, endoscopy data and outcomes from electronic records.
Results: There were 500 patients with a mean age of 66.4. Male: Female - 291:209. Rebleeding rate was 6%; mortality 10.8% and 1% required radiological/surgical interventions. Non Variceal accounted for 69% (344), variceal 9% (44) and no cause for bleeding 22% (112). NVGIB endoscopy findings were - 15% duodenal ulcer, 8% gastric ulcer, 33% Oesophagitis/Gastritis/Duodenitis, 7% others, 4% malignancy, 2% oesophageal ulcer.
Conclusion: Our audit shows that 24/7 AUGIB service in a tertiary centre can provide highly successful endoscopic treatment in preventing rebleeding (6% compared to 13% national data[2]) but does not improve mortality. The reason for non improvement in mortality is unsurprising[1] but compared to national data, slight increase could be multifactorial and we feel it is related to the deprivation score[4]. Currently, we see the role of topical haemostatic therapy in 24/7 tertiary centres to be in select population and does not require change of protocols from dual endoscopic treatment.

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P1367 ENDOSCOPIC ANTERIOR FUNDOPLICATION WITH THE MEDIGUS ULTRASONIC SURGICAL ENDOSTAPLER (MUSE^{TM}): RESULTS FROM AN EX-VIVO SIMULATION TRIAL TO ASSESS THE EFFICACY OF THE PROCEDURE BY COMPARING STAPLING POSITION AND GASTRIC YIELD PRESSURES

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Introduction: GERD is the result of lower esophageal sphincter (LES) dysfunction caused by inappropriate transient LES relaxation or diminution of resting basal pressure. Recently, the Medigus Ultrasonic Surgical Endostapler (MUSE^{TM}, Medigus, Omer, Israel), a combined video- and ultrasound-guided transoral surgical stapler, has been FDA-cleared and CE-cleared for endoscopic anterior fundoplication.
Aims & Methods: Aim of this study is to determine the ideal position of the staples in relation to the gastroesophageal junction (GEJ) in a validated simulation model. MUSE procedures were performed in the EASIE-R simulator (Endosim LLC, Hudson, MA) using fresh ex-vivo porcine stomachs. As a surrogate for LES function, the gastric yield pressure (GYP) was determined by inserting an 18-Gauge cannula into the stomach lumen, which was connected to a pressure transducer. The stomach was gradually filled with methylene-blue dyed normal saline using a roller pump. The GYP was determined by detection of reflux of the methylene-dyed water in the esophagus with a gastroscope positioned above the GEJ. Four different techniques were compared by varying the distance of stapling location from the GEJ and the angle between the staples in the horizontal plane. Group A: 2 staples each at 3cm distance, angle 180 degrees; Group B: 2 staples at 3cm, angle 90 degrees; Group C: 2 staples at 4cm; angle 180 degrees; Group D: 3 staples at 3cm; 90 degrees between each staple (180 degrees total).
Results: We performed 10 MUSE procedures in each group. Baseline GYP before the procedure was 0 mmHg in all groups. Mean GYPs (±SD) after the procedure were as follows: Group A 16.9 ± 8.7; Group B 8.1 ± 7.9; Group C 12.2 ± 9.4; Group D 22.7 ± 13.3. Comparisons of each group was done using the student *t* test and were as follows:

Comparison	p-value
Group A vs Group B	0.03
Group A vs Group C	0.26
Group A vs Group D	0.26
Group B vs Group C	0.31
Group B vs Group D	0.01
Group C vs Group D	0.06

Conclusion: We observed significant differences in GYP among the tested 4 groups. Based on our results, we recommend the placement of 3 staples at 3 cm distance from the GEJ with an angle of 90 degrees between each staple position (1st and 2nd; 2nd and 3rd), which resulted in the most efficient LES valve mechanism. Limitations of this study are the small sample size and the use of an ex-vivo model with lack of intrinsic LES pressure.

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P1368 EFFICACY OF HEMOSTASIS USING HOT BIOPSY FORCEPS FOR ACUTE UPPER GASTROINTESTINAL BLEEDING

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Introduction: Hemostatic forceps is increasingly used acute upper gastrointestinal bleeding (UGIB) to achieve hemostasis as it has become readily available for Endoscopic mucosal dissection (ESD). Hot biopsy forceps (Radial Jaw^{TM} 4 Hot Biopsy Forceps, Boston Scientific, Marlborough, MA, USA) is particularly useful in hot biopsy forceps polypectomy and achieving hemostasis in ESD. We previously reported the efficiency and safety of hot biopsy forceps for ablation of gastric antral vascular ectasia[1]. Besides, in recent days it has also been used for cold polypectomy during colonoscopy[2].
Aims & Methods: The aim of the current study was to evaluate the efficacy of achieving hemostasis for non-variceal UGIB using hot biopsy forceps. A total of 188 cases were evaluated retrospectively between January 2009 and December 2014. We divided the cases into two groups, and compared the hemostasis, re-bleeding rate, and clinical background. Group A consisted of 141 cases where endoscopic hemostasis with hot biopsy forceps for acute UGIB was performed. Group B consisted of 47 cases where hemostasis was achieved with the other conventional endoscopic methods. Endoscopic treatment for UGIB was performed when cases presented with active spurting and oozing (Forrest classification Ia and Ib), and visible non-bleeding vessel (Forrest classification IIa).
Results: Clinical characteristics among groups (A/B) were male: female [89:52/39:15], average age [$70.0 \pm 14.5/67.9 \pm 14.9$] years, use of anti-coagulant agents [27.7%/21.3%], and non-steroidal anti-inflammatory drug use was [12.8%/8.5%]. The average of Hemoglobin (Hb) level was [$8.4 \pm 2.8/9.2 \pm 2.7$], and Blood urea nitrogen (BUN) / Creatinine (Cr) ratio was [$45.5 \pm 20.0/48.9 \pm 30.0$]. There were no statistically significant differences between the two groups in hemostatic rate [99.3%/100%], and re-bleeding rate [2.9%/2.1%].
Conclusion: Our use of hot biopsy forceps in active UGIB shows this method is equivalent to conventional endoscopic methods in achieving hemostasis. This method is easy, cost-effective and doesn't require special preparations or ability. Further prospective studies can confirm our finding.

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P1369 THE DIAGNOSTIC PERFORMANCE OF CONVENTIONAL ENDOSCOPY FOR DIAGNOSING SUBMUCOSAL INVASION BY EARLY GASTRIC CANCERS: THE "NON-EXTENSION SIGN" AS A SIMPLE DIAGNOSTIC MARKER

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Introduction: Differentiation between mucosal (M) or microinvasive submucosal (SM1: less than 500 micrometer) and invasive submucosal (SM2: 500 micrometer and over) cancer, as an indicator of the depth of invasion, is an important determinant of the method of treatment of early gastric cancer (EGC). Therefore, the present study sought to determine the ability and the inter-observer agreement of conventional endoscopy (CE) to diagnose SM2 cancer using only ''non-extension sign'' under unified viewing methods.
Aims & Methods: This study examined consecutive cancerous lesions detected in successive patients who underwent CE prior to either endoscopic or surgical resection at this hospital between January 2006 and December 2013.
EGCs were diagnosed according to invasion depth as M-SM1 or SM2. Each endoscopic examination was performed by a single independent endoscopist, with the diagnoses recorded in a database immediately following each procedure. SM2 cancer was diagnosed when one of two criteria is fulfilled according to the CE findings [1]: (I) massive elevation; or (II) mucosal convergence with elevation. These non-extension signes findings relate to the increased thickness and rigidity caused by massive submucosal invasion by the cancer. When the gastric wall is strongly extended by endoscopic insufflation of a large volume of air, the SM2 invasive area can be seen as a trapezoid protrusion. So this ''non-extension sign'' was assessed only when the entire stomach wall is strongly distended.
In terms of the endoscopic diagnostic criterion, lesions that were positive for the ''non-extension sign'' were classified as SM2 cancers, and those negative for the ''non-extension sign'' were classified as M-SM1 cancers. The histopathological findings were used as the gold standard.
Results: We examined a total of 981 lesions from 822 patients. There were 127 true positive lesions, 824 true negative, 11 false positive, and 19 false negative. This yielded a sensitivity of 87.0% (95% CI 81.5-92.4%), specificity of 98.6% (95% CI 97.9-99.4%), positive predictive value of 92.0% (95% CI 87.5-96.5%), negative predictive value of 97.8% (95% CI 96.7-98.7%), and diagnostic accuracy of 96.9% (95% CI 95.8-98.0%). The values of inter-observer variation for diagnosing submucosal invasion by EGC using ''non-extension sign'' was 0.839 (excellent agreement [2]) between 2 endoscopists.
Conclusion: In the present study, the ''non-extension sign'', detectable using CE, is a straightforward and effective means for accurately determining the suitability of minimally-invasive endoscopic treatment.

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P1370 EDUCATION FOR WIDESPREAD OF ENDOSCOPIC CELL SHEET TRANSPLANTATION TO PREVENT A STRICTURE AFTER ESOPHAGEAL ESD

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Introduction: Endoscopic cell sheet transplantation to prevent a stricture after esophageal endoscopic submucosal dissection (ESD) was developed in our university hospital. Cell sheet was harvested by each patient's own oral mucosal tissue. Isolated epithelial cells from the oral mucosal tissue were cultured for 16 days using culture dishes with intelligent temperature-responsive surface. We were able to get transplantable epithelial cell sheets by reducing temperature without protein enzyme. Then, the autologous cell sheets were endoscopically transplanted onto the bed of the esophageal ulcer after ESD. We reported the result of regenerative medical clinical research on *Gastroenterology* in 2012.
Aims & Methods: The aim of our study is feasibility of cell sheet transplantation in other institutes. We educated endoscopic cell sheet transplantation by animal examinations before the clinical research and directly taught in each 10 cases from 2011 at Karolinska Institute in Sweden and Nagasaki University.
Results: Selected medical staff at Karolinska Institute in Sweden received training from us on this technology. They, then, adapted the techniques to their clinical studies, which focused on Barrett's esophagus with high-grade dysplasia. Ten patients participated in the study and results were collected. Currently, the Institute is preparing for the randomized control study.
Nagasaki University conducted a study to determine the possibility of transferring collected oral mucosal tissue to the cell processing center at our university by air. Many variables, such as temperature, humidity, vibration, were taken into considerations. Cells collected from 10 subjects were transported to us successfully.
Conclusion: This is the first successful model on cell sheet transplantation for the prevention of stricture. We hope that this technology will be widely used around the world in the future.

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P1371 PILOT STUDY EVALUATING SEE-THROUGH HEAD-MOUNTED DISPLAY FOR CLINICAL USE – LABORATORY EXPERIMENT USING UPPER GASTROINTESTINAL ENDOSCOPIC SIMULATOR –

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Introduction: Observing an X-ray monitor and an endoscopic monitor is necessary for fluoroscopy-guided therapeutic endoscopic procedures such as ERCP. However it is difficult to view the two monitors simultaneously. A see-through head-mounted display (SHD, Moverio BT-100; Seiko Epson Corp., Azumino, Japan) was developed for viewing moving images projected 20–30 cm in front of the eyes. The images do not obstruct the surrounding view.
Aims & Methods: The aim of this study was to evaluate the utility of SHD for clinical use. We conducted two experiments. Experiment 1 verified the non-inferiority of SHD-guided endoscopic procedures to normal monitor-guided endoscopic procedures. Subjects were three doctors and one nurse; the nurse had no endoscopy experience. The times necessary to conduct a series of endoscopic observation procedures and head movements during observations were compared between normal monitors and SHD. Endoscopy was performed by insertion through the esophagus. The stomach to the duodenal papilla and the stomach interior were observed. Each subject performed two runs of observations using each monitoring method. The shortest time was used as the procedure time. The head movement was measured using the inertial measurement unit of the SHD. Examination 2 used the gastrostomy model as the model to perform endoscopic procedures while observing multiple monitors. Subjects were four doctors with gastrostomy experience. They performed two runs of the procedure

using each monitoring method to compare the procedural times and head movements.
Results: Experiment 1) The median of the procedure time of four subjects was 51.5 s (range 48–69 s) by normal monitoring, and 53 s (range 46–76 s) by SHD. None of the four subjects, including the nurse, showed even slight up and down or left and right shifting of the head position. Experiment 2) The median procedure time of the four subjects was 36 s (range 26–41 s) by normal monitoring, and 32 s (range 25–41 s) by SHD. Regarding head movement, all subjects exhibited up and down or left and right shifting of the head position by normal monitoring every time their eyes moved between the monitor and the gastrostomy site, although all subjects were able to perform the procedure while exhibiting almost no head position shift using SHD.
Conclusion: When guided by SHD, the procedure performance was not inferior to that of normal monitor-guided endoscopic procedures. Additionally, it was possible to perform procedures during which multiple monitors were observed simultaneously without shifting the head position, suggesting the possibility of its usefulness for therapeutic endoscopy where an X-ray monitor is also used.
Disclosure of Interest: None declared

P1372 SINGLE CLIP VERSUS MULTI-FIRING CLIP DEVICE FOR CLOSURE OF SUBMUCOSAL ENTRANCE AFTER PER-ORAL ENDOSCOPIC MYOTOMY (POEM)

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Introduction: Per Oral Endoscopic Myotomy (POEM) is an alternative treatment for achalasia. With this technique an esophageal myotomy is completely performed endoscopically. After the myotomy the 2-3 cm long entry site of the submucosal tunnel is closed with endoscopic clips. After placement of each clip a next clip has to be introduced through the working channel of the endoscope. A new endoscopic clip system has recently been introduced (Clipmaster3, Medwork, Germany). With this system it is possible to place up to 3 consecutive clips without having to reload and therefore could reduce closure time.
Aims & Methods: We performed a prospective study with this new multi-firing device looking at efficacy, safety and ease of use. Moreover, closure using Clipmaster3 was compared to closure with standard endoscopic clips. Patients diagnosed with achalasia who underwent POEM were prospectively studied. Both physician and endoscopy nurse were trained to use Clipmaster3 prior to the first procedure. The following variables were collected for both groups: sex, age, achalasia subtype based on high-resolution manometry, disease duration, length of the mucosal incision, successful closure, closure time of the mucosal incision, number of clips used for successful closure, unsuccessfully placed clips, adverse events and postoperative stay. Handling of the Clipmaster3 was evaluated by both endoscopist and endoscopy nurse by means of a VAS score (0 = impossible, 10 = very easy).
Results: Twelve POEM closures with Clipmaster3 were compared to 24 standard-POEM procedures based on the same physician and assisting endoscopy nurse for all procedures. Data of the procedures were compared in a 1:2 manner. The Clipmaster3 and the standard group did not differ in sex distribution, age (42 yrs [29-49] vs 41 yrs [34-54] p 0.379) and type of achalasia (p 0.181). Median disease duration differed between groups, 24 months [10-66] for Clipmaster3 vs 2 months [1-32] (p 0.018) for standard closure. Length of the mucosal incision did not differ between groups (25.0 mm [20-30] vs 20.0 mm [20-30], p 1.0). Successful closure could be performed in all patients in both groups. Closure time did not differ between the groups (622 s [438-909] vs 598.5 s [488-664] p 0.72). The number of clips that were placed to achieve successful closure did not differ (9 vs 8). The proportion of all used clips that was either displaced or discarded was larger for Clipmaster (8.8%) compared to standard closure (2.0%, p 0.00782). The number of adverse events did not differ between groups (n = 3, 25.0% vs n = 6, 25.0%). In none of the patients leakage of water-soluble contrast was seen during X-swallow at day 1. Postoperative stay was 1 day for all patients. In both groups there was no readmission or mortality. VAS score for ease of handling of the Clipmaster3 for closure did not differ between the endoscopist and endoscopy nurse and was 7 ([6-8][6-9]) out of 10.
Conclusion: This study demonstrates that Clipmaster3 for closure of the mucosal incision after POEM was safe and feasible in all patients. Compared to standard endoscopic clips Clipmaster3 was not associated with reduced closure time as was hypothesized. Compared to standard closure, more clips of Clipmaster3 were displaced or discarded to achieve successful closure. A training effect cannot be excluded as cause of these results.
Disclosure of Interest: None declared

P1373 ENDOSCOPIC TREATMENT FOR SUPERFICIAL BARRETT'S ESOPHAGEAL ADENOCARCINOMA: UTILITY OF MAGNIFYING NBI ENDOSCOPY AND NEGATIVE BIOPSY AROUND THE LESION FOR DIAGNOSIS OF ITS EXTENT

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Introduction: Treatment strategies for superficial Barrett's esophageal adenocarcinoma(s-BEA) and high-grade dysplasia differ substantially between Japan and Western countries. In Japan, targeting biopsy and endoscopic submucosal dissection (ESD) is favored, but sometimes horizontal extent is a difficult issue. In our hospital, horizontal margin is diagnosed in all cases by narrow-band imaging magnifying endoscopy (NBI-ME) before ESD, and recently, negative biopsies around the lesion is actively taken for confirm horizontal margin.
Aims & Methods: This study aimed to investigate the utility of NBI-ME and negative biopsies. The subjects comprised 67 lesions in 63 cases with pathologically defined s-BEA (SSBE, 56; LSBE, 7) that were endoscopically resected (ESD/EMR) in our hospital in December 2014 or before. The horizontal extent was diagnosed preoperatively in all cases by NBI-ME based on the presence or absence of a demarcation line and irregularity of the surface patterns and vascular patterns. Then, a horizontal margin-negative rate was compared between two groups: Group A, biopsy from 0 to 3 peripheral points (22 lesions in 18 cases); and Group B, biopsy from 4 peripheral points or more (45 lesions in 45 cases). Lesions with at least one of the findings of double-layered lamina muscularis mucosae, esophageal glands, and squamous cell islets detected by postoperative pathology were defined as Barrett's esophageal adenocarcinoma and subjected to analysis.
Results: Overall, the horizontal margin-negative rate was 97.0% (65/67 lesions). It was 96.5% (55/57 lesions) and 100% (10/10 lesions) with the background of SSBE and LSBE, respectively. All were negative in Group B, while it was 90.9% (20/22 lesions) in Group A in 2 of which development under the squamous epithelium was observed. Pearson's chi-square test revealed a significant difference between two groups with a p value at 0.040.
Conclusion: In diagnosis of the horizontal extent of s-BEA, NBI-ME and negative biopsies were useful. Negative biopsies from at least 4 points can be necessary to prevent misdiagnosis of the horizontal extent.
Disclosure of Interest: None declared

P1374 UTILITY OF MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING IN THE DIFFERENTIAL DIAGNOSIS OF SUPERFICIAL-ELEVATED TYPE GASTRIC EPITHELIAL NEOPLASMS BY NON-EXPERTS

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Introduction: Magnifying narrow-band imaging (M-NBI) has been reported to be superior to conventional white-light imaging (C-WLI) in its ability to differentially diagnose gastric cancers and adenomas [1]. However, these results have been achieved when examinations are performed by experts. The diagnostic ability of non-experts with fewer years of experience has not been reported.
Aims & Methods: This study investigated the diagnostic abilities of experts and non-experts when using C-WLI and M-NBI to distinguish superficial-elevated type gastric epithelial neoplasms as cancer or adenomas. Among consecutive patients with a gastric epithelial neoplasm who underwent endoscopic resection at our hospital between 2006 and 2011, this study included 1) superficial-elevated type lesions, 2) lesions evaluated preoperatively by both C-WLI and M-NBI, and 3) lesions that were histopathologically examined. Cases of resected lesions with a histopathological diagnosis of cancer or adenoma were reviewed in random order by two endoscopists (expert: endoscopic experience 20 years, magnified endoscopic experience 8 years; non-expert: endoscopic experience 7 years, magnified endoscopic experience 3 years). These endoscopists, who were unaware of the diagnosis, were asked to distinguish these lesions as cancer or adenoma based on the following criteria. The diagnosis by C-WLI was based on lesion color [1]. Lesions that appeared red compared to the background mucosa were diagnosed as cancer. Non-red lesions (same color or discolored compared to background mucosa) were diagnosed as adenomas. The VS classification system (VSCS), proposed by Yao et al, was used as the diagnostic criteria for M-NBI. The resected lesions were classified, based on their histopathological findings as the gold standard, into low-grade adenoma (LGA) and early cancer/high-grade adenoma (EC/HGA). Diagnostic sensitivity and specificity for EC/HGA based on C-WLI and M-NBI, when performed by an expert and non-expert, were compared. McNemar's test was used for statistical comparison between the two groups. The level of statistical significance was $p < 0.05$.
Results: There were 147 superficial-elevated type gastric epithelial neoplasms (LGA group 48; EC/HGA group 99). As for the sensitivity (95% Cl) of C-WLI vs. M-NBI in Expert, 68.6% (59.5-77.8) vs. 93.9% (89.2-98.6), the specificity were 89.5% (80.9-98.2) vs. 87.5% (78.1-96.8). In expert, M-NBI significantly had higher sensitivity than C-WLI. As for the sensitivity of C-WLI vs. M-NBI in non-expert, 67.6% (89.2-98.6) vs. 89.9% (83.9-95.8), the specificity were 84.3% (71.7-96.9) vs. 70.8% (57.9-83.6). In non-expert, M-NBI significantly had higher sensitivity than C-WLI as well as expert.
Conclusion: The diagnostic sensitivity of M-NBI using the VSCS is superior to the diagnostic sensitivity of C-WLI in the differential diagnosis of superficial-elevated type gastric epithelial neoplasms as cancer or adenoma. M-NBI had similar diagnostic ability when performed by an expert and a non-expert.

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Disclosure of Interest: None declared

P1375 A NOVEL HIGH-PRESSURE CARBON DIOXIDE SUBMUCOSAL INJECTION TECHNIQUE IN ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) can be used for successful en bloc resection of early stage gastrointestinal tumors including large lesions. However, this requires an effective submucosal (SM) injection agent that is safer and more effective. We previously reported on the effectiveness of carbon dioxide (CO_2) as a SM injection agent during ESD procedure[1)]. CO_2 was filled into a 50ml syringe and then injected by hand into the SM layer which resulted in physical dissection of that layer. However, additional injection solution was necessary for maintaining the SM cushion based on previous feasibility study[2)]. Hence, we developed a high pressure CO_2 SM injection (HPCSI) technique to facilitate ESD.
Aims & Methods: The aim of this preclinical study was to assess the feasibility of this novel technique in a live pig model. Twelve domestic female pigs of about 30 kg underwent gastric ESD in two groups. Two different areas of artificial lesions measuring 3×3 cm were marked with soft coagulation in each of the six pigs. HPCOSI system consisted of a prototype electrosurgical knife which has the gas emitting lumen at the tip of the sheath with a CO_2 insufflation regulator connected to a CO_2 bottle. By alternate allocation, circumferential incision using a prototype electrosurgical knife of HPCSI, followed by SM dissection using HPCSI was performed (HPCSI group). Large vessels in the SM layer were coagulated using the tip of a knife. In the other group, conventional ESD was performed following SM injection of normal saline solution. All procedures were performed by one of two endoscopists. The area of the resected pieces was calculated by using the formula for calculating the area of a circle: (Area = Pi × radius^2) SM dissection speed was calculated by dividing the area of the resected piece in relation to the total dissection time (speed = area/time). Second look gastroscopy was performed on day 3. The thickness of submucosal layer in the resected specimens and the degree of inflammation (score: 1 to 3) around ESD-induced ulcer were evaluated histopahologically between two groups by an independent pathologist in a blind fashion.
Results: All procedure achieved en bloc resection. SM dissection speed was significant faster in the HPCSI group than the control group (8.1 ± 3.7 vs. 4.8 ± 2.2 cm^2/sec, $p = 0.017$). No perforation occurred and one delayed bleeding occurred in the control group. Second look gastroscopy did not observe any necrotic changes of gastric mucosa around ESD-induced ulcers. There were no statistically significant differences of the thickness of submucosal layer (270.8 ± 125.6 vs. 431.3 ± 107.0 μm, $p = 0.17$) and the inflammation score (1.8 ± 0.8 vs. 1.6 ± 0.5 μm, $p = 0.45$), respectively.
Conclusion: A novel HPCSI technique may represent advancement in safe and effective SM dissection procedure. The value of this technique for clinical use awaits further study.

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P1376 THE EFFICACY OF ON DEMAND LIQUID SIMETHICONE IN IMPROVING ENDOSCOPIC VISIBILITY DURING UPPER GASTRO-INTESTINAL ENDOSCOPY (UGIE): A PROSPECTIVE RANDOMIZED PLACEBO CONTROL STUDY

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Introduction: Intraluminal foam and bubbles can hamper endoscopic visibility, potentially missing lesions and extending time of procedure. Simethicone is a defoaming agent which decreases surface tension, leading to coalescing of foam and bubbles. Simethicone is not absorbed from gastrointestinal tract and is not attached to other drugs, rarely has adverse effects. Previous studies reported that the addition of simethicone with bowel preparation before performing colonoscopy and small bowel capsule endoscopy is useful by increasing endoscopic visibility, diagnostic accuracy and endoscopist satisfaction. Nevertheless, there have been limited data on its usefulness in UGI endoscopy on demand basis.
Aims & Methods: To evaluate the effectiveness of liquid simethicone washing on enhancing endoscopic visibility in patients undergoing UGI endoscopy.
Randomized prospective placebo-controlled trial, adults aged 18-60 years undergoing elective UGIE included. Exclusion criteria were nasogastric tube insertion, stenosis and retention in upper digestive tract, history of gastric surgery, cardiac and coronary artery diseases within 6 weeks, uncontrolled pulmonary diseases, pregnancy, thrombocytopenia (platelet less than 20,000/mm3), coagulopathy (INR over 2.5), non co-operative and history of simethicone use within 2 weeks. Study group was given adjunctive simethicone washing, 3 ml of liquid simethicone (120 mg) in 50 ml of water and placebo group was given 50 ml of plain water. Grading system of Mc Nally used for severity of foam and bubbles as following: grade 1 (no foam, bubbles), 2 (minimal), 3 (moderate) or 4 (abundant, obscuring of mucosal surface) at stomach or duodenum. The mean value of Mc Nally scores at the stomach and was compared.
Results: A total of 144 patients were prospectively enrolled to the present study. Seven patients were excluded due to non co-oprtiveness (n = 3), NG tube feeding (n = 1), gastric surgery (n = 2), asnd recent myocardial infarction one patient. Finally 137 patients were randomized into two groups: 71 patients were given adjunctive simethicone washing, and 66 patients received placebo. Both groups were comparable on demographic and clinic parameters. In simethicone group reduction of mean value of foam and bubbles scores wass better (2.4 vs 3.8, $p < 0.001$). Endoscopist satisfaction was graded by self-rated endoscopic visibility scale as very good, good, fair, bad, very bad (30 %vs 5%, 40% vs 5%, 25% vs 30%, 5%vs 45% and 0%vs 15%). The results revealed that simethicone enhanced endoscopist satisfaction significantly by showing higher proportion of very good and good endoscopic visibility scale in this group compared to placebo (72.0% vs. 13.4%, $p < 0.001$).
Conclusion: Using on demand simethicone during UGIE, enhances endoscopic visibility, increases endoscopist satisfaction. Further studies required to prove its benefit for small lesion detection.
Disclosure of Interest: V. Sharma: None declared, G. Gandhi Conflict with: nil

P1377 SINGLE-CENTRE CLINICAL EXPERIENCE OF HEMOSPRAY ENDOTHERAPY IN PATIENTS WITH ACUTE UPPER GASTROINTESTINAL BLEEDING

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Introduction: Acute upper gastrointestinal bleeding (AUGIB) is a common medical emergency associated with a hospital mortality of 10%. Therapeutic endoscopy with conventional combined injection and mechanical application is the recognised 1st-line intervention to achieve haemostasis. However, 5-10 % of patients experience recurrence of bleeding after initial endoscopic haemostasis. Hemospray (TC-325; Cook Medical, Winston-Salem, USA) endotherapy is now becoming widely available as a novel agent to augment hemostatic efficacy.
We report on the 'real-life' single-centre experience in the UK, of the efficacy and safety of Hemospray in the management of AUGIB.
Aims & Methods: A single-centre retrospective analysis of all patients treated with Hemospray from September 2013 -April 2015 was performed. Case notes were reviewed and data collected including demographics, Rockall score, endoscopic modality, length of hospital stay, repeat procedures and transfusion requirements.
Results: 58 patients (42 male) with a mean age of 64.7 years (range 26-92) were treated with Hemospray at endoscopy. The indications for endoscopy were melaena (29, 50 %), profound anaemia (16, 28 %), haematemesis (6, 10%), oesophagogastric varices (5, 8.6%), dysphagia (1, 1.7%), dyspepsia (1, 1.7%). The mean pre-endoscopy Rockall score was 3 (range 0-7), post-endoscopy Rockall score 5 (range 1-10).
Hemospray was applied as the single modality in 16 cases (2 oesophageal tumours, 4 gastric tumours, 4 peptic ulcers, 1 peptic stricture, 1 Dieulafoy lesion, 1 unidentified D2 bleeding source). Adjunctive modality occurred in 31 cases (54.8% following variceal band ligation as the primary modality). 11 cases required rescue therapy (10 peptic ulcers, 1 polyp bleeding).
Successful haemostasis with Hemospray was achieved for all but one patient (98.3%). This patient (Dieulafoy lesion with Hemospray as solitary modality) required repeat endoscopic dual therapy (adrenaline/clips). 2 cases of bleeding DU required Hemospray despite radiologic embolization of oozing visible vessels.
No procedural complications during and immediately post-application were reported. There were no treatment-related adverse events. There was one in-patient death, not attributable to AUGIB/endoscopy. The mean length of hospital stay was 12 days (range 1-51).
Conclusion: Our experience confirms Hemospray to be an effective endoscopic modality for achieving successful haemostasis in the vast majority of cases of AUGIB, when used as single, adjunctive, or rescue endotherapy, for a wide-range of causes for AUGIB. Our 'real-life' single-centre UK experience supports Hemospray for all major causes of AUGIB; a modality that is easy to apply, and safe to use.
Disclosure of Interest: None declared

P1378 ENDOSCOPIC UNROOFING PROVIDES HISTOLOGY OF SMALL GASTRIC SUBEPITHELIAL TUMORS AND MAY ALSO LEAD TO TUMOR REMISSION IN MANY CASES: A RETROSPECTIVE STUDY INCLUDING FOLLOW-UP

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Introduction: Accurate diagnosis of small gastric subepithelial tumors (SETs) is essential in order to assess their malignant potential. Endoscopic unroofing by conventional snare or needle knife has been reported to yield sufficient tissue samples for histological evaluation including immunohistochemical staining.
Aims & Methods: We aimed to evaluate endoscopic unroofing in patients with small gastric SETs regarding its safety and diagnostic accuracy as well as a

potential therapeutic effect of this technique over time. In the context of a retrospective analysis, we identified patients who underwent endoscopic unroofing of small SETs of the stomach at our department. Demographic data, indication for intervention, safety of the procedure and follow-up were assessed.

Results: Between 2003 and 2012 a total of 14 patients (7 male, 7 female, median age 70 years, range 51-95 years) underwent endoscopic unroofing of 14 SETs with a mean diameter of 26 ± 13mm at endosonography. Indications were histology sampling for risk stratification (9 cases) and treatment of symptoms including bleeding or abdominal pain in patients unfit for surgical resection (5 cases). Unroofing was performed with a standard polypectomy snare and technically successful in all but one case where the cutting failed due to the big diameter (30mm) of the SET. Bleeding was the only adverse event (in 4 cases) and could always be managed by clip application and argon plasma coagulation, respectively. Histological assessment revealed mostly gastrointestinal stromal tumor (GIST) (8 cases, all of which were low risk GISTs) and one case each of leiomyoma, fibroid polyp, glomus tumor and ectopic pancreas. In one case, the specimen was not diagnostic. Histology proved complete resection of the glomus tumor, all other lesions were partly resected. Endoscopic follow-up including endosonograghy was available for 10 patients over a median time span of 8 months (range 2-81 months). Of these patients, 8 cases (6 with GIST, 1 with leiomyoma, 1 with glomus tumor) showed a complete and 2 cases (both with GIST) a partial remission of their SET over time. Until now, 1 patient with partial remission underwent surgical resection due to an increase in size of his GIST, the patient with the fibroid polyp died from an unrelated cause.

Conclusion: Unroofing of small gastric SETs is a safe procedure that showed a high diagnostic yield. In our study, this technique led to a complete remission of the SET in a majority of patients (in 62% of patients with successful unroofing), including also 6 GIST cases. For patients with gastric SETs who are unfit for surgical resection, endoscopic unroofing might be a safe and effective diagnostic and therapeutic strategy that deserves further investigation.

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P1379 ESOPHAGEAL INVOLVEMENT IN LICHEN PLANUS - A NOT SO RARE CONDITION

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Introduction: Lichen planus is a common disease. According to various epidemiological data up to 0.5% of the population is affected. Its pathogenesis is unexplained, but an autoimmune component is highly probable. Histopathology shows a band-like predominantly T-lymphocytic inflammation at the dermo-epidermal junction with interface dermatitis. Main manifestations are skin and oral mucosa, less frequently genital mucosa. There are only few case reports and case series about an involvement of the esophagus.

Aims & Methods: In order to investigate the frequency of an esophageal involvement patients with lichen planus who were treated in our dermatological outpatient clinic were invited to undergo an esophago-gastro-duodenoscopy at the interdisciplinary endoscopical unit. Most patients were examined by one gastroenterologist (WK). The following criteria were regarded as visible macroscopical signs of esophageal lichen planus: Friability or sloughing of the mucosa, whitish areas, mucosal tears, stenosis as late sequelae. Histological criteria were (in analogy to dermal lesions): mainly lymphocytic infiltration, denudation of the epithelium, deposits of fibrinogen and/or IgG along the basement membrane in immunofluorescence.

Results: In 8/24 patients with skin and/or oral lichen planus macroscopical and histological criteria for esophageal involvement were fulfilled. in further 4 patients we found histological lesions in the esophagus. In 4/8 patients with macroscopical lesions dysphagia was the leading symptom. One patients had a scarring stenosis that required endoscopical dilatation. 3 of these 8 patients did not indicate any esophageal symptoms. Esophageal involvement of lichen planus responded well to therapy with systemic and/or local therapy with corticosteroids. However, in patients with severe dysphagia systemic corticosteroid therapy seems to be necessary for induction of symptomatic remission.

Conclusion: Even if our patients cannot be regarded as an unselected cohort, these data suggest that esophageal involvement in lichen planus is more frequent than anticipated. Surprisingly severe lesions can be found not only in patients with dysphagia but also in asymptomatic patients. Our data also suggest that endoscopic and histological criteria for esophageal involvement should be better defined, in particular the differential diagnosis to mucous membrane pemphigoid may be challenging. Currently there is no standard therapy. In patients presenting with dysphagia dermatological diseases must be considered. Vice versa in patients with skin involvement in lichen planus possible esophageal involvement should be investigated, to prevent stenosis as long-term consequence.

Disclosure of Interest: None declared

P1380 A NOVEL ENDOSCOPIC SUTURING DEVICE FACILITATES ENDOSCOPIC SUBMUCOSAL DISSECTION, AND DECREASE THE COMPLICATIONS

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Introduction: Endoscopic submucosal dissection (ESD) of early-stage gastrointestinal cancer improves the rate of successful en bloc resection, but it is associated with serious complications, such as bleeding and perforation. The common endoscopic suturing devices are almost expensive and based on special equipment. We designed a novel suturing device that is cheap and suitable for conventional endoscopy. Using the new device, we reported the pulley method to facilitate ESD procedures and the closure of large mucosal defects after ESD.

Aims & Methods: Fifteen patients with early-stage gastrointestinal cancers or adenomas larger than 20 mm were enrolled. The pulley method with standard clips and suturing device was used to provide traction to improve visualization of the dissection plane during ESD. The large mucosal defects post-ESD were completely closed with the novel suturing device. All operations were completed using the common single-channel endoscopy.

Results: Pulley-ESD followed by endoscopic suturing of the mucosal defects was performed in 15 patients (mean age, 64 years, 3 lesions in esophagus, 8 lesions in the stomach, 4 lesions in the colon) over a period of 10 months. All lesions (100%) were removed en bloc. No perforation or emergent surgery was noted. There were no immediate or delayed adverse events in any of the study patients. The process of pulley method was successfully completed in all patients, and the mean operating time was 10 ± 3min. Closure of post-ESD defects with the novel suturing device was technically feasible and fast (mean closure time, 10 ± 5min per patient).

Conclusion: The novel suturing device is technically feasible and fast. It can significantly facilitate en bloc ESD and decrease the complications during and post ESD.

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P1381 CLINICAL OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL DUODENAL NEOPLASM IN 60 LESIONS

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Introduction: Superficial duodenal neoplasm is a rare disease. Recently, the improvement of endoscopic technologies has been suggested to lead to better recognition of duodenal adenoma and early cancer. Radical resection techniques such as pancreaticoduodenectomy should be avoided if possible when treating non-invasive duodenal cancer or adenoma because they cause more serious postoperative dysfunction in the duodenum than in other parts of the gastrointestinal tract. The advantage of ESD over EMR is the higher rate of en bloc resection. However, ESD is technically more difficult than ESD for lesions of other parts of the GI tract. In this study, we conducted consecutive duodenal ESD and evaluated its safety and efficacy.

Aims & Methods: Between July 2010 and December 2014, superficial duodenal neoplasm in 60 lesions was treated with ESD at our institution. The ESD procedure was carried out using a Dual Knife and/or Hook Knife through a gastroscope with waterjet functions and a CO2 insufflation system. A soft transparent hood was attached to the gastroscope tip. In most cases we performed under general anaesthesia. Data were collected and evaluated in terms of the clinical outcome.

Results: The mean tumor size was 26.5 mm in diameter (range: 2-75 mm). The en bloc resection rate was 98%. The complete en bloc resection rate was 85%.

The mean procedure time was 93.4 min. Histopathologically, there were 27 lesions of adenocarcinoma and 33 adenomas. There were 11 cases of complications (9 cases of perforation and 2 cases of delayed bleeding). Only one case with perforation required surgery; the others were managed endoscopically. Both cases with delayed bleeding were managed endoscopically. No patient died from any associated complications or duodenal neoplasm. Incomplete en bloc resection was observed in 9 cases in our institution. The estimated median follow-up period was 767 days (range 120–1436 days). Local recurrence occurred in one case. It was well controlled by hotbiopsy and argon plasma coagulation.
Conclusion: On the basis of our results, although ESD is apparently much more reliable than EMR, it should be performed only by experienced experts at advanced high-volume centers since duodenal ESD is technically demanding and risky compared with ESD in any other part of the GI tract.
Disclosure of Interest: None declared

P1382 USEFULNESS AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING A GRASPING-TYPE SCISSORS FORCEPS FOR THE REMOVAL OF EARLY GASTRIC CANCERS

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Introduction: Endoscopic submucosal dissection (ESD) with conventional knife devices was been developed to improve the rate of successful en bloc resection. However, ESD using knife device is technically difficult and carries a high risk of perforation and bleeding, and thus requires skillful techniques. Conventional devices for submucosal incision such as the IT knife and needle knife merely bring the knife in contact with the submucosal tissue and cutting is performed using an electrosurgical current. These cutting methods without fixing the knife to the target have a potential risk of incomplete resections or major complications due to unexpected incision due to pulsation or respiratory movement. To resolve the problems related to ESD using a conventional knife device, the grasping-type scissors forceps (GSF) was developed. This study compared ESD using the GSF and ESD using the knife in terms of tumor size, en bloc resection rates, duration of the ESD procedure relative to tumor size and location, and complication rates.
Aims & Methods: Forty-two patients with early gastric cancers (EGCs) between April 2014 and February 2015 underwent ESD using the knife devices (knife group), and thirty-three patients with EGCs between April 2014 and February 2015 also underwent ESD using the GSF (GSF group). The clinical results were then retrospectively compared between the two groups.
Results: The mean duration of ESD for resected lesions of <20 mm in diameter was shorter in the GSF group than in the knife group ($p < 0.05$). On the other hand the mean duration of the procedure for resected lesions of >20 mm did not significantly differ between the two groups. The mean duration of ESD was not also associated with tumor locations between the two groups. In the knife group, complications comprised perforations in 2 patients (4.8%) and delayed bleeding that required endoscopic treatment in 3 patients (7.1%). However, there was no patient with complications in the GSF group. Although the number of complications tended to be lower for ESD with GSF, the differences did not reach the level of statistical significance. The curative en bloc resection rate in the GSF group was 100 % in tumors of <20 mm and 96.5 % in tumors of ≥ 20 mm. On the other hand the curative en bloc resection rate in the knife group was 100 % in tumors of <20 mm and 94.7 % in tumors ≥ 20 mm. There was no significant difference in the rate of curative en bloc resection between the two groups.
Conclusion: ESD using GSF was technically simpler and thus less time-consuming regardless of the location of lesions, especially when lesions of <20 mm in size. ESD using GSF was considered safe, and it can be universally applied to conventional ESD.
Disclosure of Interest: None declared

P1383 A NOVEL ENDOSCOPIC VESSEL SEALING USING FORCED COAGULATION MODE WITH LOW ELECTRIC OUTPUT DURING ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: To prevent bleeding during endoscopic submucosal dissection (ESD) is an important subject to perform ESD smoothly and safely. We have so far reported the way to decrease bleeding during ESD on the basis of submucosal vessel structures, and the vessel sealing method by soft coagulation mode (E7, 100W, VIO300D) with Flush Knife BT. On the other hand, reports about dissection and vessel sealing using forced coagulation mode with low electric output have recently been seen. Based on these suggestions, we introduced a novel vessel sealing method using forced coagulation mode with low electric output (E1, 10W).
Aims & Methods: The aim of this study is to compare the efficiency of vessel sealing using soft coagulation mode (S method) or forced coagulation mode with low electric output (F method) during ESD. Eight cases each for S method and F method were retrospectively reviewed. ESD was performed by a single operator who has more than 4000 ESD experiences before. None of the patients took any antiplatelet or anticoagulation medicine. The procedures were carried out as follows; 1) submucosal layer tissue surrounding a blood vessel was isolated, 2) both sides of the isolated vessel were cramped with the tip of the Flush Knife BT and coagulated in each coagulation mode until the blood vessels turned white, 3) the blood vessel was cut utilizing the forced coagulation mode (E3, 50W). The frequency of cramps until the vessels turned white, time between the start and finish of coagulation, and the bleeding after cutting the vessels in both method groups were recorded and they were compared statistically.
Results: The total numbers of precoagulated vessels in each group were 55 (S method) and 134 (F method). The average frequency of vessel cramps were 2.4 and 2.19 times ($p = 0.156$), the median time of coagulation were 10 and 9 seconds ($p = 0.490$), and the rate of bleeding were 31% (17/55) and 13% (17/134) ($p = 0.0031$) respectively. Most bleeding could be stopped by forced coagulation mode (E3, 50W), and the number of bleeding which needed hemostasis forceps were 1.8% (1/55) and 2.2% (3/134) ($p = 1.000$) respectively.
Conclusion: The vessel sealing using forced coagulation with low electric output less causes bleeding after precoagulation compared to that with soft coagulation mode. Considering that it takes about 20 seconds only to replace devices if we use hemostasis forceps to precogulate the vessels, this new vessel sealing method seems to be a less time consuming and efficient with low bleeding rate.
Disclosure of Interest: None declared

P1384 ADVANTAGE OF MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING FOR DETERMINING THE HORIZONTAL EXTENT OF EARLY GASTRIC CANCER OVER CHROMOENDOSCOPY, IN TERMS OF DECREASING THE SPECIMEN AREA

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Introduction: Previous study has shown that wide resected specimen is significant factor of delayed bleeding after endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) [1]. Thus, it is required to determine the horizontal extent of EGC with horizontal margin-negative and to decrease the specimen area. The standard method for determining demarcation line is standard endoscopy with dye spraying – chromoendoscopy (CE), with previous study confirming its usefulness. In recent years, the development of magnifying endoscopy with narrow-barrow imaging (M-NBI) has taken advantage of determining a clear demarcation line over CE. While successful delineation was defined that cancerous tissue was limited within the markings, no reports exist regarding the advantage of M-NBI in terms of decreasing the specimen area.
Aims & Methods: The aim of this study is to demonstrate the usefulness of M-NBI for determining the horizontal extent of EGC compared to CE, in terms of the specimen area. Between April 2012 and March 2014, ESD for solitary EGC was carried out at Chiba Cancer Center in a total of 230 consecutive lesions diagnosed by using M-NBI (M-NBI group) which met the following criteria: (?) the predominant histological type was differentiated; and (?) en bloc resection was achieved. As a control group (CE group), we selected 195 consecutive lesions between April 2007 and March 2008, which were diagnosed by using CE and met the same criteria. When the lesion showed clear margins, the periphery of the lesion was marked by electrocoagulation. On the other hand, when the lesions demonstrated unclear margins, we took multiple biopsy samples. Then we put markings, after confirming the histological findings. After the ESD, the extent of the carcinoma was reconstructed on macroscopic photograph according to histological findings. We calculated length from the carcinoma margin to the lateral margin at the short and long axis ($= a + b + c + d$ as shown in Figure 1), and compared it between M-NBI group and CE group.
Results: Differences in clinical and histological characteristics between the two groups were not significant. The horizontal margin-positive with M-NBI group and CE group were observed in 1 of 230 (0.4%) versus 2 of 195 (1.0%), respectively, with no significant difference. The frequency of taking biopsy samples with M-NBI group and CE group were 22 of 230 (9.6%) versus 63 of 195 (32.3%), respectively, with the latter significantly higher. The median length ($= a + b + c + d$) of M-NBI group and CE group were 38mm versus 41.5mm, respectively, with the former significantly shorter. In relation to different macroscopic types, those were 41mm versus 44.5mm for the flat and depressed type, respectively, showing significant difference. In relation to tumor size, those were 37.5mm versus 44mm for that >20mm, respectively, showing significant difference.
Conclusion: M-NBI took advantage of determining the horizontal extent of EGC over CE, and made a contribution to decrease specimen area in size.

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Disclosure of Interest: None declared

P1385 THE INCIDENCE OF SYNCHRONOUS AND METACHRONOUS GASTRIC CANCER AFTER ENDOSCOPIC RESECTION OF EARLY GASTRIC CANCER ACCORDING TO THE DEGREE OF DIFFERENTIATION OF THE PRIMARY GASTRIC CANCER

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Introduction: Endoscopic resection (ER) is widely used as a standard treatment for early gastric cancer (EGC) these days. However, gastric cancer can develop synchronously or metachronously after ER treatment.
Aims & Methods: The aims of this study were to investigate the predictors of recurrence of EGC after ER, especially regarding to the degree of the differentiation of primary gastric cancer. We enrolled a total of 293 patients who met the

extended criteria for ER and underwent this procedure from January 2007 to December 2012 at Kyung Hee University Hospital in Seoul, Korea. And, we retrospectively analyzed baseline characteristics and clinicopathological information about primary gastric cancer. Patients were classified into two groups, the differentiated group and the undifferentiated group. Annually, we followed up the patients with esophagogastroduodenoscopy (EGD) after ER. We excluded the patients whose follow up period was less than 6 months after ER. Synchronous gastric cancer (SGC) and metachronous gastric cancer (MGC) were counted in each group and then performed analysis which factor can influence the development of gastric cancer.
Results: Of the 293 patients, SGC developed in 41 patients (15.2%) in the differentiated group and only one patients (4.2%) in the undifferentiated group ($p = 0.221$). MGC developed in 19 patients (7.1%) in the differentiated group and none in the undifferentiated group ($p = 0.382$). Intestinal metaplasia was seen in 91.5 % of the patients in the differentiated group and 58.3 % of the patients in the undifferentiated group ($p = 0.001$). Although age was the only significant predictor of SGC in both univariate ($p = 0.047$) and multivariate analysis (OR 3.193; $p = 0.010$), it did not show significance in occurrence of MGC. Alcohol showed significant difference between the non-metachronous group and the metachronous group with *p*-value 0.036 in univariate analysis, but failed to show significant result in multivariate analysis ($p = 0.077$). Other factors including sex, smoking, *Helicobacter pylori* infection and baseline gastric mucosal atrophy did not show any statistical significance.
Conclusion: Differentiated type of gastric cancer may be a predictor of occurrence of SGC and MGC because of its high portion of intestinal metaplasia. We should consider the degree of differentiation of primary cancer, age and history of alcohol consumption together with scheduled follow-up EGD after ER. Furthermore, large scale, prospective, long-term follow-up study will be needed to validate our results.
Disclosure of Interest: None declared

P1386 OBSERVER AGREEMENT AMONG BEGINNERS IN IMAGE ASSESSMENT OF BARRETT'S ESOPHAGUS USING A SIMPLIFIED NARROW-BAND IMAGING CLASSIFICATION: A RETROSPECTIVE MULTI-CENTER STUDY

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Introduction: We demonstrated the usefulness of a simplified narrow-band imaging (NBI) classification of surface patterns in Barrett's esophagus (BE) using high-definition magnification endoscopy with NBI (HDME-NBI) (Kato M, et al. *UEGW* 2014). It is, however, unclear whether this classification is useful for beginners. We conducted this study to validate the interpretation of the NBI classification among beginners.
Aims & Methods: A total of 248 HDME-NBI images from non-dysplastic and flat-type dysplastic areas in patients with BE were retrieved and randomized for review by eight beginners (four students and four fellows). All beginners took the 1st exam before receiving the lecture about the classification, the 2nd immediately after the lecture, and the 3rd six weeks after the lecture. The primary endpoint was observer agreement of NBI surface patterns and predicted histology (dysplasia vs. non-dysplasia), and the secondary endpoint was the classification-based diagnostic accuracy values.
Results: The overall inter-observer agreements were substantial for mucosal pattern ($\kappa = 0.65$) and predicted histology (0.61) and moderate for vascular pattern (0.56) in the 2nd. The overall intra-observer agreements were all substantial for mucosal pattern (0.73), vascular pattern (0.74) and predicted histology (0.78) between the 2nd and 3rd exams. The mean values of sensitivity, specificity and overall accuracy for all beginners in the 2nd exam were 88%, 90.2% and 89.7%, respectively.
Conclusion: The simplified NBI classification seems to be easily understandable and reliable and to have high diagnostic accuracy for beginners.
Disclosure of Interest: None declared

P1387 ANALYSIS OF THE CURATIVE EFFECT OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR THE EARLY CANCER AND PRECANCEROUS LESIONS IN THE REMNANT STOMACH

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Introduction: Endoscopic submucosal dissection (ESD) was initially developed in Japan for the resection of early stage gastric cancers.
Aims & Methods: To determine the feasibility and effectiveness of endoscopic submucosal dissection (ESD) for treating early gastric cancer (EGC) in the remnant stomach of patients after gastrectomy.
From January, 2008 to December, 2013, we investigated 36 patients undergoing ESD for EGC in the remnant stomach in Endoscopy Center, Zhongshan Hospital, Fudan University. Pre- and postoperative conditions and long-term follow-up of these patients were evaluated.
Results: Both the success rate and the complete resection were 100%. The median maximum diameter of the tumor size was 1.5 (range 0.6-4.5) cm. During the ESD process, two bleeding cases were treated successfully by endoscopic hemostasis. The average operation time was 40 (10~80) min. The delayed hemorrhage was happened in 2 cases within 1-3 days after operation, and were also treated successfully by endoscopic hemostasis. There was no perforation or delayed perforation. Twelve cases were diagnosed as mild-moderate dysplasia, 7 cases were high grade intraepithelial neoplasia, 16 cases were hyperplastic polyps, and 1 case was signet ring cell carcinomawhich was at the T1 stage and the patient underwent operation for resecting gastric stump and lymph node dissection at 7 days after ESD. The postoperative follow-up was lost. The curative resections rate achieved 92.7%. The median follow-up of the remaining 35 patients was 36 (6~78) months with no discomfort and recurrence.
Conclusion: Although ESD for EGC in the remnant stomach is a time-consuming procedure and requires advanced techniques compared with ESD in normal stomach. ESD performed by endoscopists with sufficient experience appears to be feasible and effective.
Disclosure of Interest: None declared

P1388 ENDOSCOPIC ENUCLEATION OF UPPER GASTROINTESTINAL SUBMUCOSAL TUMORS ORIGINATING FROM MUSCULARIS PROPRIA

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Introduction: Submucosal tumors (SMT) originating from muscularis propria of upper gastrointestinal tract is challenging to remove by conventional endoscopic submucosal dissection (cESD) method due to high perforation rate. Proper closure of mucosal defect is essential to prevent perforation related complications. Metallic clip is the most common method to close perforation. However, the failure rate is high since the size of mucosal defect is usually large. Endoscopic enucleation (EN) has been proposed previously to preserve mucosa and facility clip closure, but comparative studies had been scarce.
Aims & Methods: The purpose of this study was to compare endoscopic enucleation to cESD in clarifying its safety and efficacy in treating submucosal tumor. In this retrospective, single-center study, endoscopic enucleation was attempted in 35 patients (12 male, mean 54.3 ± 11.6 years) with submucosal tumor of esophagus (11) or stomach (24) from Mar 2010 to Mar 2013, and thirty-five submucosal tumors from 35 patients (13 male, mean 50.4 ± 11.3 years) removed by cESD were included as control. All lesions was removed by using needle-tip HybridKnife and insulated-tip knife**.** Mucosal defect closure rate and time were observed.
Results: The median size of the submucosal tumor was 18.0 mm (12.0-25.0 mm) in EN group compared to 25.0 mm (12.0-30.0 mm) in cESD group ($p = 0.260$). A total of 49 cases (23 cases in EN group, 26 cases in cESD group, $p = 0.434$) were originating from deep muscularis propria. All tumors were successfully removed in EN group, while one patient in cESD group was transferred to emergency surgery due to unsuccessful closure of perforation (100% vs. 97.1%, $p = 0.310$). The en bloc rate was 97.1% in EN group compared to 82.9% in cESD group ($p = .046$). Perforation rate was 22.9% in EN group compared to 31.4% in cESD group ($p = .612$), and clip closure was attempted in 33 and 20 cases, respectively. Satisfactory closure was achieved in 32 patients (97.0%) in EN group compared to 9 patients (45.0%) in cESD group ($p < 0.001$). Twelve patients with unsatisfactory closure were treated conservatively by extending fasting time and gastric tube drainage. The median procedure time was 28.0 min (20.0-38.0 min) in EN group compared to 57.0 min (33.0-79.0 min) in cESD group ($p < 0.001$). The median mucosal closure time was 6.0 min (4.0-9.0 min) in EN group compared to 11.0 min (7.0-24.5 min) in cESD group ($p = .001$). Twenty-four hours after the procedure, Oral intake was resumed in patients without perforation. Endoscopy one month later revealed complete healing of the iatrogenic ulcer in 32 cases of EN group and 14 cases of cESD group, and all iatrogenic ulcer was completely healed two month later. No recurrence of tumor has been observed during follow-up.
Conclusion: Both EN and cESD were safe and effective to remove submucosal tumors originating from muscularis propria of upper gastrointestinal tract, but EN had more satisfactory mucosal closure and appears to be less time consuming compared to cESD.

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Disclosure of Interest: None declared

P1389 IRON DEFICIENCY WITHOUT ANAEMIA IN ASYMPTOMATIC PATIENTS: ARE WE DOING ENOUGH

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Introduction: Iron deficiency (ID) without anemia determined by low ferritin levels, is a common phenomenon.[1] There is controversy and little evidence in regards to the diagnostic cascade in these asymptomatic patients at risk of gastrointestinal (GI) malignancy.[2,3] Current guidelines for this group lack consensus and available evidence is quite old.[4-6]
Aims & Methods: This study was planned primarily to evaluate current practices at our hospital to see how thoroughly patients have been investigated and

determine whether or not the current set of investigations are enough to identify all the potential causes of iron deficiency, especially GI malignancy. We identified asymptomatic patients with ID but without anaemia from our local database. Men and post-menopausal women with age over 50 years and without prior diagnosis of any cause of ID were included. Patients were labeled to have ID if serum ferritin was low (less than 15mg/dl) with a normal haemoglobin level (Hb > 115mg/dl). Proportion of patients screened for coeliac disease (CD) was also calculated. Data was analyzed to find out new cases of CD and colorectal carcinoma.

Results: Clinical notes of 444 patients were analyzed and only 76 patients (15.09%) met the eligibility criteria, having a median age 66.5 ± 9.4 years. Fifty two patients (68.4%) were male. Screening for CD was carried out in 29 (38.2%) patients. All the patients had upper GI endoscopy done. Only 23 patients (30.3%) had undergone either colonoscopy or CT colonogram. None of the patients were found to have upper gastrointestinal malignancy. Two new cases of celiac disease (2.9%) and one new case of colorectal malignancy (1.4%) were diagnosed. GI inflammation or ulceration was diagnosed in 32 (42.1%) patients.

Conclusion: We may conclude that all men and post-menopausal women with evidence of iron deficiency but without anemia should be investigated exactly in the same way as we investigate patients with iron deficiency anaemia. Special emphasis on lower gastrointestinal endoscopy if no significant cause of anaemia is found on upper GI endoscopy.

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P1390 CLINICAL OUTCOMES OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSSECTION AND RISK FACTORS ASSOCIATED WITH PIECEMEAL ESD

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Introduction: Endoscopic Submucosal Dissection (ESD) enables en bloc resection of large colorectal neoplasia. However, because of the technical difficulty in colorectal ESD, en bloc resection cannot be achieved in all ESD cases. The aim of our study is to compare the outcomes between en bloc ESD and piecemeal ESD and to identify the risk factors of piecemeal ESD for colorectal neoplasia.

Aims & Methods: We reviewed the medical records of patients who underwent ESD for colorectal epithelial neoplasia, between January 2005 and April 2014 in Asan Medical Center. Patients who did not undergo follow-up endoscopy or who needed subsequent surgery and/or chemoradiation were excluded from the analysis. We analyzed complication, histologically complete resection, and recurrence rate between en bloc ESD cases and piecemeal ESD cases.

Results: Among a total of 494 patients who underwent ESD for colorectal epithelial neoplasia, en bloc ESD and piecemeal ESD were performed in 426 (86.2%) cases and in 68 (13.8%) cases, respectively. The mean tumor size was not different between en bloc ESD (32.4 ± 16.4 mm) and piecemeal ESD group (31.9 ± 10.8 mm) (p = 0.738). The proportion of adenoma, mucosal adenoacrarcinoma and submucosal adenocarcinoma was not statistically different between two groups. Histologically complete resection was more frequent in the en bloc ESD group compared with the piecemeal ESD group (80.5% vs. 61.8%, respectively; p = 0.001). The overall local recurrence rate was 1.6% (8/494). The local recurrence rate was higher in the piecemeal ESD group than in the en bloc ESD group (5.9% vs. 0.9%; p = 0.015). In univariate analysis, piecemeal ESD (OR = 6.59, 95% CI 1.61-27.03; p = 0.015), tumor size ≥35 mm (OR = 13.74, 95% CI 1.68-112.65; p = 0.003), histologically incomplete resection (OR = 6.12, 95% CI 1.44-26.04; p = 0.015), and moderate experienced endoscopist who had performed between 100 and 200 ESD cases (OR = 10.63, 95% CI 2.11-53.41; p = 0.002) were associated with local recurrence after ESD. There was no difference in perforation rate and delayed bleeding between the two groups. Piecemeal ESD was associated with sessile tumor (OR = 1.81, 95% CI 1.04-3.16; p = 0.035), hybrid ESD method (OR = 35.71, 95% CI 18.18-71.43), intraprocedural bleeding (OR = 3.55, 95% CI 1.63-7.69; p = 0.002) in the univariate analysis. Level of endoscopists' experience in ESD was not associated with piecemeal ESD. Multivariate analysis revealed that hybrid ESD (OR = 36.09, 95% CI 18.09-71.99; p < 0.001) and intraprocedural bleeding (OR = 3.71, 95% CI 1.26-10.93; p = 0.017) were independent risk factors of piecemeal ESD.

Table 1: local recurrence of en bloc and piecemeal ESD

	En bloc ESD (n = 426)	Piecemeal ESD (n = 68)	p value
Number of follow up endoscopy	1.9 ± 1.2	2.1 ± 1.3	0.154
Median follow up (IQR), months	15.5 (12.3 - 30.7)	13.7 (6.9 - 33.5)	0.278
Local recurrence	4 (0.9)	4 (5.9)	0.015

Conclusion: Local recurrence was significantly frequent in piecemeal ESD compared with en bloc ESD. Hybrid ESD technique and intraprocedural bleeding were independent risk factors for piecemeal ESD.

Disclosure of Interest: None declared

P1391 PSYCHOMOTOR AND COGNITIVE EFFECTS OF A 15 MINUTE INHALATION OF METHOXYFLURANE IN HEALTHY VOLUNTEERS: IMPLICATION FOR POST-COLONOSCOPY CARE

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Introduction: In addition to its use in ambulance services, portable inhaled methoxyflurane (Penthrox®, 3ml) has been successfully used as a form of patient-controlled analgesia for colonoscopy in both unselected and high-risk patients (Nguyen *et al* 2013, Nguyen *et al* 2015). More importantly, the use of Penthrox® for colonoscopy has been shown to be safe, cost effective and allowed earlier discharge due its lack of sedation. It remains unclear, however, whether it is safe for patients to drive and/or return to work after short-term Penthrox® inhalation.

Aims & Methods: The aim is to evaluate the psychomotor and cognitive effects of 15 minutes inhalation of Penthrox® in adult healthy volunteers. Each of the 50 healthy volunteers, age from 18 to 80 years, were studied on 2 occasions with either Penthrox® or placebo (normal saline with methoxyflurane odor) in a randomized, double-blind fashion. On each occasion, the subject's psychomotor function was examined before, immediately after, and at 30, 60, 120, 180 and 240 min after completion of a 15-min inhalation of the studied drug. Psychomotor and cognitive performance was evaluated by validated Digit Symbol Substitution Test (DSST), auditory reaction time (ART) test, eye-hand coordination (EHC) test trail making test (TMT) and logical reasoning test (LRT).

Results: Compared to placebo, a 15-min Penthrox® inhalation led to an immediate modest impairment of DSST (P < 0.001), ART (P < 0.001), EHC (P < 0.01), TMT (P = 0.02) and LRT (P = 0.04). In all subjects, the performance of all five tests normalized by 30 minutes after inhalation, and was comparable to that of placebo. Although increasing age associated with a deterioration in the performance of all five psychomotor tests, the effects of Penthrox® remained similar and were comparable amongst all age groups.

Conclusion: In all age groups, a 15 minute inhalation of methoxyflurane induces an acute but very short-lasting impairment of psychomotor and cognitive performance, which returns to normal within 30 minutes after inhalation. These findings indicate that subjects who use inhaled Penthrox® for colonoscopy can safely return to tasks that require high psychomotor skills such as driving and work on the same day.

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Disclosure of Interest: None declared

P1392 THE AER-O-SCOPE COLONOSCOPE SYSTEM IS SAFE AND EFFECTIVE FOR COLONOSCOPY IN HUMANS

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Introduction: The self-propelled, disposable Aer-O-Scope Colonoscope (AOS) with 360° view is designed to enhance visualization as well as minimize risk for perforation and infection transmission, while shortening operator training time associated with conventional colonoscopy (CC).

Aims & Methods: We evaluated AOS safety and efficacy for cecal intubation. Prospective patients presenting for colorectal cancer screening underwent AOS immediately followed by CC. Initial patients necessary for AOS operators to achieve proficiency made up the "training cohort". Subsequent enrolled patients made up the "study cohort".

AOS colonoscopy was performed to the cecum, where anatomic landmarks were photographed and mucosal suction-marks placed. During AOS withdrawal, polyps were recorded and similarly marked. At second-pass (using CC), any potential mucosal damage and suction-marks from the AOS, as well as polyps, were recorded.

Main endpoints included: 1) AOS cecal intubation rates, confirmed by anatomic landmarks and residual marks seen at subsequent CC. 2) Frequency and severity of adverse events and mucosal damage with AOS. Secondary endpoints were: 1) Subjective procedure-proficiency, evaluated by the operator based on the training cohort 2) Documenting pathologies visualized with AOS.

Results: 56/58 enrolled patients completed the study. Proficiency with AOS was attained after 8-10 procedures. Cecal intubation was successful in 98.2% (55/56 subjects, 95%CI 90.4-99.9%), including 100% (95%CI 90.7-100%) of the study cohort and 94.4% (95%CI 72.7-99.9%) of the training cohort. No mucosal damage or adverse events were reported. AOS detected 87.5% of polyps seen in tandem CC, including all polyps > 5 mm.
Conclusion: AOS was highly successful, simple to use and safe in attaining complete colonoscopy (cecal intubation).
Disclosure of Interest: N. Gluck: None declared, A. Melhem: None declared, Z. Halpern Consultancy: Consulting fees for GI View, K. Mergener: None declared, S. Goldfarb Conflict with: employee of GI-View, E. Santo: None declared

P1393 ONE-YEAR FOLLOW-UP COLONOSCOPY AFTER CURATIVE RESECTION OF COLORECTAL CANCER: IS IT WORTHWHILE?

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Introduction: Colonoscopic follow-up after colorectal cancer resection (CRC) is recommended to screen for metachronous neoplasia. Although a one-year interval has been suggested, guidelines vary in the timing recommendation for the first investigation
Aims & Methods
Aim: To determine the prevalence of, and risk factor for metachronousneoplasia after curative resection of colorectal cancer among patients undergoing one year follow-up colonoscopy.
Methods: The baseline clinical and colonoscopic data and follow-up details of patients who had a one-year follow-up colonoscopy after curative colorectal resection between January 2004 and October 2014 in a teaching hospital were analyzed. Metachronous colonic lesion was defined as the presence of adenomas, advanced neoplastic lesions (ANL) (>75% villous component, high-grade dysplasia or size > 10mm) or CRC occurring after 12 month of the indexcolonoscopy. Univariate and multivariate analyses were performed to identify risk factors for metachronous adenoma, ANL and CRC. Risk was expressed in odds ratio (OR) with its corresponding 95% confidence intervals (CI).
Results: A total of 143 patients who underwent surveillance colonoscopy between 12 and 18 months after index colonoscopy, were included. The median age was 64(30-90) years and 55% were male. The prevalence of metachronousadenomas and ANL was 28/143(15%) and 7/143(4%) respectively. No metachronous CRC was found. Among the clinical and colonoscopic baseline characteristics the presence of synchronous adenoma (OR 4.2 CI 1.7 – 10.78, p0.001) and ANL (OR 3.21 CI 1.21 – 7.74, p 0.013) were independently associated with presence of metachronous adenomas on one-year follow-up colonoscopy. Presence of ANL on index colonoscopy was the only independentpredictor of metachronous ANL on one-year follow-up colonoscopy.
Conclusion: We found a relatively low prevalence of metachronous ANL and no CRC on one-year follow-up colonoscopy after curative resection of colorectal cancer. However patients with adenomas and ANL at baseline colonoscopy showed a higher risk of presenting metachronous colonic neoplasia, and therefore may benefit from this endoscopic interval.
Disclosure of Interest: None declared

P1394 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR DYSPLASTIC LESIONS IN ULCERATIVE COLITIS

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Introduction: Endoscopic resection of dysplastic lesions in colitis (UC) has been controversial. En bloc resection of the lesion is preferable to allow precise pathologic assessment and minimize recurrence. Endoscopic Submucosal Dissection (ESD) offers this possibility but the comprehensive submucosal fibrosis from long term inflammation may increases the procedural risks and reduces complete resection.
Aims & Methods: In order to assess technical feasibility, multicentres experiences in ESD for UC dysplasia were retrospectively reviewed. Submucosal (sm) condition, namely fibrosis and fat deposition were carefully scored.
Results: Total 26 dysplastic lesions were enrolled (18 UK and 8 Japan). Patient mean age was 62 (49-86) and mean UC duration was 17 years (12-30). Macroscopically lesions were classified into IIa 2, IIa + IIb 6, IIa + IIc 1, Is 2, Is+IIa 2, LST-G 8 and LST-NG 5. Median size was 28.0mm (range5-68mm). They were located in rectum (18) including 4 lesions extended over dentate line , RS (3), SC (4) and on pouch anastomosis (1). Sm fibrosis was observed in all cases (mild 10, mod 11, severe 5) and fat deposition was observed in 9 cases (fat deposition only upper sm 5, whole sm 4).
Enbloc resection was possible in 23/26 cases. Failure of enbloc resection was due to patient intolerance (2), severe fibrosis (1) and extensive fat deposition (1). One patient had delayed bleeding on day3 post procedure. R0 resection was confirmed in 17 cases. Histology showed T1 cancer (2), high-grade dysplasia (6), low-grade dysplasia (17) and regenerative atypia (1). Three patients received panproctocolectomy afterwards. At the first follow up one patient had tiny recurrence (3 mm) which was further treated endoscopically. Hence no recurrence was observed in all patient (n = 16) who had further follow up within median 31 months (3-60).
Conclusion: ESD was feasible for UC dyplasia without an increase rate of complications. However, submucosal fibrosis and fat deposition were frequently observed which contributed to technical complexity. Due to lesions' subtlety, extra wider margin was warranted in order to achieve R0 resection.
Disclosure of Interest: None declared

P1395 OPTICAL DIAGNOSIS OF DIMINUTIVE COLON POLYPS: EXPERIENCED ENDOSCOPISTS BASELINE PERFORMANCE IS NO DIFFERENT TO MEDICAL STUDENTS - A CLEAR TRAINING PATHWAY IS REQUIRED

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Introduction: Accurate optical diagnosis of diminutive colon polyps (DCPs) has been identified as a key goal for advanced endoscopic imaging techniques by the ASGE and ESGE. In-vivo studies show differences in performance between expert and non-expert endoscopists. Training and accreditation pathways for optical diagnosis of DCPs have yet to be established.
Aims & Methods: We aimed to compare the baseline optical diagnosis skills for characterising DCPs of 3 groups with varying experience of colonoscopy, and assess the impact of a novel web-based training module. Participant groups comprised Medical Students (n = 7, 0-5 colonoscopies observed), Gastroenterology Trainees (n = 7, median 120 colonoscopies performed) and Consultants (n = 7, median 3000 colonoscopies performed).
Participants undertook a test module comprising 90 randomised images of diminutive colonic polyps viewed with high definition white light (30), Pentax i-Scan image enhancement (30) and 0.2% indigocarmine chromoendoscopy (30) for which histology was predicted (adenomatous vs hyperplastic). Confidence ratings were also assigned to all predictions. Results were compared to known histopathology.
2 expert endoscopists validated the test module and obtained 86.7% accuracy. Participants then completed an interactive web-based training module before repeating the test module.
Results: Overall accuracy did not differ significantly between the three groups prior to the training module (P = 0.322) or following the training module (p = 0.708). Overall accuracy improved significantly following the training module for all 3 groups. However it remained below that of the 2 expert endoscopists (P < 0.02 for all 3 comparisons).
No significant difference in mean accuracy between the three modalities (HDWL/i-Scan/Chromo) was found pre-training. Post-training mean accuracy for WL and IC images was significantly higher than for i-Scan images (P = 0.002 & P < 0.001).
Mean kappa values and the proportion of high confidence predictions increased significantly for all 3 groups following the training module (Pre training MS/Trainees/Cons 0.106/0.298/0.216, post training 0.472/0.541/0.371). The proportion of high confidence predictions also increased significantly for all 3 groups following the training module.
Conclusion: Baseline optical diagnosis skills amongst experienced endoscopists are no higher than medical students or trainees. It appears that optical diagnosis is a specific skill which cannot be gained through experience of colonoscopy alone.
A brief web-based training intervention produces significant improvement but overall accuracy levels remain below that required to replace histopathology and hence formal training pathways need to be established and incorporated into gastroenterology training programmes.
In this study HDWL imaging was at least as accurate as advanced endoscopic imaging and chromoendoscoy before and after training.
Disclosure of Interest: None declared

Abstract number: P1395

Group	Medical Students				Trainees				Consultants			
Modality	HDWL	i-Scan	Chromo	Overall	HDWL	i-Scan	Chromo	Overall	HDWL	i-Scan	Chromo	Overall
Pre-Training	60.9%	54.3%	61.9%	59.1%	67.6%	67.1%	61.9%	65.7%	65.7%	58.6%	62.8%	62.4%
Post-Training	73.3%	63.3%	71.0%	69.2%	71.9%	66.7%	74.8%	71.1%	73.3%	65.2%	75.2%	71.3%

P1396 DEFINING THE OPTIMAL I-SCAN SETTINGS FOR SMALL COLONIC POLYP CHARACTERISATION – RESULTS FROM A LARGE PROSPECTIVE SERIES

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Introduction: Characterisation of small colonic polyps has been identified as a key goal for advanced imaging modalities by the ASGE and ESGE. Pentax i-Scan is an endoscopic digital contrast technology which has been shown to be accurate tool for characterising small colonic polyps in-vivo. I-Scan combines features which accentuate dark-light borders (surface & contrast enhancement, SE/CE) and suppression of red light whist enhancing blue/green light (tone enhancement, TE). The optimal settings for use of i-Scan in the colon have yet to be determined.

Aims & Methods: High-quality digital images of 100 small colonic polyps were recorded as part of a prospective study (NCT 01761279). Images of each polyp were recorded in 3 i-Scan modes: i-Scan 1 (SE/CE), i-Scan 2 (TE) & i-Scan 3 (SE/CE/TE). Randomised images were viewed by 2 blinded endoscopists who rated visibility of diagnostic features predicted polyp histology (neoplastic vs non-neoplastic).

Results: The proportion of adenomas rated as having visible pericryptal vessels were 59%, 81% and 82% for i-Scan 1, 2 & 3 respectively. The differences between i-Scan 1 and 2 ($P = 0.001$) and i-Scan 1 and 3 ($P < 0.001$) were statistically significant.

The difference in proportion of adenomas with no visible surface pattern between i-Scan 1 and 2 was statistically significant (26% vs 8%, $P = 0.001$), as was the difference between i-Scan 1 and 3 (26% vs 9%, $P = 0.003$). There was no significant difference between i-Scan 2 and 3 (8% vs 9%, $P = 1.00$).

Mean sensitivity for adenomatous histology between the two endoscopists was 69% for polyps viewed with i-Scan 1. Compared to i-Scan 1 assessments sensitivity was significantly higher with i-Scan 2 (86%, $P = 0.006$ for comparison), and with i-Scan 3 (87%, $P = 0.003$ for comparison). There was no significant difference in sensitivity between i-Scan 2 and i-Scan 3 assessments (86% vs 87%, $P = 1.000$).

No significant differences in specificity were found between the 3 i-Scan modes (i-Scan 1 vs i-Scan 2 $P = 0.828$, i-Scan 1 vs i-Scan 3 $P = 1.000$, i-Scan 1 vs i-Scan 3 $P = 1.000$).

Overall accuracy increased from 79% with i-Scan 1 to 86.5% with i-Scan 2 and 87.5% with i-Scan 3. There was no significant difference in overall accuracy between i-Scan 1 and i-Scan 2 ($P = 0.063$) or i-Scan 2 and i-Scan 3 ($P = 0.882$). However there was a significant difference between i-Scan 1 and i-Scan 3 assessments ($P = 0.032$).

	i-Scan 1 (SE + CE)	i-Scan 2 (TE)	i-Scan 3 (SE + CE + TE)
Sensitivity	69/100 (69%)	86/100 (86%)	87/100 (87%)
Specificity	89/100 (89%)	87/100 (87%)	88/100 (88%)
Accuracy	158/200 (79%)	173/200 (86.5%)	175/200 (87.5%)

Conclusion: Tone enhancement appears to be the most effective component of the i-Scan system for accurate small colonic polyp characterisation, with no additional benefit from the addition of surface/contrast enhancement.

Disclosure of Interest: None declared

P1397 COMPARISON OF DIATHERMY SNARE AND COLD SNARE POLYPECTOMY IN SMALL AND DIMINUTIVE ADENOMATOUS POLYPS WITH REGARDS TO COMPLETENESS OF RESECTION

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Introduction: The proper choice of polypectomy instrument and resection method is crucial regarding completeness of resection. To our knowledge, to date no study compared hot and cold snare regarding completeness of resection.

Aims & Methods: We analyzed data from the Austrian colorectal cancer screening program which was provided by participating endoscopists using a standardized form, between 2012 and 2015. In order to accurately attribute histologic findings regarding completeness of resection, exclusively procedures with resection of only one adenomatous polyp, reporting details on snare resection type, were analyzed.

Results: An overall of 1383 resections of diminutive and small polyps were analyzed.

Within the group of diminutive polyps (< 5mm, $n = 388$), resection was graded complete in 81.6% when using hot snare (HS) versus 81.2% (RR 0.99; $p = 0.91$) when using cold snare (CS). In an equal share of polypectomies completeness was graded as uncertain (HS 17.2% vs. CS 17.4%; RR 1.01; $p = 0.96$). Complete resection clearly could not be achieved in 1.2% in the HS groups vs. 1.4% in the CS group (RR 1.21; $p = 0.79$).

As for small polyps (5-10mm, $n = 995$), resection was graded complete in 87.5% when using hot snare (HS) vs. 92.4% (RR 1.06; $p = 0.037$) when using cold snare (CS). Completeness of resection was graded as uncertain in 10.7% in the HS group versus 6.8% in the CS group (RR 0.64; $p = 0.07$), while complete resection clearly failed in 1.7% in the HS groups vs. 0.8% in the CS group (RR 0.46; $p = 0.45$).

Conclusion: With regards to completeness of resection in polypectomy of diminutive adenomatous polyps, HS and CS performed equally well. As for polypectomy of small adenomatous polyps, a higher rate of complete resection might be achieved when using CS.

Disclosure of Interest: None declared

P1398 COLORECTAL ESD AND MANAGEMENT OF PERFORATION BY SECOND GENERATION MASTER ROBOTIC PLATFORM IN ANIMAL MODEL

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Introduction: Our group previously reported a multicenter clinical trial on the safety and efficacy of Master and Slave Transluminal Endoscopic Robot (MASTER) for performance of gastric endoscopic submucosal dissection (ESD) in 5 patients with early gastric neoplasia [1]. The first prototype of MASTER is limited by the inability to exchange the robotic arms, as well as incapability to move the endoscope independent of the arms [2]. The second prototype was developed to address these issues.

Aims & Methods: The second-generation prototype of MASTER was developed with additional degrees of freedom from the robotic arms, the ability to exchange the two arms during dissection, as well as an independent platform to allow separate movement of the endoscope. With the improvement, a standardized protocol for performance of Robotic endoscopic ESD was commenced. The performance of colonic ESD using new MASTER system with the standardized protocol was tested in an ex-vivo porcine model as well as a live porcine model. Moreover, the management of perforation after ESD using the MASTER robotic platform was also examined.

Results: This is a preclinical experiment on three procedures conducted by 2nd generation MASTER. The first procedure was the performance of ESD for resection of a 5 x 5cm imaginary lesion in ex-vivo porcine model. After submucosal injection, mucosal incision was performed using the diathermy hook of one robotic arm at the proximal mucosa. The mucosal was then grasped with the second arm and further mucosal incision was performed around the lesion. Submucosal dissection was performed with clear exposure through adequate retraction of the mucosa. After complete submucosal dissection, the remaining mucosal attachment was resected. The same technique was applied for performance of MASTER robotic rectal ESD in live pig model. The procedure was successful with the specimen size of 30 x 30mm and the operative time was 53 minutes. After the procedure, an artificial perforation was created using the needle knife. The perforation was first grasper by the robotic arm at one edge, pulled laterally to reduce its size thereby minimizing gas leakage, and allowing targeted clip closure. The perforation was successfully closed by endoclip.

Conclusion: The second generation of MASTER robotic system allowed intuitive manipulation, dissection as well as clear endoscopic view for performance of colorectal ESD. The robotic arm also allowed grasping of the perforation to facilitate closure with endoclips.

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Disclosure of Interest: None declared

P1399 PROSPECTIVE RANDOMIZED MULTICENTER TRIAL TO COMPARE ADENOMA DETECTION RATE OF G-EYE™ HIGH DEFINITION COLONOSCOPY WITH STANDARD HIGH DEFINITION COLONOSCOPY – INITIAL RESULTS

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Introduction: The prevention of colorectal cancer (CRC) by colonoscopy is attributed to the identification and removal of adenomas. A significant number of adenomas are missed during Standard Colonoscopy (SC), e.g., due to polyps hidden behind colon folds and flexures. The newly developed G-EYE™ Endoscope (SMART Medical Systems Ltd, Ra'anana, Israel) combines a forward viewing endoscope with an integral, reusable balloon at its bending section. During withdrawal of the G-EYE™ Endoscope, the balloon is partially inflated, allowing for the flattening of colon folds, centralization of the optical image, and

reduction in bowel slippage, thus providing enhanced visualization of the colon and increased detection of polyps and adenomas.
Aims & Methods: The aim of this study is to compare the adenoma detection rate (ADR) of G-EYE^{TM} high definition (HD) colonoscopy with that of standard HD colonoscopy. From May 2014 to April 2015, patients (age > 50) referred to colonoscopy for screening, surveillance, following positive fecal occult blood test (FOBT), or due to change of bowel habits, were randomized to either SC group or G-EYE^{TM} group. The G-EYE^{TM} Endoscope was based on the same instrument as the conventional HD-colonoscope.
Results: 360 subjects were enrolled to the study, of which 177 subjects were randomized to the SC group and 183 subjects were randomized to the G-EYE^{TM} group. The ADR, adenoma per patient, number of advanced adenomas and large-size adenomas for each group are presented in Table 1. Compared with conventional colonoscopy, G-EYE^{TM} colonoscopy increased ADR by 58%. Special attention should be given to 55% and 56% increase in number of advanced adenomas and large-size adenomas, respectively. Procedural times were similar between the two groups.
Table 1: Results summary

	SC	G-EYE	% increase
ADR	31%	49%	58%
Adenoma per patient	0.48	0.89	85%
Advanced adenomas	22	34	55%
Large adenomas (≥10mm)	16	25	56%

Conclusion: Our study has shown that the G-EYE^{TM} endoscope has a substantially higher ADR, compared to SC, which is considered to be one of the indicators for quality in colonoscopy. Moreover, the G–EYE^{TM} endoscope is able to detect not only small and diminutive adenomas but also a larger number of advanced and large size adenomas. It is therefore concluded that the G-EYE^{TM} has the potential to reduce colonoscopic miss rates and reduce interval cancer incidents.
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P1400 ENDOSCOPIC SHIELDING TECHNIQUE WITH A NEWLY DEVELOPED HYDROGEL ON COLONIC MICROPERFORATION IN AN EXPERIMENTAL MODEL WITH RATS

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Introduction: Electrocautery may induce deep thermal injury with transmural necrosis of the bowel, named coagulation syndrome (CS). Prevention of CS is important to avoid unnecessary surgical procedures given the increasing number of endoscopic resections performed every year. To date we do not have any approved endoscopic treatment to avoid the development of CS.
Aims & Methods: The aims of this study were to assess the efficacy of a newly developed hydrogel (patent pending) to prevent CS and to verify experimentally the safety of this treatment procedure.
Colonic microperforation secondary to thermal injury was obtained according to our rat model (1). Lesions were performed in 24 male Sprague-Dawley rats (400-450 g) under general anesthesia. Animals were randomized to receive on of the following sprayed treatments (8-rats each) onto the lesions, as a shield (Endoscopic Shielding Technique or EST): saline control (SC), sodium hyaluronic acid sodium salt 1% w/w (comparative example) and the developed hydrogel (product). Rats underwent endoscopic follow-up at 48h and 1 week. TNF-a plasma levels were determined at 48h. All survival animals were sacrificed after 7 days and ulcers sites were macroscopically and histopathologically evaluated.
Results: Animals treated with product obtained the best results in comparison with control and comparative groups, avoiding mortality (0% vs 50% and 25%; $p = 0.038$), and avoiding or reducing the risk of perforation at 7 days (0% vs 100% and 33.3%; $p = 0.02$); respectively. Mucosal healing rate (percentage of mucosal restoration) at 7 days was significantly higher with product (70% vs 30.3% and 47.2%; $p = 0.003$). Physiological healing (absence of submucosal fibrosis) was significantly higher with product (6 of 8 animals, 75%) than in saline (0 of 4 animals, 0%) and hyaluronic acid (4 of 6 animals, 66.6%) ($p = 0.02$). TNF-α levels were significantly lower with product and hyaluronic acid than in control group (344.5 ± 28.2 and 338.1 ± 17.2 vs 627.58 ± 52; $p < 0.05$).
Conclusion: Our study has demonstrated that the application of this newly hydrogel in a rat model of colon microperforation is able to prevent CS.

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P1401 PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY (PCLE) FOR ANGIOGENESIS EVALUATION IN LOCALLY ADVANCED RECTAL AND GASTRIC CANCERS

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Introduction: Probe-based Confocal Laser Endomicroscopy (pCLE) is an innovative endoscopic technique that allows taking high resolution images of the mucosa, facilitating the identification of cellular and subcellular microstructures allowing an evaluation of the microvasculature during endoscopic examination. Angiogenesis is a hallmark of cancer development inducing the formation of new vasculature to support its growth.
Aims & Methods: The aim of our study was to evaluate tumor neoangiogenesis through pCLE imaging in locally advanced gastric and rectal cancer patients, before and after neoadjuvant radio-chemotherapy (RT/CT).
68 consecutive patients affected by Rectal Cancer (RC, 17F, 51M mean age: 64 years) and 23 consecutive patients with Gastric Cancer (GC, 6F, 17 M mean age: 65 years) underwent endoscopy with pCLE-GastroFlex UHD probe (Mauna Kea Technologies) and i.v. fluorescein infusion in order to evaluate intratumoral vascularization and to evaluate the efficiency of blood flow. After RT/CT treatment, 32 RC (25M, 7F) and 5 GC (1F, 4M) patients were revaluated using pCLE; neoangiogenesis was evaluated according to Cannizzaro-Spessotto (CS) scale, assigning one point to each of the following features: tortuous vessels, large vessels, leakage and defective flux.
Results: 19 out of 32 (59.4%) RC and 2 out of 5 (40%) GC patients showed an improvement of angiogenesis index, while in the remaining 13 RC (40.6%) and 3 GC (60%) there were no changes of the vascular architecture following the treatment. There was a significant difference ($p = 0.00$) in neoangiogenesis CS scores between RC pre- (median CS score: 3.0) and post-RT/CT (median CS score: 2.0), while there's not difference ($p > 0.05$) between GC patients pre- (median CS score: 2.0) and post-therapy (median CS score: 2.0).
Conclusion: Our data show a better reactivation of vessels' morphology and functions in RC patients, with an improvement of angiogenesis index. In GC patients median angiogenesis index remained unmodified, without positive changes in vascular morphology, probably due to the presence of fibrosis. The results of our work demonstrate that pCLE technique is suitable to evaluate the alterations of the intratumoral microvasculature and reveal a functional improvement of vasculature in post-therapy RC patients. It may constitute a innovative approach in order to identify subjects that respond to the therapy, improving the outcome of the patients.
Disclosure of Interest: None declared

P1402 LARGE LOW RECTAL VS. HIGH RECTAL POLYPS: OUTCOME DATA FROM A LARGE PROSPECTIVE SERIES

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Introduction: Low rectal polyps are considered to be more challenging to resect than high rectal polyps.
Aims & Methods: We aim to compare the safety, feasibility and outcomes of endoscopic resection of low rectal polyps (originating within 5cm of dentate line) versus the mid to high rectal polyps. Cohort study of patients referred to our centre. All patients who had endoscopic resection (EMR or Knife assisted resection) of rectal polyps over 20mm in size from 2009 to July 2014 were included. All procedures were performed by a single experienced endoscopist. Benign LST-G type lesions were resected by conventional EMR technique but polyps close to dentate line, those with scarring, and flat LST-NG type lesions were resected either by full ESD or Knife assisted resection technique.
Results: 181 polyps resected in 179 patients. Average patient age 71 years. Mean polyp size 50mm (range 20-170mm). Mean patient follow up 3 years. Referrals were due to large polyp size, proximity to dentate line, growth on haemorrhoidal bed, more than 50% circumference involvement or scarring due to previously failed EMR attempts. Polyp characteristics: 61 (33.7%) > 50mm, 34 (18.8%) scarred, 109 (60.2%) high rectum, 72 (39.8%) low rectum.
110/181(60.8%) were resected by ESD and 71/181(39.2%) by EMR. 60/181(33.2%) were resected en bloc. Histology showed 8(4.4%) cancers, 27(15%) HGD and 146(80.5%) LGD/non dysplastic lesions. There was no significant difference between high and low rectal lesions.

Follow up was available for 158. Endoscopic cure rate: 147/158(93%). Of these 124/147(84%) required 1 attempt, 17/147(11.5%) required 2 and 6/147(4.5%) required more than 2 attempts to achieve complete cure. Recurrence/residual polyp after first attempt was seen in 30/158 (19%) of patients. Univariate analysis showed that recurrence was significantly linked to size > 50mm, piecemeal resection, low rectal lesions and the presence of scarring (table).
The complication rate was 14/181(7.7%) which were all managed conservatively. There was 1(0.5%) significant intraprocedural bleed. There were 7(3.9%) delayed bleeds (2 needing transfusion), 1(0.5%) post polypectomy syndrome and 5(2.7%) cases of exposed muscle fibres which were clipped during the procedure with no further sequelae. There were no factors significantly predictive of complications.
Table 1: Factors associated with recurrence

	SIZE		RESECTION TYPE		SITE		SCARRING	
RECURRENCE30/158 (19%)	≤50mm	>50mm	En bloc	Piecemeal	High rectum	Low rectum	Yes	No
13/108 (12%)	17/50 (34%)	3/57 (5.2%)	27/101 (26.7%)	13/93 (14%)	17/65 (26.1%)	11/28 (39.3%)	19/130 (14.6%)	
p = 0.001		p = 0.001		p = 0.05		p = 0.003		

Conclusion: Rectal polyps referred for resection are generally very large in size (mean 50mm). It is safe and feasible to resect very low rectal polyps around the dentate line. The outcome data shows no difference in complication rates between low and high rectal polyps. Given the large sizes and rectal location, the low cancer rate reflects our careful lesion selection. Recurrence after the first attempt at endoscopic resection is higher in low rectal polyps and those with large size and scarring. However, repeat attempts can achieve complete clearance.
Disclosure of Interest: None declared

P1403 WHAT IS THE TRUE IMPACT OF IATROGENIC PERFORATIONS DURING COLONOSCOPY?

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Introduction: Colonoscopy is the gold standard exam to diagnose and treat colorectal lesions. It is a safe procedure, though the risk of iatrogenic injuries, including perforations, is not negligible. Traditionally, surgery was the first-line therapy in these cases. However, experience in endoscopic closure of perforations and the marketing of devices for this exact purpose have increased, thus making endoscopy a therapeutic option.
Aims & Methods
Objective: Evaluation of the perforations occurred during colonoscopy, their characteristics, treatment and prognosis.
Methods: A retrospective study of all patients with perforations secondary to colonoscopy treated in a tertiary hospital between 01-January-2006 and 01-Oct-2014. Analysis of demographic, endoscopic, radiological and therapeutic data.
Results: We identified 53 cases of perforation, 20 in colonoscopies performed in non-hospital environment (therapeutic-45%) and only with a surgical resolution. The 33 perforations occurred inhospital represent 0.12% of all colonoscopies carried out (n = 21.481). Patients: Male sex-56%; average age-71 years; colic diverticulosis-10%; prior abdominopelvic surgery-31%. Procedures: elective-93%; under sedation-21%; poor bowel preparation-56%; resident participation-35% (resident as the first performer-10 cases). Perforations: rectosigmoid location-35%; average lesions diameter-35mm; diagnosis during the procedure-51%. Treatment of perforations occurred in our unit (73% > therapeutic colonoscopies): 2-conservative, 12-endoscopic (10 successfully), 21-surgical (including the 2 cases with endoscopic approach failure). Comparing the endoscopic treatment (n = 10, G1) versus surgery (n = 22; G2): perforation size- 9mm (G1) / 28mm (G2); perforation location- 7/10 in rectum (G1), 5/21 in rectum and 5/21 transverse colon (G2); no differences in complications or mortality at 30 days.
Conclusion: Perforations in colonoscopy are rare in our clinical practice. Endoscopic closure was effective, though limited to perforations found during the procedure. The mortality is relatively low and this approach does not worsen it. An additional effort is necessary in order to detect perforations during colonoscopy.
Disclosure of Interest: None declared

P1404 WATER EXCHANGE IS SUPERIOR TO OTHER METHODS, ENHANCING ADENOMA AND HYPERPLASTIC POLYP DETECTION IN MALE SCREENING PATIENTS

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Introduction: Patients may develop interval cancers (IC) after colonoscopy. High adenoma detection rate (ADR) is associated with reduced risks of IC, both in incidence and mortality. ICs, partly due to missed lesions, occur predominantly in the proximal colon (cecum to splenic flexure). There is only limited confirmation of the reproducibility of an increase in lesion detection by water exchange (WE, removal of water predominantly during insertion) seen largely in male colon cancer screening patients in U.S. studies [1-4]. In a mixed cohort of male European patients undergoing mainly diagnostic colonoscopy we confirmed these findings [DDW 2015 abstract #2144377].
Aims & Methods: The reproducibility of such observations in 50-70 year old Italian males undergoing first-time on-demand sedation screening colonoscopy was evaluated in a review (01.02.2012 to 31.12.2014) of a prospectively generated database. Split-dose bowel preparation was used to clean the colon. Insertion techniques: air insufflation (AI), water immersion (WI, removal of water predominantly during withdrawal) and WE. Primary outcome measure: overall ADR. Secondary outcome measures: proximal colon ADR, bowel preparation scores and real-time maximum insertion pain.
Results: 379 males were analysed (WE = 121; WI = 125; AI = 133). Demographics, cecal intubation rates, insertion and withdrawal times (around 13.4') were comparable in all study groups. Table 1 shows that **compared to AI**, **WE** achieved significantly higher overall and proximal colon ADR, and decreased the need for sedation. **WE (vs WI and AI)** achieved significantly higher Boston Bowel Preparation Scale scores and lowest real-time maximum insertion pain. Limitations: single-centre, unblinded study. The lack of significance in overall ADR of WE vs WI may be a type II error. Strengths: largest sample size compared with all previous reports.
Conclusion: As in male U.S. Veterans, WE is superior to air insufflation in enhancing overall and proximal colon ADR and in decreasing the need for sedation in male Italian patients undergoing screening colonoscopy. WE is superior to all the other techniques in enhancing colon cleanliness and minimizing insertion pain. Confirmation of these significant impacts in screening cases is important. WE, with the highest adenoma yield, may be relevant in addressing the issue of IC due to missed lesions. WE, with the lowest discomfort and decreased need for sedation, lessens patients' burden.

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P1405 SCREENING COLONOSCOPY WITH THE SYSTEMATIC MAPPING OF PROXIMAL COLON: COMPARATIVE STUDY

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Introduction: According to the published date, most of the missed colorectal lesions during screening colonoscopy are located in proximal colon. The aim

Abstract number: P1404 Table 1

		WEN ± 121	WIN ± 125	AIN ± 133	P value		
					WE vs WI	WE vs AI	WI vs AI
Overall ADR, n (%)		70 (58)	61 (49)	58 (44)	0.155†	0.023†	0.403†
Overall proximal colon ADR, n (%)	All sizes	35 (29)	31 (25)	21 (16)	0.467†	0.012†	0.072†
< 10 mm	29 (24)	25 (20)	20 (15)	0.454†	0.072†	0.294†	
Boston Bowel Preparation Scale, mean (SD)		8.4 (1.0)	7.9 (1.3)	8.1 (1.2)	< 0.0005‡	0.020‡	0.182‡
Real-time maximum insertion pain, mean (95% CI)		2.1 (1.6-2.5)	3.0 (2.4-3.6)	3.1 (2.6-3.7)	0.011‡	0.003‡	0.767‡
On-demand sedation, n (%)		9 (8)	14 (11)	24 (18)	0.310†	0.012†	0.121†

†Chi-squared; ‡ t-test; ADR, adenoma detection rate; SD, standard deviation; CI, confidence interval. Real-time maximum insertion pain (Numeric Rating Scale, 0=none, 1-2=discomfort, 10=maximum).

of our study was to assess the detection rate of colorectal lesions by comparing colonoscopy with the systematic mapping of proximal colon and white light colonoscopy.
Aims & Methods: In one institution, 222 asymptomatic patients (mean age 50.5) participated in study of screening colonoscopy, performed by a single endoscopist using colonoscope CF HQ190 (Olympus Medical Systems). Informed consents were obtained in all cases. Patients were excluded if the bowel preparation was inadequate, if they had an earlier diagnosed colorectal neoplasia or inflammation, or if they were receiving anticoagulant medication. Patients received intravenous propofol prior to intubation of the colonoscope. Complete colonoscopy was performed in 222 (100%) cases.
A conventional examination was performed in 98 patients. A further 124 patients were examined with the systematic mapping of cecum and ascending colon. Totally were performed at least 23 pictures for each patient: appendicular orifice, area proximal to ileocecal valve, overall view of cecum and four-quadrant pictures under each fold of ascending colon. All lesions identified during screening colonoscopy in both groups were removed completely. The two groups were similar with regard to age and gender. Mann-Whitney U Tests were used to determine differences between groups.
Results: There was not anything complications after colonoscopy. Results of colorectal lesions detection are shown in Table, the difference between two groups was insignificant (p value more than 0.05).

	Adenoma detection rate	Proximal adenoma detection rate	Proximal adenoma per patient	Patients with serrated polyp
Conventional colonoscopy	42%	32%	0.60	20%
Systematic mapping	42.7%	35.5%	0.59	23.4%

Conclusion: The results of our study show that there is not significant difference between conventional colonoscopy and systematic mapping for single colonoscopist. Multicenter study should be performed for evaluation of this approach of screening colonoscopy.
Disclosure of Interest: None declared

P1406 SCREENING COLONOSCOPY WITH INDIGO CARMINE DYEING: A BLUE CAP IS A SIGNIFICANT SIGN FOR SESSILE SERRATED POLYPS

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Introduction: Sessile serrated polyps (SSP) are precancerous lesions, but they are often inconspicuous during screening colonoscopy. A mucous cap was described earlier as endoscopic marker for SSP detection. But, in case if mucus is not stained with bile, the visualization of SSP keeps very difficult. The aim of our study was to assess the effectiveness of a blue cap for the detection of SSP after dyeing colon mucosa by indigo carmine solution.
Aims & Methods: In one institution, 222 asymptomatic patients (mean age 50.5) participated in study of screening colonoscopy, performed by a single endoscopist using colonoscope CF HQ190 (Olympus Medical Systems). Informed consents were obtained in all cases. Patients were excluded if the bowel preparation was inadequate, if they had an earlier diagnosed colorectal neoplasia or inflammation, or if they were receiving anticoagulant medication. Patients received intravenous propofol prior to intubation of the colonoscope. Complete colonoscopy was performed in 222 (100%) cases. Totally 105 sessile lesions were detected and stained using 0.2% indigo carmine solution. All lesions and surrounding mucosa were washed actively using "water jet". Residual liquid was removed, after those endoscopic features were evaluated. In case if indigo carmine remains on lesions surface, a blue cap sign was considered. All lesions were removed endoscopically. Results of pathology examinations were compared with endoscopic features. The results of chromoendoscopy were unknown for pathologist.
Results: There was not anything complications after colonoscopy. All 76 lesions, which have had a blue cap sign, were classified pathologically as SSP. Sensitivity and specificity for detection of SSP were 93.9% and 100% respectively. There are no cases of adenocarcinoma in all patients.
Conclusion: The results of our study show that chromocolonoscopy with indigo carmine remains the effective method for differentiation of sessile colorectal lesions. A blue cap is a significant sign for endoscopic diagnosis of SSP.
Disclosure of Interest: None declared

P1407 DIAGNOSTIC CHARACTERISTICS OF DEPRESSED TYPE COLORECTAL NEOPLASMS IN MAGNIFYING CHROMOENDOSCOPY AND ENDOCYTOSCOPY

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Introduction: Colorectal cancers are generally recognized to develop from"polyps". This "adenoma-carcinoma sequence" theory has been in the mainstream of development of colorectal cancers. But recently the existence of many depressed-type cancers has been revealed, which are considered to emerge directly from normal epithelium, not through the adenomatous stage. This theory is called "de novo" pathway. Now, it is possible to presume the histology of colorectal lesions using magnifying endoscopy (pit pattern classification) and endocytoscopy (EC). We can observe not only the structural atypia but also the cellular atypia in living colorectal lesions. The aim is to clarify the diagnostic characteristics of depressed-type colorectal neoplasms, demonstrating the validity of pit pattern diagnosis and EC classification.
Aims & Methods: A total of 23725 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our unit from April 2001 to November 2014. Of these, 15404 lesions were low-grade dysplasia, 5003 were high-grade dysplasia and 1000 were submucosally invasive (T1) carcinomas. According to the developmental morphology classification, they were divided into 3 types: depressed, flat and protruded type. We investigated the rate of T1 carcinomas and the characteristics of depressed-type neoplasms concerning pit pattern and EC classification.
Results: The rate of T1 carcinomas in depressed-type lesions reached to 63.7%, meanwhile that in flat-type and protruded-type lesions was 4.1% and 3.1%, respectively. Within less than 5mm in diameter, that was 10.2%, 0% and 0.06%, respectively. Most (88.3% and 91.2%) of the flat-type and protruded-type lesions showed typeIII_L or IV pit pattern corresponding to adenomas, whereas 94.5% of the depressed-type lesions were characterized by type III_S, $?_I$ or $?_N$ pit pattern corresponding to carcinomas. As for endocytoscopy, most of the flat-and protruded-type lesions showed EC2 corresponding to adenomas. In contrast, the depressed-type lesions were observed as EC3a (24.4%) and EC3b (73.2%) corresponding to invasive carcinomas.
Conclusion: This study revealed the diagnostic characteristics of depressed-type lesions. They show typically typeIII_S,$?_I$ or V_N pit patterns in magnifying endoscopy and type EC3a or EC3b in endocytoscopy. These lesions tend to invade the submucosal layer even when they are small. Therefore, it is important to consider deeply and examine the developmental morphology of colorectal neoplasms.
Disclosure of Interest: None declared

P1408 DO ADJUVANTS REALLY ADD TO THE EFFICACY OF SPLIT-DOSE POLYETHYLENE GLYCOL-BASED BOWEL PREPARATIONS? A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Polyethylene glycol (PEG) bowel preparations are safe and effective but require the consumption of large volumes of fluid, with relative low associated adherence. Alternatively, some data suggest adjuvants may enhance bowel cleansing quality and patient acceptance.
Aims & Methods: We performed a meta-analysis to determine the efficacy, willingness-to-repeat, and procedural outcomes of adding any type of adjuvant to a PEG bowel preparation, given as split-dose, in high (>3L) or low-volume (<2L) regimens.
We performed systematic searches of MEDLINE, EMBASE, Scopus, CENTRAL and ISI Web of knowledge from January 1980 to March 2015 for published results from randomized trials that assessed split-dose regimens of PEG with adjuvant vs split-dose PEG without adjuvant. We excluded studies that included pediatric, hospitalized, or inflammatory bowel disease patients, or trials in which the control group also received an adjuvant. Adjuvants were categorised as osmotic laxatives, irritant laxatives, antifoam products or other (prokinetics). The primary outcome was efficacy of bowel cleansing. Secondary outcomes included patients' willingness to repeat the procedure, polyp and adenoma detection rates.
Results: Of 2,813 citations, 11 trials (n = 2,252 intention to treat patients) fulfilled the overall inclusion criteria. Split PEG low-dose preparations complemented by an adjuvant were not inferior to split PEG high-dose (odds ratio (OR) = 0.82; 95% confidence interval (CI):0.62-1.08; 7 studies). Split PEG high-dose preparations plus an adjuvant resulted in a significantly greater proportion of patients with adequate preparations (OR = 2.98, 95%CI:2.00-4.42, 4 studies). To our knowledge, no study assessed split PEG low-dose versus split PEG low-dose with adjuvants. Willingness-to-repeat was significantly greater with the use of split PEG low-dose with adjuvants compared to split PEG high-dose preparations (OR = 7.46; 95%CI:3.07-18.14; 2 studies), but was lower for split PEG high-dose with adjuvants versus split PEG high-dose (OR = 0.33; CI95% 0.13-0.85). No differences were noted in polyp or adenoma detection rates.
Conclusion: Efficacy of bowel cleansing for split PEG low-dose with the addition of an adjuvant were not inferior to split PEG high-dose, and yielded a higher proportion of patient willingness to repeat the preparation. Split PEG high-dose was more efficient with an adjuvant compared to same dosage without adjuvant but was less tolerated. No differences were noted in polyp or adenoma detection rate. Additional research is required to further characterize adjuvants' impact in split-dose PEG low-volume.
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P1409 CONSTIPATION: IS COLONOSCOPY ALWAYS NEEDED? EXPERIENCE OF A MOROCCAN UNIT

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Introduction: Constipation is one of the most encountered symptoms in Gastroenterology. It may result from several causes that can be diagnosed, for the most of them, with colonoscopy. The aim of our study is to determine the frequency of different colonoscopy findings related to constipation and to evaluate risk factors associated with a pathological colonoscopy.

Aims & Methods: 5222 colonoscopies were performed between January 2006 and March 2015, 511 patients (9.7%) underwent colonoscopy for constipation alone or associated with other symptoms. We excluded incomplete colonoscopies. Statistical analysis was performed using the Spss Software 10.0.

Results: 321 females (62.8%) and 190 males (37.1%) were included. The mean age was 51.21+/-15.47 years. All procedures were performed under sedation with propofol. The Boston score average was 5.21 +/- 1.5 points. Colonoscopy was performed in 108 cases with constipation as sole symptom. In the other cases, constipation was associated with: rectal bleeding in 173 cases (33.8%), abdominal pain in 172 cases (33.6%), alternating with diarrhea in 88 cases (17.2%), weight loss in 62 cases (12.1%), tenesmus in 12 cases (2.3%) and anemia in 7 cases (1.7%). Out of 511 colonoscopies performed we reported: polyps in 88 cases (17.2%), malignant tumors in 18 cases (3.5%), diverticula in 11 cases (2.1%), inflammatory bowel diseases in 11 cases (2.1%), lipomas in 6 cases (1.17%), angiodysplasias in 6 cases (1.17%), melanosis coli in 5 cases (0.9 %), solitary rectal ulcer in 2 cases (0.3%) and 1 case of extrinsic compression (0.1%) and 1 case of rectal varices (0.1%). Colonoscopy was normal in 335 / 511patients (65.5%) all symptoms combined, and in 100/108 patients who had constipation as the only symptom (92.5%). After univariate and multivariate analysis, only age (OR: 0.69, IC 95%: 0.30-0.92, p = 0.04) and rectal bleeding (OR: 0.31, IC 95%:0.15-0.70, p = 0.01) was significantly associated with a pathological colonoscopy (adjusted to gender and abdominal pain).

Conclusion: In our unit, 9.7% of colonoscopies were performed for constipation. Tumors were found in 20.7% cases of which 3.5% were malignant. The contribution of colonoscopy in isolated constipation is close to that of screening colonoscopy, but it keeps a major role when constipation is associated with other warning signs such as rectal bleeding, unintentional weight loss or anemia.

Disclosure of Interest: None declared

P1410 VALIDITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL T1 (SUBMUCOSAL INVASION) CANCER

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Introduction: Endoscopic submucosal dissection (ESD) has allowed the achievement of histologically curative en bloc resection of early colorectal cancer regardless of size, level of fibrosis, or location. Recently, ESD has been performed not only for therapeutic purposes, but also for diagnostic purposes to obtain total incisional biopsies in order to determine the necessity of additional therapy. However, owing to the presence of fibrosis from cancer submucosal (SM) invasion, ESD for patients with pSM is considered more difficult than ESD for patients with pM or adenoma. We investigated the safety and validity of ESD for patients with pT1 (SM) colorectal cancer at our institution.

Aims & Methods: The subjects were 403 patients who underwent ESD for colorectal cancer from January 2009 to August 2014. They were classified into an A group (adenoma/pM cancer) and B group (pSM cancer). Statistical analysis was performed to examine how pT1 (SM) was affected by different factors, including patient characteristics (age, sex), lesion characteristics (site, tumor diameter, macroscopic type), and outcome (en bloc resection rate, mean operation time, non-lifting signs [NLS], presence/absence of fibrosis, complications). Next, the outcomes for pT1 (SM) cases were compared between a vertical margin (VM)-positive group and VM-negative group.

Results: There were 348 lesions in the A group and 55 in the B group. In univariate analysis, the B group had significantly higher fibrosis (p = 0.0105) and NLS (p = 0.0236); in multivariate analysis, only fibrosis remained a significant factor in the B group. Outcomes for pT1 (SM) were 31/24 cases of SM1/SM2, respectively. Further, 83.6% of patients in group B underwent en bloc complete resection, and the complication was only postoperative hemorrhage. Seven cases of the patients in group B were VM-positive, and all were SM2 lesions. There were no significant differences in operation time, tumor diameter, presence/absence of fibrosis, or NLS between the VM-positive and VM-negative groups. The depth of SM invasion was significantly deeper in the VM-positive group than in the VM-negative group (P = 0.0346).

Conclusion: These results suggest that the ESD procedure might be safe and effective irrespective of the depth of invasion. However, this investigation examined cases where ESD was performed by skilled doctors, and there was significantly higher rates of fibrosis in pT1 (SM) colorectal cancer in this investigation, so the level of difficulty is anticipated to be higher. In case of deep SM invasion, there is the possibility of VM-positivity, and a preoperative diagnosis is important; we believe that when deep SM invasion is suspected, it is necessary to perform ESD after having affirmed additional therapy.

Disclosure of Interest: None declared

P1411 VALIDITY OF THE "RESECT-AND-DISCARD" STRATEGY FOR DIMINUTIVE COLORECTAL CARCINOMAS

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Introduction: The "resect-and-discard" strategy has been drawing attention as allowing diminutive and small colorectal tumors, the majority of which tend to be benign, to be resected and discarded without pathologic assessment, as long as they can be endoscopically diagnosed as adenomas with confidence, thus saving the cost of such assessment. However, endoscopic evaluation of these lesions may be associated with the risk of submucosal invasive cancers of the colon being missed inadvertently.

Aims & Methods

Aims: To clarify the clinicopathological features of diminutive carcinomas of the colon measuring < 5 mm in size and to evaluate the validity of the "resect-and-discard" strategy for these lesions.

Methods: A total of 4.934 neoplastic lesions < 5 mm in size which were endoscopically resected between July 2003 and March 2015 and whose histological diagnoses became available were included for analysis. In this analysis, in addition to adenocarcinoma, high-grade dysplasia was handled as consistent with the definition of diminutive carcinoma.

Results: 1) Of all neoplastic lesions examined, malignant lesions accounted for 0.4% (22/4.934), with the histological diagnoses obtained being well differentiated adenocarcinoma (n = 2), one of which contained a depressed-type lesion measuring 1 mm, moderately differentiated adenocarcinoma (n = 1), high-grade dysplasia (n = 19), and low-grade dysplasia (n = 4.912); 2) a majority of the diminutive adenomas were found in the right colon, with 54.5% (12/22) of the diminutive carcinomas found in the transverse colon; 3) in terms of gross appearance, depressed-type lesions (IIa + IIc or IIc) were common and accounted for 45.5% (10/22) of the diminutive carcinomas, while depressed-type lesions accounted for 3.3% (162/4.912) of the low-grade dysplasia; 4) 68.5% (3.367/4.912) of the diminutive adenomas and 63.6% (14/22) of the diminutive carcinomas were subjected to magnifying observation; 5) the treatments implemented included endoscopic mucosal resection (EMR) in 50% (11/22) of the diminutive carcinomas and hot biopsy forceps polypectomy (HB) in 77.2% (3.791/4.922) of the diminutive adenomas.

Conclusion: Diminutive carcinomas were commonly found in the transverse colon as well as in depressed-type lesions, suggesting that diminutive lesions need to be examined for presence of depressed-type lesions using dye spraying and magnifying endoscopy, and all depressed-type lesions need to be completely resected, without resorting to the "resect-and-discard" strategy.

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P1412 FEATURES OF ELECTROCOAGULATION SYNDROME AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL NEOPLASM

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Introduction: *Background and study aims:* Endoscopic submucosal dissection (ESD) is a promising treatment for large gastrointestinal superficial neoplasms, although the method is technically difficult, and perforation and delayed bleeding are well-known adverse events. However, there have been no large studies about electrocoagulation syndrome after colorectal ESD.

Aims & Methods: The aim of this study was to evaluate the incidence and clinical significant risk factors of post-ESD coagulation syndrome (PECS).

This was a retrospective cohort study conducted in a referral cancer center. A total of 336 patients with colorectal neoplasms (143 adenomas or serrated lesions, and 193 carcinomas) underwent ESD from January 2011 to June 2013. Incidence, outcome, and factors associated with occurrence of PECS were investigated. The study protocol was approved by the local ethics committee in our center as No. 1406025042.

Results: PECS occurred in 35 patients (9.5%). The median time until PECS was 15.5 h, and the median period of PECS was 32.5 h. Fever (≥37.6°C) after ESD was found in 41% of the PECS group and 9% of the non-PECS group ($P < 0.001$). All PECS cases were managed conservatively. On multivariate analysis, female patients [odds ratio (OR) = 3.2, $P = 0.002$], lesion location at ascending colon and cecum (OR = 3.5, $P = 0.001$), and resected specimen ≥40 mm (HR = 2.1, $P = 0.05$) were independent risk factors for PECS.

Conclusion: PECS occurred in 35 patients (9.5%) with colorectal ESD, however, all cases had a good outcome with conservative management. Female sex, tumor location at the ascending colon and cecum, and resected specimen ≥40 mm were independently significant risk factors for PECS.

Disclosure of Interest: None declared

P1413 THE TREATMENT OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECTAL NEUROENDOCRINE TUMOR (NET) IN GENERAL HOSPITALS; A MULTICENTRE RETROSPECTIVE COHORT STUDY BY OSAKA GUT FORUM

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Introduction: Endoscopic subumucosal dissection (ESD) for rectal neuroendocrine tumors (NETs) has been reported from referral institutions. However, little is known about the treatment outcome of ESD for rectal NETs in general hospitals.

Aims & Methods: The aim of the present study is to clarify the clinical short- and long-term outcomes in general hospitals and to raise issues concerning ESD for rectal NET. The present study is a retrospective cohort study conducted by Osaka Gut Forum. Patients undergoing endoscopic resection for rectal NETs from 2003 to 2012 were retrospectively investigated. Short-term outcomes (R0, R1 resection rate, and complications) were compared between the conventional EMR and the ESD group. Unclear resection margin was also analyzed as Rx resection. Follow-up survey was performed for patients followed more than 12 months, and long-term outcomes (local recurrence, distant metastasis rate, and survival) were investigated in these patients.

Results: Total 117 patients treated by endoscopic resection for rectal NETs were enrolled. Among these cases, 14 strip biopsy and 7 cap aspiration method were excluded. ESMR-L method was not performed in the present series. Patient age, gender, lesion site, and ulcerations were similar between groups. The lesion size was significantly larger in the ESD group than in the EMR group (6.6 ± 2.1 vs. 5.3 ± 1.7 mm, $p = 0.001$). ESD significantly decreased the R1 resection rate compared to EMR (5.9% vs. 23.3%, $p = 0.001$). The R0 resection rate, however, was similar between both groups because vertical Rx resection is more occurred in the ESD group than in the EMR group. The perforation and delayed bleeding rates were similar between groups. A multivariate analysis showed that ESD was an independent risk-reducing factor for R1 resection [OR = 0.183 (95%CI; 0.036-0.701), $p = 0.012$]. We performed follow-up in 79 patients, including 10 patients with Rx resection. There were no local recurrences or distant metastases [median follow-up period 42 months (19-115)].

Conclusion: In general hospitals, complete resection rate of rectal NET was similar between ESD and conventional EMR despite a decreased incidence of R1 resection in the ESD group. To improve the clinical outcomes of ESD for rectal NET, attention to the possible Rx resection should be paid.

Disclosure of Interest: None declared

P1414 ADVANTAGE OF THE ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) COMPARED TO THE CAP-ASSIST ENDOSCOPIC MUCOSAL RESECTION (EMR-C) IN RECTAL NEUROENDOCRINE TUMORS (R-NETS)

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Introduction: Conventional endoscopic mucosal resection (EMR) for Rectal neuroendocrine tumors (R-NETs) took the suggestions in vertical margin positives frequently. In the past we basically have resecting R-NETs by choosing the cap-assist and aspirational EMR method(EMR-C), and we thought the efficacy and conveniently it. However we experience lack of safety in some cases with EMR-C. Recently we treated R-NETs having the incident with endoscopic submucosal dissection (ESD).

Aims & Methods: The aim was to compare the clinical usefulness of ESD with EMR-C for the thorough resected R-NETs. In the period from January 2004 to October 2013, there were 110 cases of R-NETs that were estimated to be 10mm or less in diameter and without lymph node enlargement. The complete resection rate, incidence of complications, and procedure times associated with each two procedures (EMR-C, ESD) were analyzed.

Results: The 98 lesions were resected using EMR-C, and 12 lesions were resected by ESD. The complete resection rate was 93% (91/ 98) in the EMR-C group and 100% in the ESD group. All of them were pathologically negative findings of the involved lymphovascular or the muscle layer invasion. The average time of procedure was longer in ESD which was taken 32minutes than in EMR-C on 5minutes. One case has perforation in EMR-C for residual lesion after EMR at another hospital, the reason why that case had some fibrosis at submucosal layer. Such as the residual lesion with fibrosis should have taken ESD to avoid perforation and also thorough treatment. There was not any perforation case in ESD.

Conclusion: This comparison has some selection bias such as total cases and indication with two procedures. We recognize that EMR-C was not inferiority against ESD due to most R-NETs. However there are some cases lack of safety and also difficult of thorough resection with EMR-C. Such as the residual lesion with fibrosis and the unclear lesion of border should have taken ESD to avoid perforation and also thorough treatment.

Disclosure of Interest: None declared

P1415 AN INVESTIGATION OF DIAGNOSTIC ENDOSCOPY OF SESSILE SERRATED ADENOMA / POLYP (SSA/P): HOW TO SKILLFULLY PERFORM DIAGNOSTIC ENDOSCOPY

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Introduction: Serrated lesions of the colorectum are classified as hyperplastic polyp (HP), traditional serrated adenoma (TSA), and sessile serrated adenoma/polyp (SSA/P). TSA and SSA/P are thought to undergo malignant transformation through the serrated pathway. The endoscopic and pathological characteristics of TSA have been elucidated, but the pathological diagnostic standards for SSA/P have only recently been established. Much is still unknown about its characteristics including those related to endoscopic findings.

Aims & Methods: 183 lesions identified via colonoscopy as possible serrated lesions and endoscopically resected prior to December 2014 were subjected to pathological diagnosis and classified as SSA/P (Yao et al. classification; 120 lesions), HP (46 lesions), and TSA (17 lesions). The 120 SSA/P lesions were compared to HP, from which they are difficult to differentiate, and the endoscopic characteristics of SSA/P were investigated.

Results: Our investigation of lesion location were as follows: 25 HP (54%) and 21 HP (46%) in the right-sided and left-sided colon respectively, 105 SSA/P (88%) and 15 SSA/P (12%) in the right-sided and left-sided colon respectively, indicating that SSA/P lesions in the right-sided colon were in the majority. Median values for the maximum diameter of the lesions were 7 mm (4-20) for HP and 10 mm (3-20) for SSA/P, indicating that SSA/P lesions were significantly larger. Gross examination of the morphology types of HP and SSA/P respectively indicated that there were 9 lesions (20%) and 13 lesions (11%) that were 0-I, and that there were 37 lesions (80%) and 107 lesions (89%) that were 0-II. In addition, of the SSA/P lesions that were 0-II, one lesion was IIb, 7 lesions were accompanied by small elevations (Is), all were 12 mm or larger, and in 6 cases the Is component was confirmed to be TSA. None of the HP lesions had co-existing lesions. It has been previously reported in Japan DDW that viscous yellowish mucus and a lobulated surface on the lesions were characteristic findings indicating SSA/P. In the present study these findings were observed in both HP and SSA/P in the following numbers: Viscous yellowish mucus was observed on 14 HP lesions (30%) and 107 SSA/P lesions (89%), lobulated surfaces were observed on 19 HP lesions (41%) and 108 SSA/P lesions (90%), indicating that SSA/P displayed these characteristics at a higher rate. Pit pattern diagnosis indicated that 31 HP lesions (67%) and 43 SSA/P lesions (36%) were type II, 15 HP lesions (33%) and 77 SSA/P lesions (64%) were either enlarged type II, type IIIH, or type IVH pit. SSA/P sensitivity was 88.4% and specificity was 71.1% for viscous yellowish mucus, and SSA/P sensitivity was 85.0% and specificity was 69.2% for lobulated surface. Sensitivity was 83.7% and specificity was 41.9% for enlarged type II-, type IIIH-, or type IVH-positive. In the present study, one case of SSA/P (0.8%) had comorbid intramucosal carcinoma.

Conclusion: SSA/P occurs more frequently in the right-sided colon. Conventional observation as type 0-II lesions with viscous yellowish mucus and lobulated surfaces and the additional use of magnifying endoscopy in pit pattern diagnosis for lesions can be expected to improve diagnostic accuracy.

Reference

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Disclosure of Interest: None declared

P1416 ENDOSCOPIC MANAGEMENT FOR SIGMOID VOLVULUS: SHOULD WE PERFORM ENDOSCOPIC DETORSION IN ALL CASES?

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Introduction: Sigmoid volvulus (SV) is a relatively common medical emergency. Endoscopic management is the first choice as an initial therapy for SV for the reasons of technical easiness and less invasiveness.

Endoscopic detorsion, untwist of sigmoid colon using colonoscope under radiographic guidance, is applied first, however, the successful rate of endoscopic detorsion is not actually high. Endoscopic exsufflation, just suction the gas into the lumen, is second choice after failure of endoscopic detorsion. However, it has not been clarified the outcomes of endoscopic management for SV, especially the difference between detorsion and exsufflation.

Aims & Methods: The aim of this study is to compare outcomes of these two different managements.

This was a retrospective cohort study from a tertiary hospital. SV was suspected in patients with intestinal obstruction symptoms, and was diagnosed with computed tomography finding of dilated sigmoid colon around its own mesentery. A total of 42 patients with SV hospitalized for the first time from April 2004 to December 2014 were enrolled. Recurrence cases were excluded in this study. Of these, 5 cases who underwent urgent surgery (3 due to colon gangrene, 2 due to repeated SV history), 4 cases who were not followed up after discharge and 1 case who refused surgery regardless of apparent colon gangrene sign were excluded, and a total of 32 patients were included into data analysis. It was

unknown whether detortion was superior as compared with exsufflation following unsuccessful detortion or not. Therefore we compared complication rate and hospitalization length as short-term outcomes and cumulative recurrence rate and mortality as a med- and long-term outcomes between detorsion and exsufflation group. Student's t analysis or Fischer's exact analysis was used for comparison of short-term outcomes and Kaplan-Meier method and log rank analyses were used to compare cumulative recurrence rate.
Results: Male-to-female ratio was 2.6: 1. Mean age was 80.5 ± 8.4 years old. Median observation period was 189 days [IQR 67-504]. Fifteen cases (47%) were initially managed by endoscopic detorsion and seventeen cases (53%) tried to untwist by endoscopy were managed by exsufflation alone. There were no adverse events associated with endoscopic management. Mean hospitalization length was significantly shorter in detorsion group than in exsufflation group (6.1 days vs 11.8 days, $p = 0.0008$). One-year cumulative recurrence rate of all included patients was 66%. There was no difference of cumulative recurrence rate between detorsion and exsufflation group ($p = 0.45$). Of 23 patients with recurrence, one (4%) died of colon gangrene at the time of first recurrence.
Conclusion: The outcomes of endoscopic detorsion and exsufflation were equivalent as management for SV except length of hospitalization. When considering the high recurrence rate of both treatments and the risk of death due to colon gangrene, elective surgery was recommended, if at all possible.
Disclosure of Interest: None declared

P1417 QUALITY IN ENDOSCOPY: A RETROSPECTIVE AUDIT OF RECTAL RETROFLEXION IN LOWER GI ENDOSCOPY

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Introduction: Retroflexion in the rectum is recommended during lower GI endoscopy to avoid missing adenomatous polyps/cancer in the difficult to visualise anorectal region.[1] It is a recognised component of colonoscopy improvement bundles.[2] Retroflexion aids in detection of lesions missed by the straight viewing scope.[3] There is lack of data about quality standards of retroflexion in current clinical practice. The aim of this study was to audit practice of rectal retroflexion and image documentation at lower GI endoscopy in a non-tertiary endoscopy unit.
Aims & Methods: A retrospective analysis was performed of all flexible lower GI endoscopic examinations over a 2-month period between 1st January and 28th February 2015. Reports were accessed from the hospital endoscopy reporting system (HICSS) and corresponding images for each procedure performed were analysed for evidence of photodocumentation of rectal retroflexion and image quality. Image quality was recorded as either adequate or poor.
Results: A total of 1402 Lower GI endoscopies were performed between 1st Jan and 28th Feb 2015. Of the 1402 examinations 136 patients were excluded from the analysis. Overall there was evidence of retroflexion in only 31% of patients. There was variation of practice amongst different endoscopists with the highest percentage of photodocumentation of retroflexion being recorded by physician endoscopists (see table 1) Of the cases where there was evidence of retroflexion, image quality was of an acceptable standard in only 62%. Taking this into consideration, overall there was clear image documentation of retroflexion in only 19.1% of patients.
Table 1

Endoscopist	Adequate Reftroflexion	Poor retroflexion	No retroflexion
Physician(n = 509)	144(28.2%)	103(20.2%)	262(51.4%)
Surgeon(n = 607)	80(13.17%)	37(6.09%)	490(80.72%)
Nurse(n = 92)	11(11.9%)	7(7.6%)	74(80.4%)
GP(n = 58)	7(12.06%)	1(1.72%)	50(86.2%)

Conclusion: This study demonstrates the rectal retroflexion is poorly performed at flexible endoscopy. Photodocumentation was of an acceptable quality in the minority. Endoscopists should be educated about the importance of routine retroflexion and photodocumentation at flexible sigmoidoscopy and colonoscopy. Endoscopists should take time and care when examining the rectum in retroflexion to avoid missing low rectal lesions. There should be as great an importance given to photodocumentation of the rectum in retroflexion as a quality indicator of completion of colonoscopy /flexible sigmoidoscopy as is given to documentation of caecal intubation.

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Disclosure of Interest: None declared

P1418 THE NOVEL ABILITY OF ENDOCYTOSCOPY TO DIAGNOSE THE HISTOLOGICAL DEGREE OF DIFFERENTIATION IN EARLY-STAGE COLORECTAL CARCINOMAS

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Introduction: Ultra-high magnifying endoscopy (Endocytoscopy: EC) enables us to observe *in vivo* cellular images at approximately 400x magnification. We have reported that EC images could distinguish between neoplastic and non-neoplastic lesions, and revealed that our EC classification had a good correlation with the degree of submucosal invasion. The aim of this study is to assess whether EC is capable of diagnosing the histological degree of differentiation that is recognized as one of the most important prognostic factors in colorectal cancers.
Aims & Methods: Between April 2001 and November 2014, a total of 23725 colorectal neoplasms excluding advanced carcinomas were resected endoscopically or surgically, and 678 lesions were examined by EC before resection at Showa University Northern Yokohama Hospital. Of these, a detailed verification between both EC images and histopathology of resected specimens were performed in 94 lesions. Histological differentiation was diagnosed according to the WHO classification. In addition, focusing on the size, shape and arrangement of carcinoma glands and nuclei, we divided the EC images into following types; Finding (A): enlarged nuclei and tubular gland lumen, finding (B): enlarged nuclei and unclear gland formation, finding (C): clumpy enlarged nuclei and fused gland formation, finding (D): fine granular structure. Finally, we compared these findings with their histological grade of differentiation in the superficial layer of the resected specimen.
Results: Histopathological examination of the 94 resected lesions revealed that 65 lesions were well differentiated adenocarcinoma (WELL) and 29 lesions were moderately differentiated adenocarcinoma (MODE). There was no poorly differentiated adenocarcinoma on the superficial layer. In 65 WELL lesions, finding (A) was observed in 65 lesions (100%), finding (B) in 20 lesions (30.8%), finding (C) in six lesions (9.2%) and finding (D) in 18 lesions (27.7%). On the other hand, in 29 MODE lesions, finding (A) was observed in 22 lesions (75.8%), finding (B) in 28 lesions (96.6%), finding (C) in 27 lesions (93.1%) and finding (D) in 15 lesions (51.7%). The sensitivity, specificity, accuracy and positive likelihood ratio that the presence of finding (C) predicted MODE were 93.1%, 90.7%, 91.5% and 10.1, respectively. Furthermore, they were 92.3%, 96.6%, 93.6% and 26.8, respectively for the presence of finding (A) and the absence of finding (C) predicting WELL.
Conclusion: The EC finding of clumpy enlarged nuclei and fused gland formation is possibly associated with the cribriform pattern that is peculiar to moderately differentiated adenocarcinoma. Endocytoscopy could have the promising ability of diagnosing the histological grade of differentiation in colorectal carcinomas.
Disclosure of Interest: None declared

P1419 EFFICACY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING AN ADVANCED SCISSORS-TYPE KNIFE FOR EARLY COLORECTAL NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) is one of the most useful methods for treating early colorectal neoplasms, and conventionally utilizes an IT knife, hook knife, or needle knife. However, because these devices are used without fixation to target, there is the potential risk for complications due to unexpected incision. To reduce risk of complications from ESD performed using a conventional knife, we utilized a scissors-type knife (SB knife: Akita Sumitomo Bakelite) that allows keeping an adequate dissection layer and preventing unexpected muscular layer injury. Nevertheless, a longer procedure time has been identified as a disadvantage of the SB knife. Recently, an advanced SB knife was developed to prevent scorching of the knife. In the study, we report the efficacy and safety of ESD using this advanced SB knife for early colorectal neoplasms.
Aims & Methods: The aims of our study were to evaluate the efficacy and safety of ESD performed with the advanced SB knife compared with the conventional SB knife in the treatment of early colorectal neoplasms. The procedure was performed in 160 lesions from 148 patients (M:F = 78:70; median age = 70), from October 2010 to February 2015. ESD was performed with the conventional SB knife in 115 lesions (Group A) and with the advanced SB knife in 45 lesions (Group B). We evaluated the en-bloc resection rate, complete resection rate, specimen size, tumor size, procedure time, and complications. Complete resection was defined as en-bloc resection, where both lateral and vertical margins were negative.
Results: The en-bloc resection rate was 96.5% (111/115) in Group A and 100% (45/45) in Group B ($p = 0.58$). The complete resection rate was 93.0% (107/115) in Group A and 95.6% (43/45) in Group B ($p = 0.73$). The mean diameter of the resected specimens was 34.0 mm (range, 12–112 mm) in Group A and 37.0 mm (range, 7–72 mm) in Group B ($p = 0.19$). The mean diameter of tumors was 26.6 mm (range, 4–99 mm) in Group A and 29.8 mm (range, 3–67 mm) in Group B ($p = 0.23$). The median procedure time was 80 min (range, 20–400 min) in Group A and 65 min (range, 15–420 min) in Group B ($p = 0.49$). The mean ratio of resected specimen area (diameter^2) to procedure time (min) was 15.2 mm^2/min in Group A and 18.9 mm^2/min in Group B, and therefore the resected specimen area per minute was significantly wider in Group B than in Group A ($p < 0.05$). In relation to complications from the procedure, there were no perforations in both groups. Only 5 cases of delayed hemorrhage occurred in Group A (4.3%), and all these cases were controlled with endoscopic hemostasis.
Conclusion: ESD performed using either the conventional or advanced SB knife can be adequately adopted as a technically efficient and safe method for resecting

early colorectal neoplasms. Moreover, the advanced SB knife offers the possibility of making the overall procedure time even shorter.
Disclosure of Interest: None declared

P1420 ANALGOSEDATION IN ENDOSCOPY SUITE USING A MIXTURE WITH 02/N20: EVALUATION OF EFFICACY AND SAFETY

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Introduction: Colonoscopy is the most popular examination in the diagnosis of colorectal diseases, but pain and discomfort generally require analgosedation performed with intravenous technique. Recently the use of conscious sedation with a mixture of 50% N_2O and O_2 (Livopan®) was introduced. A sufficient number of air exchanges through the use of scavenger systems should be provided because the exposure to N_2O is a risk factor for health personnel.
Aims & Methods: The aim of our study was to evaluate the efficacy and safety of N_2O/O_2 mixture vs. midazolam/meperidine (Mid/MEP), and the exposure to N_2O of health personnel both in presence or absence of a collecting system and active evacuation of N_2O.
The study was carried out in Endoscopy Suite of our University Hospital. The patients were divided into 3 groups: patients sedated with N_2O/O_2 mixture with the aid of a mobile system of evacuation with double mask (NIKI group); patients sedated with the same mixture without the aid of the system NIKI (NO NIKI group) and patients sedated with Midazolam 0.5-1.5mg and Meperidine 1-5mg (Mid/MEP group). To evaluate the clinical efficacy and safety were considered: vital signs (heart rate, blood pressure and SpO_2); Ramsay Agitation Sedation Scale (RASS); satisfaction of the operator; VAS; psycho-motor recovery time. The diffusion of environmental N_2O/O_2 was evaluated with infrared photoacoustic spectroscopy across five sampling points located within ambulatory endoscopy. Measured results were processed using descriptive statistical analysis using software "IC Stata 9.2 for Mac." The comparison analysis between groups were made using t-test and the "one way ANOVA", while for concentrations of N_2O between the two groups the Mann-Whitney U test was used, whereas, as statistically significant, a value of $p < 0.05$ was considered.
Results: We enrolled 86 patients of which 39 in NIKI group, 6 in NO NIKI group and 40 in Mid/MEP group. The three groups had similar demographic characteristics. The Mid/MEP group reported a mean VAS lower than NO NIKI group ($p < 0.05$). NIKI group reported a mean VAS lower than NO NIKI group but higher than Mid/MEP group. Mid/MEP group reported a mean RASS higher than NIKI and NO NIKI groups. Recovery time was higher in Mid/MEP group compared with both NIKI and NO NIKI group. Mean N_2O/O_2 concentrations in NO NIKI group was 450 ± 347 ppm, while in NIKI group was 28 ± 55 ppm ($p \leq 0.001$).
Conclusion: During colonoscopy the use of an anesthetic short-acting agent would be the best choice for providing adequate sedation and comfort and quick recovery of psycho-motor functions. Our study showed that the mixture of 50% nitrous oxide and oxygen offers these benefits and may represent an effective alternative to intravenous sedation. The environmental monitoring shows that the N_2O/O_2 concentrations varies considerably depending on the utilization, or not, of the scavenger system that is a valid tool to ensure the safety of the operators.
Disclosure of Interest: None declared

P1421 HIGH DEFINITION WHITE LIGHT ENDOSCOPY (HDWLE) VERSUS HIGH DEFINITION WITH CHROMOENDOSCOPY (HDCE) IN THE DETECTION OF DYSPLASIA IN LONG STANDING ULCERATIVE COLITIS: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Patients with ulcerative colitis (UC) have an increased risk for colorectal cancer (CRC) compared to the general population. The yield of surveillance can be improved by addition of newer endoscopic methods that enhance the detection of subtle mucosal abnormalities like chromoendoscopy (CE)[1] and HDWLE[2] when compared to standard definition endoscopy. CE however is still not widely adopted and no studies have compared HDCE and HDWLE.
Aims & Methods
Aims: To compare the rate of detection of dysplasia in patients with long standing UC with HDWLE compared to high definition with CE (HDCE)
Methods: Parallel group randomized controlled trial (clinicaltrials.gov number NCT02138318) in which patients with long standing (>10 years) extensive UC requiring surveillance colonoscopy were randomized to either HDWLE or HDCE (with 0.2% indigo carmine spray). HD scopes (Olympus CF260L or 290L) and processors (Olympus Spectrum CV260 or Elite CV290) and HD monitors were used for all procedures. Time to reach caecum and withdrawal time was recorded. Presence of dysplasia was confirmed by two expert GI histopathologists. Data was analysed according to the number of patients who had dysplastic endoscopic lesions detected (per patient analysis) and also to the number of dysplastic lesions (per lesion analysis).
Results: In total 53 patients were randomized to HDWLE and 50 to the HDCE arm. Baseline characteristics including duration of disease, bowel preparation, endoscopists, concomitant PSC and previous dysplasia were similar in both arms. A total of 14 dysplastic lesions (1 with high-grade and 13 with low-grade dysplasia) were detected in 11 patients (22%) in the HDCE arm and 6 dysplastic lesions (all low grade dysplasia) in 5 patients (9.4%) in the HDWLE arm. HDCE was significantly better ($p = 0.04$) than HDWLE on a per patient basis for the detection of endoscopically visible dysplastic lesions. HDCE (0.26 ± 0.6) detected more dysplastic lesions per-patient than HDWLE (0.12 ± 0.4). Withdrawal time was significantly ($p < 0.001$) higher in HDCE (21.2 ± 5.8 min) compared to HDWLE (13.6 ± 3.3 min).
Conclusion: HDCE significantly improves the detection of dysplastic lesions in patients with long standing UC undergoing surveillance endoscopy and should be the procedure of choice in these patients. On average it increases procedure time by 8 minutes over HDWLE.

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Disclosure of Interest: None declared

P1422 EFFECTS OF PLATELET-RICH PLASMA ON ENDOSCOPIC MUCOSAL RESECTION IN RAT AND PORCINE MODELS

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Introduction: Platelet-rich plasma (PRP) is a concentrate from blood that contains 3 to 5 times more platelet than the normal concentration. PRP promotes several types of cell activity all of which are necessary in the process of wound and soft tissue healing. Endoscopic resection techniques produce mucosal lesions.
Aims & Methods: In this study we assess the efficacy of endoscope application of PRP to prevent complications and to induce mucosal healing after endoscopic resections. Colonic EMR-induced lesions were performed in rats ($n = 16$) and pigs ($n = 4$). Animals were randomized to receive one of the following sprayed treatments onto the lesions, as a shield (Endoscopic Shielding Technique or EST): saline (control; 8 rats and 2 pigs), and PRP (product; 8 rats and 2 pigs). Pigs underwent endoscopic follow-up at weeks 1 and 2. Rats were followed at 48 h and 7 days, being sacrificed at week 1 to perform histological evaluation of the lesions. Thermal injury was assessed with a 1-4 scale: (1) mucosal necrosis; (2) submucosal necrosis; (3) muscularis propria necrosis; and (4) serosal necrosis.
Results: All rats treated with PRP were alive after 7 days, whereas saline treatment showed 50% of mortality ($p = 0.02$). Mean ulcerated area after 48h and 7 days were significantly lower with PRP than saline (0.27 ± 0.02 cm^2 and 0.08 ± 0.01 cm^2 vs. 0.56 ± 0.1 cm^2 and 0.40 ± 0.06 cm^2; $p < 0.001$). Thermal injury was significantly lower with PRP (1.25 ± 0.46) than in controls (2.25 ± 0.50); $p = 0.006$. Descriptive analysis of porcine model showed a trend to higher mucosal restoration in animals treated with PRP than saline, at weeks 1 and 2 (Median area in cm^2: 0.55 and 0.40 vs 1.32 and 0.79).
Conclusion: The use of sprayed PRP onto EMR-colonic mucosal lesions showed strong healing properties in rat and porcine models.
Disclosure of Interest: None declared

P1423 ENDOSCOPIC SHIELDING TECHNIQUE WITH A NEWLY DEVELOPED HYDROGEL ON MUCOSAL THERMAL INJURY IN A PORCINE MODEL

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Introduction: The incidence of deep thermal injury secondary to therapeutic endoscopy will increase in the future with the widespread use of advanced resection techniques. To prevent this coagulation syndrome we have developed a newly hydrogel (patent pending), that can be sprayed onto the lesions as a shield (Endoscopic Shielding Technique or EST), providing a direct administration through the endoscope channel.
Aims & Methods: The aims of this study were to evaluate the healing process of colonic EMR-induced ulcers in animals with the application of this hydrogel (product), and to verify experimentally the safety of this treatment procedure. Colonic EMR was performed in 8 pigs under general anesthesia. Three ulcers sites were prepared in each pig in left colon: one EMR-ulcer was performed with prior saline submucosal injection (A; EMR-saline), other EMR-saline ulcer was treated by applying a product shield (B; EMR-saline-P), while the other EMR-ulcer was performed with prior submucosal injection of the product and posterior EST with product (C; EMR-P-P). All animals underwent weekly endoscopic follow-up (weeks 1 and 2). At the end of the treatment period new lesions (EMR-saline; EMR-saline-P and EMR-P-P) were performed in healthy colonic mucosa to assess acute injury. All animals were

euthanized at week 2, and ulcers sites were macroscopically and histopathologically evaluated. Thermal injury was assessed with a 1-4 scale: (1) mucosal necrosis; (2) submucosal necrosis; (3) muscularis propria necrosis; and (4) serosal necrosis.
Results: Basal mean ulcerated area induced by EMR was comparable in the three groups (A = 2.12 ± 1.45 cm^2, B = 2.57 ± 1.53 cm^2, C = 2.66 ± 1.64 cm^2; p = n.s.). Submucosal injection of product induced a marked trend to less deep thermal injury (C = 2.25 ± 0.46 vs A and B = 2.75 ± 0.46; p = 0.127). Mucosal healing rate at week 2 (percentage of mucosal restoration) were significantly higher in animals treated with product (B = 90.2 ± 3.9%, C = 91.3 ± 5.5% vs A = 73.1 ± 12.6%; p = 0.002).
Conclusion: The application of this newly hydrogel in a porcine model with EMR-colonic ulcers has demonstrated strong healing properties. Otherwise, submucosal injection of this product is able to avoid high thermal load of the gastrointestinal wall. This technique is safe and easy to learn, and we can solve many drawbacks we have in the field.
Disclosure of Interest: V. Lorenzo-Zúñiga Conflict with: Patent authorship, R. Bartoli Conflict with: Patent authorship, V. Moreno de Vega Conflict with: Patent authorship, A. Hernández: None declared, J. Boix Conflict with: Patent authorship

P1424 PREDICTIVE ACCURACY OF HIGH-RISK SERRATED LESIONS AND THE IMPACT OF A BRIEF EDUCATIONAL INTERVENTION

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Introduction: Real-time characterisation of advanced lesions during colonoscopy informs the therapeutic approach. Sessile serrated polyps (SSP) may be missed but even when detected are almost four times as likely as adenomas to be incompletely resected, especially if large. SSP with dysplastic foci (SSP-D) are considered high risk for malignant transformation. They may be mistaken for other lesions if only the dysplastic (adenoma-like) area of the lesion is appreciated, risking incomplete resection. However, dysplasia in serrated lesions may be detected endoscopically. The ability of expert and trainee endoscopists to do this is unknown.
Aims & Methods: To determine baseline accuracy for *in vivo* histology prediction of SSP-D and the impact of a brief educational intervention.
Seventy high-quality representative images were selected from a database of large sessile and flat polyps. Histopathology was used as the gold standard. The images were presented, in randomised order, to Australasian self-identified ''expert'' and ''trainee'' colonoscopists. Participants were asked to predict the underlying histology of each lesion from five options (SSP-D, SSP with no dysplasia (SSP-ND), tubulovillous adenoma, tubular adenoma, submucosal invasive cancer (SMIC)). Subsequently, a 60-minute educational session explaining the characteristic features of SSP-D was provided. Participants then repeated the test using the same polyp set with images in a different order.
Results: Responses were collected from 37 participants: 16 Trainees and 21 Experts. The groups were differentiated by years of colonoscopy (1.4 vs 12.8; $p < 0.001$) and average number of colonoscopies per week (8.5 vs 19.2; $p < 0.001$). Baseline accuracy (Table 1) was 66% for SSP-ND and 22% for SSP-D with experts demonstrating a significantly better predictive accuracy for SSP-D (p = 0.042).
Post training testing showed a threefold improvement in recognition of SSP-D for the whole cohort ($p < 0.001$). This effect was more pronounced for trainees (17.1% to 67.1%) than for experts (26.0% to 68.2%). Following training there was no significant difference in SSP-D recognition between trainees and experts (p = .837).
Table1: Proportion of responses correct by level of training

	Proportion correct	Mean score (%)	Difference in mean score (95% CI) (%)	Sig. (2-tailed)
Overall score	Whole cohort			<.001
	Pre	55.37		<.001
	Post	60.65	5.28 (2.58-7.99)	.171
	Trainees			
	Pre	46.61		
	Post	55.10	8.49 (5.72-11.27)	
	Experts			
	Pre	62.04		
	Post	64.88	2.84 (-1.33-7.01)	
SSP-D	Whole cohort	22.11	45.62 (38.10-53.14)	<.001
	Pre	67.73	50.06 (37.54 – 62.59)	<.001
	Post	17.06	42.24 (32.33-52.15)	<.001
	Trainees	67.13		
	Pre	25.95		
	Post	68.19		
	Experts			
	Pre			
	Post			
SSP-ND	Whole cohort	66.24	3.22 (-1.42-7.85)	.168
	Pre	69.46	6.75 (-2.34-15.84)	.134
	Post	61.44	0.52 (-4.29-5.34)	.823
	Trainees	68.19		
	Pre	69.91		
	Post	70.43		
Adenomas	Whole cohort	67.95	–11.35 (-16.97–5.37)	<.0010
	Pre	56.60	-8.13 (-16.94-0.69)	.68
	Post	53.75	-13.81 (-21.58–6.04)	.001
	Trainees	45.63		
	Pre	78.77		
	Post	64.95		
	Experts			
	Pre			
	Post			
SMIC	Whole cohort	49.87	–7.59 (-14.55–0.64)	.033
	Pre	42.27	-6.31 (-17.60-4.97)	.252
	Post	42.25	-8.57 (-18.17-1.03)	.077
	Trainees	35.94		
	Pre	55.67		
	Post	47.10		
	Experts			
	Pre			
	Post			

Conclusion: SSP-D lesions are under diagnosed by both expert and non-expert endoscopists. A brief educational intervention can significantly improve the predictive accuracy of lesions encountered at colonoscopy and particularly improves the performance of trainees.
Disclosure of Interest: None declared

P1425 A SIGNIFICANT PROPORTION OF PATIENTS STILL REQUIRE COLONOSCOPY AFTER CT COLONOGRAPHY WITHIN THE NHS BOWEL CANCER SCREENING PROGRAMME

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Introduction: Patients within the Bowel Cancer Screening Programme (BCSP) who are unsuitable for or decline colonoscopy are instead usually offered CT colonography (CTC). Whereas patients with a normal CTC are either discharged or returned back to biennial screening, colonoscopy is usually indicated if CTC demonstrates a suspected colorectal cancer (CRC) or large polyp/s (>10mm). Patients who have intermediate-sized polyps (6-9mm) or multiple diminutive polyps (<5mm) either proceed to colonoscopy (flexible sigmoidoscopy for left-sided polyps) or interval CTC. We investigated the number of patients who required colonoscopy after CTC within the BSCP. We hypothesised that a significant proportion of patients still require colonoscopy, thus questioning the utility of CTC in patients in the BCSP.
Aims & Methods: Patients who had a CTC within the BCSP at UCLH between September 2007-14 were identified retrospectively. All CTC examinations were performed using faecal tagging with laxatives wherever possible with or without intravenous contrast. Results of CTC were classified as normal, low-risk (1-2 polyps both <10mm), intermediate-risk (3-4 polyps <10mm or at least one ≥10mm), high-risk (≥5 small polyps or ≥3 intermediate-sized polyps with at least one ≥10mm) and suspected CRC.
Results: In total, 319 CTCs were performed in 292 patients. 39 patients (13%) had CTC after incomplete colonoscopy and were excluded. 253 patients (136 male, median age 70 years) underwent CTC as their primary investigation and their outcomes analysed.
98 patients (39%) proceeded to having a colonoscopy after their CTC. There was no significant difference in the reported study quality between those patients requiring a colonoscopy (good 44%, poor 10%) and not (good 52% poor 7%). 57 patients (92%) who had either intermediate/high-risk polyps or suspected CRC on CTC underwent colonoscopy. Of these 57 patients, 15 (26%) had either low-risk polyps (n = 9) or no abnormality at colonoscopy (n = 6). 37 patients (20%) whose CTC was either normal (n = 10) or revealed low-risk polyps (n = 27) were also referred for colonoscopy. No patient had their CTC diagnosis upstaged after colonoscopy.
The median time from CTC to colonoscopy was 35 days (5-1852 days). 72 patients (74%) had their colonoscopy within 3 months of their index CTC.
Conclusion: A significant proportion of patients who undergo CTC within the BCSP will still require a colonoscopy. Although the sensitivity of polyp detection between CTC and colonoscopy is comparable, CTC confers a not insignificant radiation burden. It is essential that all patients be counselled with this information upon entrance into the BCSP and in doing so, may reduce the number of CTCs as the primary investigation within the BCSP.
Disclosure of Interest: None declared

P1426 EFFICACY AND SAFETY OF ENDOSCOPIC BALLOON DILATION IN THE INFLAMMATORY BOWEL DISEASE: RESULTS OF THE ENEIDA DATABASE (TEDEII STUDY)

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Introduction: Endoscopic balloon dilation (EBD) is the endoscopic treatment of choice for short stenosis in Crohn's diseases (CD). Several uncontrolled observational studies have shown that EBD in selected patients is a safe and an effective alternative to surgery. Previously published series have limitations due to heterogeneity of technique and different endpoints which makes comparisons difficult, and generally with small series of patients and performed at tertiary care centres.

Aims & Methods: To asses efficacy and safety of EBD in clinical practice setting in Spanish hospitals adhered to ENEIDA project. We identified all patients undergoing EBD from ENEIDA database. Additional information not included in the database was requested to the 16 participating centres: patient's clinical information; stenosis data;and information about effectiveness and complications of EBD. Technical success was defined when endoscope got pass through stricture after the procedure and therapeutic success when it was not necessary another endoscopic or surgical treatment after 1 year or until the end of the follow-up. A logistic regression analysis was performed to assess factors associated with therapeutic success. A survival analysis was done to evaluate predictive factors related to remain free of surgery.

Results: A total of 335 dilations were performed in 162 patients (147 CD, 13 UC and 2 IC) with a median of 2 dilation/patient. In 43.1% of cases strictures were in the anastomotic site. Technical and therapeutic success was achieved in 80.2% and 52.2% of EBD respectively with a median follow-up of 36 months (0-276). 72.4% of the patients were free of surgery or stent placement, 32% with one EBD. In the multivariate analysis, technical success with an OR of 2.62 ($p = 0.012$), the balloon diameter (>12 mm) with an OR of 2.5 ($p = 0.006$) and no need of anti-TNF therapy for the disease control with an OR of 1.71 ($p = 0.031$) were associated with therapeutic success. No related factors were found in the survival analysis. The rate of major complications was 2%.

Conclusion: In a clinical practice environment, EBD has a similar efficacy and safety than has been reported in tertiary care centres. Technical success, the balloon diameter (>12 mm) and not needing anti-TNF for disease control were the only factors associated with the therapeutic success. Randomized prospective studies are required to set what other factors are related to the response to EBD.

Disclosure of Interest: None declared

P1427 NATURAL HISTORY OF COLORECTAL ADENOMATOUS POLYP: LONG-TERM RETROSPECTIVE STUDY USING COLONOSCOPY

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Introduction: Endoscopic resection of colorectal adenomatous polyps effectively prevents colorectal cancer[1)]. But natural history of untreated colonic adenomatous polyps is uncertain. At our hospital, adenomatous polyps with a size of ≥6 mm or in which cancer is suspected on magnifying chromoendoscopy are subject to resection, and a follow up approach is adopted for adenomatous polyps with a size of ≤5 mm.

Aims & Methods: We retrospectively observed the natural history of adenomatous polyps and investigated the risk factors for polyp enlargement. We investigated 94 patients (362 adenomatous polyps) who underwent initial colonoscopy between 2007 and 2014 at our hospital and then continuously underwent at least four colonoscopies each year. For all polyps images taken by conventional white light endoscopy and magnified indigo carmine spraying, no polyps were biopsied. Endoscopic pit pattern diagnosis was performed using Kudo's classifications and, with III L pit patterns as subcategories, polyps were categorized into III L1 pit pattern composed of III L pit only, and III L2 pit pattern composed of both III L pit and I pit. Size was evaluated on comparison with the non-traumatic tube (outer diameter, 2.8 mm) in all polyps. Endoscopic reports and endoscopic images were reviewed and re-evaluated for the location, macroscopic type, size, and pit pattern of all polyps. We retrospectively investigated risk factors for polyp enlargement using univariate and multivariate analysis.

Results: A total of 284 polyps could have been followed up until the final endoscopy. The follow-up rate was 78.4%, the median follow-up period was 60 months (range, 46–84 months), and the median polyp size at initial colonoscopy was 3 mm (range, 2–13 mm). At the final endoscopy, 33 polyps (11.6%) had enlarged in size; the mean amount of enlargement was 1.78 ± 0.9 mm. When investigating the risk factors for polyp enlargement, univariate analysis indicated no significant differences in age, gender, initial size, or aspirin use; however, significant differences were noted for IV pit pattern ($P < 0.001$), III L1 pit pattern ($P = 0.009$), rectosigmoid colon ($P < 0.001$) and Is morphology ($P < 0.001$). Multivariate analysis results indicated that IV pit pattern ($P < 0.001$; OR 13.8, 95%CI: 3.5-55.3), III L1 pit pattern ($P = 0.004$; OR 4.3, 95%CI: 1.6-12.0) and rectosigmoid colon ($P = 0.01$; OR 3.0, 95%CI: 1.3-6.8) were independent risk factors for polyp enlargement.

Conclusion: Most polyps with III L2 pit pattern, size does not have a change even long-term follow-up. But resection should be considered for IV pit pattern polyps located in the rectosigmoid colon.

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Disclosure of Interest: None declared

P1428 THERAPEUTIC STRATEGY OF ESD FOR COLORECTAL TUMORS ACCOMPANIED BY SEVERE DEGREE FIBROSIS IN THE SUBMUCOSAL LAYER

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Introduction: The difficulty of one-piece resection of a colorectal tumor using ESD sometime due to the presence of fibrosis. We examined the causes and endoscopic findings of fibrosis in the submucosal layer (SM) in order to establish an appropriate therapeutic strategy for such lesions. From these observations, we developed a safe ESD technique we used.

Aims & Methods: We performed ESD on 981 colorectal tumors in 958 patients (male: female = 565:393; mean age, 65.8years). Among these 981 cases, 238 cases were accompanied by fibrosis in the SM. These cases were divided into three groups; absence of fibrosis (type A), fibrosis due to benign causes (due to biopsy, recurrence after EMR, etc. type B), and fibrosis due to cancer invasion in the SM layer (type C). The degree of fibrosis was classified into mild (grade 1), moderate (grade 2), and severe (grade 3) degree. In this study, we analyzed these lesions in order to establish a safe and curative ESD technique.

Results: These 238 cases accompanied by fibrosis were including 11 withdrawal cases, 84 cases were considered related to cancer invasion (type C), and 154 cases were related to benign cause (type B). The one-piece resection rates were as follows: Type A; 724/743(97.4%), type B-1; 73/76(96.1%), B-2:36/40(90.0%), B-3:22/38 (57.9%), type C-1:42/42(100%, average SM depth:713.8μm), C-2:15/16(93.8%, average SM depth:1.907.0μm), C-3:13/26(50%, average SM depth:2.800.0μm). We experienced three cases (0.3%) of perforation in type B. The tumors accompanied by mild to moderate fibrosis should be dissected carefully just above the muscle layer. In cases accompanied by severe degree fibrosis (type B-3), ESD becomes more difficult due to the risk of perforation. From the analysis of one-piece resection cases in type B-3, we developed the safe ESD technique to break these difficulties. The feasibilities to complete one-piece resection with type B-3 were as follows: 1) recognition of the narrow translucent area just above the muscle layer, 2) identification of the dissection line by linking with the normal SM layer of both ends of fibrosis, 3) using an endo-clip on the muscle layer to prevent perforation before dissection. Other cases of type B-3 were impossible to design the dissection line due to wide and firm fibrosis. The limitation of ESD is thought to be existed in these lesions from the viewpoint of safety and curability. From these reasons, we established the laparoscopy endoscopy cooperative surgery (LECS) procedure to complete a safe one-piece resection with adequate surgical margin. Otherwise, type C-3 was showing a deep cancer invasion about 3.000μm in the SM, and revealed very low one-piece resection rate. From these results, type C-3 endoscopic finding was thought to be an indication of laparoscopic surgery (LAC) due to the risk of lymph node metastasis.

Conclusion: The usefulness of ESD for lesions with fibrosis is limited from the viewpoint of safety and curability. We classified the endoscopic findings of fibrosis in order to establish a safe and curative ESD technique. The tumors accompanied by fibrosis of a mild to moderate degree become a standard indication for ESD. And the tumors accompanied by severe degree fibrosis without deep cancer invasion in the SM will become a relative indication of ESD and laparoscopy endoscopy cooperative surgery (LECS) procedure.

Disclosure of Interest: None declared

P1429 CLINICAL USEFULNESS OF DUAL RED IMAGING DURING COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Dual red imaging (DRI), which is a new modality of image-enhanced endoscopy developed by Olympus, consists of 3 wavelengths different from narrow band images: the 540-nm wavelength can visualize small blood vessels in shallow tissue, and the 600-nm and 630-nm wavelengths can penetrate deep into the tissue. These wavelengths enable visualization of thick vessels, which is expected prompt identification of bleeding point in case of arterial hemorrhage. Because DRI results in a change in the color of the artery to orange, it is possible to discriminate between arteries and veins with clockwork

precision. However, there are no reports regarding the clinical usefulness of DRI during colorectal endoscopic submucosal dissection (ESD).
Aims & Methods: To assess the clinical usefulness of DRI during colorectal ESD, we evaluated the improved visibility of vessels, submucosal fibrosis, and the demarcation line of the muscle layer.
Seven physicians compared DRI to 17 corresponding white-light images during colorectal ESD. The physicians counted the number of vessels, and rated demarcation line between the submucosal and muscle layer after injection of hyaluronate sodium with minute indigo carmine, and the existence of fibrosis. The visibility from each image was rated as follows: +2 (improved), +1 (somewhat improved), 0 (equivalent to white light), -1 (somewhat decreased), and -2 (decreased). The 7 scores for each image were totalled and evaluated. If an image earned a total score of +8 or more, the image was considered improved, a score between +7 and –7 indicated no change, and a score of –8 or less indicated decreased visibility. Interobserver agreement was also examined using the kappa statistic. We also counted the number of arteries visible as orange vessels with DRI in comparison to the actual number of arteries identified by observing beating vessels or spurting bleeds on the video.
Results: The average number of vessels per picture was 5.1 ± 0.2 in white-light images and 4.1 ± 0.2 in DRI. The number of vessels visualized with DRI was significantly less than that seen with white-light images ($p < 0.01$). In regard to vessels, improved visibility was found in 59% (10/17) of images, equivalent visibility was found in 41% (7/17) of images, and there was no decreased visibility. In regard to the demarcation line of the muscle layer, improved visibility was found in 66% (11/17) of images, equivalent visibility was found in 35% (6/17) of images, and there was no decreased visibility. In regard to submucosal fibrosis, equivalent visibility was found in all images and there was no improved or decreased visibility. Interobserver agreement was 0.63 for vessels, 0.62 for the demarcation line of the muscle layer, and 0.47 for the existence of fibrosis. The average number of arteries per picture counted by using DRI (2.2 ± 1.4) was statistically equivalent to that counted by observing the video image (2.1 ± 1.5).
Conclusion: DRI improves the visibility of vessels, especially that of arteries, as they appear orange, and the demarcation line of the muscle layer. DRI may help to make colorectal ESD safer and faster.
Disclosure of Interest: None declared

P1430 A COHORT STUDY TO EVALUATE THE EFFECT OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUBMUCOSAL INVASIVE RECTAL CANCER

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Introduction: Endoscopic submucosal dissection (ESD) can be used to treat submucosal invasive rectal cancer (SM-RC). Patients who are at low risk for lymph node metastasis and local recurrence may simply undergo observational follow-up, while additional surgery is recommended for those with high-risk features. However, patients can suffer from persistent anorectal dysfunction after disfiguring rectal surgeries, such as the Dixon or Miles operations. Therefore, the objective of our study was to evaluate the outcomes of patients with SM-RC managed with either ESD or surgery to determine if ESD might be a suitable option with fewer negative side effects.
Aims & Methods: We retrospectively analyzed patients with SM-RC receiving treatment between 2009 March and 2013 September. SM-RCs with (1) a well or moderately differentiated adenocarcinoma, (2) negative vertical margins, (3) no sign of lymphovascular invasion, and (4) an invasion depth < 1000 μm were classified as low risk. Patients with SM-RCs without these characteristics were classified as high risk. Outcomes were assessed by complication rate, hospital stay length and cost, persistent anorectal dysfunction rate, recurrence rate, timeline for recurrence-free survival (RFS), and overall survival.
Results: During the study period, 76 patients with SM-RC who underwent ESD or surgery (32 ESD, 44 surgery) were enrolled (median follow-up ~35.0 months). There were 29 patients classified as low risk (16 ESD, 13 surgery) and 47 patients classified as high risk (16 ESD, 31 surgery). After we compared the complication rate, recurrence rate, recurrence-free survival, and overall survival, we found no obvious differences between ESD and surgery groups in both low-risk and high-risk patients. However, ESD had a lower occurrence of persistent anorectal dysfunction compared to surgery (low-risk: 6.3% vs. 61.5%, $p = 0.003$; high-risk: 0% vs. 41.9%, $p = 0.002$). At the same time, the average hospital stay length and cost of was lower with ESD for both high- and low-risk patients (low risk: 2.25 ± 1.39 days vs. 8.85 ± 3.31 day, $p = 0.000$; 10858.9 ± 1968.9 RMB vs. 26293.0 ± 6991.1 RMB, $P = 0.000$; high risk: 2.31 ± 0.95 day vs. 12.4 ± 15.8 day, $p = 0.015$; 11844.6 ± 2095.4 RMB vs. 32722.0 ± 5633.9 RMB, $P = 0.000$).
Conclusion: Long-term outcomes were favorable in patients with low-risk SM-RC treated with endoscopic resection alone. Endoscopic resection alone was considered an adequate treatment for this group, particularly with the interests of minimizing the occurrence of persistent anorectal dysfunction and reducing the length of hospital stay and in turn the cost. In patients with high-risk SM-RC and a clinicopathological examination showing deep invasion of the submucosa without venous or lymphatic invasion, ESD is often adequate, but follow-up is needed.
Disclosure of Interest: None declared

P1431 ENDOCUFF-VISION: IMPACT ON COLONOSCOPIST PERFORMANCE DURING SCREENING

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Introduction: Although colonoscopy is considered the optimal procedure for bowel cancer screening, it remains an imperfect tool for cancer prevention, due to missed adenomas and early cancers. The Endocuff is a simple device attached at the end of the colonoscope that opens up the field of view by retracting folds during withdrawal. Little is known regarding the Endocuff's vision (new) impact on a colonoscopist's performance.
Aims & Methods: The aim of this study was to evaluate the impact of the Endocuff-vision (ARC Design Ltd, UK) on the quality indicators for each operator. A prospective observational evaluation study was performed from April 2013 to September 2014, divided in three consecutive periods: pre-cuff (no device used), during-cuff (device used) and post-cuff (no device used). Four screening endoscopists (BPS, STG, NS, AH) utilized the Endocuff-vision™ at their own discretion when device was available to them. Quality colonoscopy indicators (Adenoma Detection Rate (ADR), Mean number of adenomas per procedure (MAP), Caecal intubation time- CIT/Withdrawal time-WT/Total procedural time-TPT) were analyzed (t-test two sample assuming equal variances) in equivalent number of procedures. The total number of procedures performed was 399, 133 per period (BPS/26, STG/53, NS/31, AH/23).
Results: The mean ADR was 55.13% in the pre-cuff period, 68.98% in the during-cuff period and 61.74% in the post-cuff period. All four operators showed significant improvement in detection when using the device, which resulted in an overall increased ADR of **13.8%** ($p < 0.05$). During the post-cuff period, the detection performance of the three endoscopists declined to similar ADR pre-cuff level while one operator improved further the adenoma detection rate.
The mean MAP was 1.2 in the pre-cuff period, 2.2 in the during-cuff period and 1.55 in the post-cuff period. The mean MAP increased significantly in all four operators at the during-cuff period (**83%**, $p < 0.05$). During the post-cuff, three endoscopists returned almost to the baseline MAP pre-cuff level while one operator maintained the high MAP score.
The mean CIT was 9.66min in the pre-cuff period, 7.5min in the during-cuff period and 9.54min in the post-cuff period. A decrease in mean CIT was featured (**22.36%**, $p < 0.005$) to all operators when using the device, returning to about the pre-cuff levels afterwards.
No complications were reported from the use of the Endocuff-vision although it was electively removed in 4 cases with severe sigmoid colon diverticulosis and one case due to anal discomfort.
Conclusion: In this pilot evaluation study, the first use of the Endocuff-vision appears to improve overall performance of the operators by making colonoscopy a quicker (decrease CIT) and more efficient (increase MAP/ADR) procedure. Further randomized evaluation of this simple novel device combining the patient comfort score and sedation required is warranted.
Disclosure of Interest: None declared

P1432 PITFALLS IN PIECEMEAL RESECTION OF COMPLEX COLORECTAL POLYPS

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Introduction: The role of piecemeal endoscopic mucosal resection (p-EMR) for sessile/flat colonic polyps previously destined for surgery is expanding. However, surgery remains appropriate in some cases. The objectives of this study were to determine the primary reasons in this decision-making, and factors associated with polyp non-excision, and the presence of submucosal invasive cancer (SMIC).
Aims & Methods: A prospective observational cohort study of all polyps referred for consideration of p-EMR to our tertiary centre between January 2010 and August 2012 was performed. For each case, a detailed endoscopic evaluation of the polyp was performed prior to the polyp being excised or not excised. The primary reason for polyp non-excision was documented. Univariable and multivariable analyses were performed to determine factors associated with (i) non-excision and (ii) submucosal invasive cancer (SMIC).
Results: Seventy-one of 419 (17%) polyps were not excised (p-EMR not attempted in 52/71 and abandoned in 19/71 cases). The primary reasons for non-excision were; suspected SMIC (36/71), polyp size +/- location, poor polyp access and patient comorbidities. On multivariate analysis, factors associated with polyp non-excision were increasing polyp size ($p < 0.001$), site (caecum and sigmoid colon, $p < 0.001$), surface features suggestive of SMIC (Paris IIc, Kudo V and NICE III, all $p < 0.001$) and female gender ($p = 0.04$). SMIC was present in 9% of polyps >2cm and was more prevalent in the rectum to the descending colon than in the transverse colon to caecum ($p = 0.04$). Although surface features were associated with SMIC on univariable analysis and the positive predictive values are relatively high (Paris IIc 80%, Kudo V 86% and NICE III 86%)., the sensitivity of these features for a diagnosis of SMIC were relatively low (Paris IIc 11%, Kudo V 49% and NICE III 51%).
Conclusion: A percentage of polyps referred to a tertiary institution were not suitable for p-EMR, most commonly because of suspicion of SMIC. Specific surface features of malignancy may be present but the physician's overall endoscopic evaluation was also useful in predicting suitability of polyps for p-EMR.
Disclosure of Interest: None declared

P1433 COMPLEX COLORECTAL POLYPS: A TERTIARY CENTRE EXPERIENCE; TAILORING THE EMR TECHNIQUE TO THE POLYP

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Introduction: The complexity of colorectal polyp referrals to tertiary centres is increasing. Features that characterise polyp complexity should be clearly defined and recognised to avert suboptimal piecemeal endoscopic mucosal resection (p-EMR) strategies and need for salvage surgery.

Aims & Methods: A prospective database of all colorectal polyps excised at our tertiary referral centre between Jan 2010 and August 2012 was collected. Standard p-EMR with a semi-stiiff snares (10mm/15mm) was performed but for polyps where this strategy was considered inadequate, p-EMR using a 20mm Spiral-snare (sp-EMR),(Olympus, KeyMed), or hybrid p-EMR (hp-EMR; p-EMR plus endoscopic-mucosal-ablation or endoscopic-submucosal-dissection) were performed. Multinomial logistic regression was performed including polyp characteristics and p-EMR techniques applied. The primary outcomes were to define characteristic features of complex polyps and factors associated with the chosen resection technique.

Results: Of 323 patients with 341 polyps (mean size 3.7cm), 81%(261/323) were tertiary and 19% were local referrals. 94/261(36%) tertiary referrals mentioned one or more previous endoscopic resection attempts. Endoscopic polyp access was described as difficult in 174/341(51%, p = .001), incomplete polyp lift in 179/341(52%, p = .002) cases and polyp size ≥4cm (median size 5cm) in 123/341(36%, p < .001) cases. Polyps ≥4cm were more frequently in a difficult position (≥4cm;63% vs <4cm;37%, p < .001). Polyps <4cm were more likely to be in the caecum or ascending colon (<4cm;35% vs ≥4cm;16%, p < .001).

Factors	Category	All polyps	≥2 - <4cm polyps	≥4cm polyps	P-value
Polyp lift	Full	162 (48%)	117 (54%)	45 (37%)	**0.002**
	Incomplete	179 (52%)	101 (46%)	78 (63%)	
Difficult polypposition	No	167 (49%)	121 (55%)	46 (37%)	**0.001**
Yes	174 (51%)	97 (45%)	77 (63%)		
Techniques used	pEMR	230 (67%)	173 (79%)	57 (46%)	**<0.001**
	Hybrid pEMR	63 (19%)	31 (14%)	24 (20%)	
	Spiral pEMR	48 (14%)	14 (6%)	34 (28%)	
Proceduralbleeding	No	306 (91%)	205 (95%)	101 (83%)	**<0.001**
Yes	32 (9%)	11 (5%)	21 (17%)		
Delayedbleeding	No	258 (78%)	181 (85%)	77 (66%)	**<0.001**
Yes	72 (22%)	32 (15%)	40 (34%)		

Endoscopically complete polypectomy was achieved in one session in 336/341(98%, p < .001) polyps. Procedural and delayed bleeding were significantly higher in the ≥4cm group where 2 of the 3 micro-perforations also occurred (3/341,0.9%) that were all treated successfully with endoscopic clipping. The overall long-term recurrence at 24 months was 17% (28% for ≥4cm/p = .02). Only eleven patients (4 benign-recurrence/7 cancer in histology,3%) in this cohort underwent surgery. Using multivariable analysis, factors associated with need for sp-EMR or hp-EMR were; **i) tertiary referrals** (sp-EMR, OR-3.41, p < .001**), ii) incomplete polyp lift** (hp-EMR, OR-8.3 > sp-EMR, OR-1.19, p < .001), **iii) previous polypectomy attempt** (hp-EMR, OR-2.77, p = .02), **iv) larger polyp size** (for an increase of 1cm - hp-EMR (OR-1.37)/sp-EMR (OR-1.66, p < .001), **v) polyps in the rectosigmoid location** (sp-EMR and hp-EMR, p < .001) and **vi) Paris IIa + IIb polyps** (sp-EMR, OR-5.01 and hp-EMR, OR-2.9, p-.007).

Conclusion: Complex colorectal polyps referred to this tertiary centre were characterised by polyp size ≥4cm, caecal location, previous unsuccessful polypectomy, difficult endoscopic access, or incomplete polyp lift. Advanced techniques such as hybrid-pEMR and spiral p-EMR were required in 33% of tertiary referrals.

Disclosure of Interest: None declared

P1434 DILATION-ASSISTED STONE EXTRACTION: AN ALTERNATIVE, EFFECTIVE AND SAFE METHOD FOR REMOVAL OF COMMON BILE DUCT LARGE STONES

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Introduction: Large stones of common bile duct (CBD) are a hard challenge after endoscopic sphincterotomy (EST) especially in those that are unable to be managed with standard techniques including mechanical lithotripsy. Dilation-assisted stone extraction (DASE) after EST can be more efficient than EST alone for removal of large CBD stones.

Aims & Methods: The aim of this study is to report the experience of a referral centre on the efficacy and complications of DASE for CBD large stones treatment. From January 2013 to March 2015 data of all consecutive patients who underwent DASE due to large stones, evidenced by CT-scan or MRI, were collected and recorded in an electronic database for the final analysis. After selective cannulation of the CBD, an initial cholangiogram was taken before balloon placement. The size of the balloon was matched to the diameters of the bile duct and stones. The balloon was gradually filled with diluted contrast medium under endoscopic and fluoroscopic guidance to observe the gradual disappearance of the waist in the balloon, which was taken to indicate progressive dilation of the orifice. Once the waist disappeared, the balloon remained inflated for 60 s.

Results: A total of 27 patients with CBD large stones were evaluated: 10 male (37%)/ 17 female (63%) with a mean age of 71.1 ± 14.2. Technical success (complete dilation) was reached in all patients (100%) with a median final dilation of 15 mm in diameter: 10 mm in 4 patients (15%), 15 mm in 11 patients (41%), 18 mm in 10 patients (37%), 20 mm in 2 patients (7%). In 6 patients (22%) EST was done before the current procedure and DASE was performed due to stones recurrence. In all patients but two (93%) large stones were successful removed from the CBD (17 with retrieval balloon and 8 with aid of mechanical lithotripsy). In those with DASE failure: 1 was treated with intracoledocical laser lithotripsy and 1 with surgical approach. Only 2 early complications were recorded (7%): both mild bleeding resolved after endoclips placement. In one patient CBD stones recurred after 2 months.

Conclusion: DASE after EST is an alternative, effective and safe method for removal of CBD large stones.

Disclosure of Interest: None declared

P1435 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY FOR PRIMARY AND SECONDARY ("RESCUE") MANAGEMENT OF PERIHILAR MALIGNANT BILIARY STRICTURES: A TERTIARY CENTRE EXPERIENCE

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Introduction: Biliary decompression and palliation of patients with perihilar malignant strictures due to cholangiocarcinoma is historically achieved via percutaneous trashepatic drainage (PTD) and placement of uncovered self expandable metallic stents (UC-SEMS). PTD in this setting carries significant morbidity (bleeding, bile leaks, biloma formation) and mortality up to 20% in retrospective audit conducted by the British society of Radiology.

Endoscopic management of perihilar malignant biliary strictures is an alternative approach adopted by very few high-volume tertiary Centres in the UK. Here we describe our experience in a total of 15 patients who were successfully managed with the placement of UC-SEMS.

Aims & Methods: To review the safety, feasibility and outcomes of the endoscopic retrograde approach as primary method of achieving biliary decompression in malignant perihilar strictures.

Retrospective case series between March 2013 to Feb 2015, 15 patients with malignant perihilar strictures were identified during the period and data collected reviewing medical notes and electronic patient records.

End-points were technical success(correct unilateral or bilateral UC-SEMS placement confirmed radiologically at the time of procedure), and clinical success (>50% fall in bilirubin 2 weeks post procedure or patient eligibility for palliative chemotherapy post intervention, or provision of initial definitive treatment in patient for best supportive care). UC-SEMS with a length of 80-100mm and diameter of 10mm were used. Depending on the type of the stricture, either a unilateral (6 patients) or bilateral (8 patients) SEMS were used.

Results: 15 patients in total (5M,10F, median age 69 years, age range -89). Table shows the primary site of malignancy.

Cholangiocarcinoma	8
Colorectal cancer with metastases	3
Pancreatic cancer with Liver metastases	2
Hepatocellular cancer	1
Metatstatic Breast cancer with liver hilar stricture	1

All patients were successfully managed with UC-SEMS at first ERCP with a procedural success rate of 100%. Clinical success was 93% (1 patient needed PTD after 12 days due to incomplete resolution of jaundice). One patient needed further ERCP 50 days after the index ERCP because of proximal extension of the stricture (type IIIa), a single UC-SEMS was successfully placed.

3 patients had previous PTD with single metal stent in situ and presented with persistent or recurrent jaundice for secondary "rescue" ERCP; 2 patients had percutaneous external biliary drain only in situ prior to the index ERCP; the remaining 10 patients had ERCP as primary biliary intervention. 5 patients received palliative chemotherapy and one patient was offered chemotherapy but subsequently declined.

No significant peri-procedural complications were recorded in our group of patients and the 30-day mortality was 0%. 5 patients reported some discomfort 24-48h post procedure attributed to stent expansion. One patient had mild pancreatitis, symptoms resolved on day 3.

Conclusion: In a high-volume Centre with expertise in the technical aspects of management of hilar lesions ERCP is highly effective and safer alternative to PTD as evident in this small retrospective study. A large prospective randomised trial is needed in order to compare PTD vs ERCP as a primary approach for biliary decompression in this group of patients.

Disclosure of Interest: None declared

P1436 RETROSPECTIVE COMPARATIVE STUDY FOR THE EFFECTIVENESS AND SAFETY OF EXTRACTING BILE DUCT STONES LESS THAN 10MM; ENDOSCOPIC PAPILLARY BALLOON DILATION BY 5-MINUTE DILATION WITH 10MM DIAMETER BALLOON VS. ENDOSCOPIC SPHINCTEROTOMY

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Introduction: Endoscopic Papillary Balloon Dilation (EPBD) has a lower risk of hemorrhage and is easier to perform but has higher incidence of pancreatitis than Endoscopic Sphincterotomy (EST). It is reported that 5-minute EPBD improves efficacy of stone extraction and reduces the risk of pancreatitis compared with conventional 1-minute EPBD. Therefore we conducted retrospective comparative study of 5-minute EPBD vs. EST with respect to stone extraction and pancreatitis.

Aims & Methods: All enrolled cases had bile duct stones less than 10mm. Consecutive 79 cases treated by 5-minute EPBD from Oct. 2013 to Apr. 2015 were compared to consecutive 82 cases treated by EST from May 2010 to Oct. 2013. EPBD balloon diameter used in this trial was all 10mm.

Results: Mean age was 74 in EPBD group and 70 in EST group ($p < 0.05$). Sex, stone diameter and number of stones did not statistically differ between two groups. The rate of complete extraction of bile duct stones in first session was 100% in both groups. Procedure time was approximately 30 minutes in both group and did not show statistical difference. Cannulation time of EPBD group and EST group was 14 minutes and 9 minutes ($p = 0.05$), respectively. The rate of novices and intermediates as 1st endoscopist was significantly higher in EPBD group (EPBD: 89% vs. EST: 71%, $p < 0.05$). Pancreatitis was seen 3.8% of EPBD group and 6.1% of EST group and bleeding occurred only in EST group (2.4%) but neither pancreatitis nor bleeding showed statistical differences.

Conclusion: 5-minute EPBD had high performance of stone extraction and low incidence of pancreatitis. It may be first choice as a method for extracting bile duct stones less than 10 mm because we can expect better long-term outcomes to EPBD than EST. However we need to conduct randomized trial and reveal long-term outcomes.

Disclosure of Interest: None declared

P1437 IS ENDOSCOPIC PAPILLECTOMY A SAFE AND EFFECTIVE OPTION?

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Introduction: Periampullary tumors represent a group of rare gastrointestinal tumors. Almost 95% of lesions of the ampulla of Vater correspond to adenomas or adenocarcinomas. These tumors can occur sporadically or in association with hereditary polyposis syndromes such as familial adenomatous polyposis (FAP). Endoscopic advances in ERCP and Endoscopic Ultrasound have changed the management of these tumors in recent years.

Aims & Methods

Aim: To present results of endoscopic papillectomy.

Patients: The database was reviewed to obtain 15 patients (8 men) with a mean age of 51.2 years (range 25-74) with papillary tumors, in whom endoscopic papillectomy was performed, between December 2006 and November 2013. The most common form of presentation was asymptomatic (53.3%), pain (40%), choledochal syndrome (13.3%) and weight loss (13.3%). Forty percent was related to FAP.

Methods: All patients had previous Endoscopic Ultrasound, biopsy with forceps, and met criteria for endoscopic resection. The procedure was performed with a duodenoscope, using the "en block" resection with snare technique, without previous injection. In all patients a 5 Fr / 3 cm length pancreatic stent was placed, after resection, as well as biliary sphincterotomy.

Results

Procedure characteristics n (%)	
Number of procedures	Total 1 61= 14 patients (93.3) 2= 1 patients (6.7)
Complications	Bleeding 3/15 (2%)
Surgery	0
Clinical success (30 days)	15 patients 13/15 (86)=2 patients with adjuvant therapy (EMR 1, APC 1)
Long-term success (>6 months)	11 patients (73) Of the 11 patients followed long-term success was achieved in 81.8% (9/11)
Follow-up mean (range)	26.4 months (6-61)
Relapses	3/11 (27)-1/11 responded to EMR + APC
RF for relapse	2/3: FAP3/3: LGDMean size: 18 mm

16 procedures were performed in 15 patients. The histological analysis of the lesions showed 11 (73.3%) had low-grade dysplasia, 2 (13.3%) had high-grade dysplasia, 1 was an intramucosal adenocarcinoma and 1 was invasive adenocarcinoma. The frequency of false negatives for cancer obtained with biopsy-forceps was 13%. The short-term treatment success, defined as absence of disease in control duodenoscopy at 30 days, was 86%.

Eleven patients were followed for 6 months or more (mean 26.45). Of these, 3 had relapses (27%), 1 was treated with ablative therapy (argon plasma coagulation). Success in monitoring for more than 6 months was 81.8% (9/11).

Immediate bleeding was the most common major complication (2%), being controlled with injection of adrenaline. No cases of acute pancreatitis (AP) were recorded. At follow-up one patient had invasive adenocarcinoma and received chemotherapy because of inoperability criteria.

Conclusion: papillectomy is a safe and proven choice, with good results in the short and long term. Forceps biopsies present a considerable false negative rate. Pancreatic plastic stent placement prophylaxis of AP is mandatory to avoid this complication. Relapse may relate, among other factors, with the association with FAP.

Disclosure of Interest: None declared

P1438 FEASIBILITY OF DIRECT PERORAL CHOLANGIOSCOPY USING AN ULTRASLIM UPPER ENDOSCOPE FOR EVALUATING RESIDUAL STONES OF COMMON BILE DUCT STONE

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Introduction: In endoscopic lithotomy for common bile duct (CBD) stone, with small residual stone in enlarged bile duct and/or maked pneumobilia, confirmation of complete removal stone is rather difficult even with balloon-occlusion cholangiography. And the frequency of residual CBD stones after stone removal was investigated that 40% had small residual stones not seen on cholangiography [1)]. Recently, direct peroral cholangioscopy (DPOCS) using an ultraslim upper endoscope has been reported to be useful for confirmation of residual CBD stone [2)]. However, accessing to biliary system and performing lithotomy is still more challenging. We performed DPOCS using an ultraslim upper endoscope, for evaluating of residual stones after endoscopic lithotomy with ERCP and technical feasibility.

Aims & Methods: From November 2009 to December 2014, thirty-seven patients (men 11) who had undergone endoscopic lithotomy for retained stone with no evidence of filling defects in balloon cholangiography were identified. The ultraslim endoscopes were used GIF-XP260N (Olympus, Tokyo, Japan) and EG-580NW2 (Fujinon, Tokyo, Japan) in this study. Endoscopic procedure for accessing biliary system followed our previous report [3)]. If any residual stone was found, it was removed directly under DPOCS with a slim basket catheter and/or suction. The rate of accessing to biliary system, present residual stone, successful residual stone removal, adverse events were analyzed.

Results: The mean age of patients was 81.4 years , the mean CBD diameter and the number of residual stones were 14.0mm, 1.6, respectively. DPOCS was successfully performed in 35 of the 37 patients (94.6%). The mean time for accessing to biliary system was 12.3 minutes in the 35 patients. The rate of application of ML was 24.3% (9/35), residual stone was identified in 7 of the patients with successful DPOCS (7/35, 20%). For all seven patients underwent endoscopic lithotomy under DPOCS, complete stone removal was accomplished (7/7, 100%). Adverse events were 16.2% (6/37), mild pancreatitis (1), mild cholangitis (5). All patients were successfully managed with conservative treatment.

Conclusion: DPOCS using an ultraslim upper endoscope is a useful and feasible endoscopic procedure for evaluation of residual CBD stones.

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Disclosure of Interest: None declared

P1439 HEMOCLIP APPLICATION USING CAP-FITTED FORWARD ENDOSCOPY TO TREAT POST-SPHINCTEROTOMY BLEEDING IN PATIENTS UNDERGOING ERCP

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Introduction: The risk of immediate or delayed bleeding following endoscopic biliary sphincterotomy (ES) during endoscopic retrograde cholangiopancreatography (ERCP) is reported from 2.0-5.3%. Clinically, bleeding can range from insignificant to life threatening. Although endoscopic clipping may effective method treatment of a wide variety of bleeding lesions of GI tract, mechanical clipping of post-ES bleeding has not been widely studied, in part due to the difficulty in placing the current generation of clips using ERCP endoscopes. A cap-fitted forward viewing endoscope can easily visualize the ampulla of Vater.

Aims & Methods: To determine the efficacy of a cap-fitted endoscopy to treat bleeding on the bleeding on the ES site in patients who undertook ERCP with ES.

Patients and methods: The study included 1.248 consecutive patients who underwent 1.248 ERCP with ES procedures between January 2011 and August 2014. ES-induced hemorrhage occurred in 45 patients (3.6%). Bleeding patterns (trickle, oozing, pulsatile, and exposed vessel) were recorded. Patients with oozing or trickle bleeding who did not respond to balloon compression or epinephrine solution injection and all the patients with pulsatile bleeding and/or exposed vessel on the ES site, received clipping.
Results: The mean age was 69.1 ± 14.3 and sex ratio (M/F) was 32 (71.1%): 13 (28.9%) in 45 patients. Thirty nine patients had immediate endoscopic visible bleeding signs during ES, and 6 patients without endoscopic visible bleeding signs during ES who did not undergo clipping (0.48%) presented with delayed hemorrhage. Visible bleeding pattern following ES were: 19 trickle (42.2 %), 22 oozing (48.9 %), 3 pulsatile (6.7 %), and 1 exposed vessel (2.2%). Hemostasis was achieved by clipping in 45 of 45 patients (100%) who included patients with antiplatelet drug (n = 9) and warfarin (n = 2). The median number of clips used in all patients was 2.0 (range: 1-3). No patients had evidence of delayed bleeding after clipping on all visible bleeding signs. No patients had evidence of complication related to this procedure after clipping.
Conclusion: Hemoclip application using cap-fitted forward viewing endoscopy is feasible, safe and may be an effective technique for the treatment and/or prevention of post-ES bleeding.
Disclosure of Interest: None declared

P1440 SPONTANEOUS HEMOBILIA AFTER LIVER TRANSPLANTATION: OUTCOME OF ENDOSCOPIC MANAGEMENT, AND ITS FREQUENCY AND RISK FACTORS

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Introduction: Liver transplantation (LT) has been applied for treatment of liver cirrhosis (LC), hepatocellular carcinoma, primary biliary cirrhosis, and fulminant hepatic failure. Spontaneous hemobilia is an uncommon LT-related biliary complication. The frequency, etiology and mechanism of spontaneous hemobilia after LT have not been known. Spontaneous hemobilia has clinical implication that blood clots in bile duct can cause biliary obstruction and cholangitis, and result in graft dysfunction. This condition may require removal of dysfunctional graft and transplantation of new graft.
Aims & Methods: This study aimed to assess outcome of endoscopic management for spontaneous hemobilia after LT, and to investigate its frequency and risk factors. The records of 53 patients who underwent ERCP to diagnose and manage hemobilia after LT at Asan Medical Center in Korea between January 2006 to April 2014 were retrospectively reviewed. To investigate the risk factors for spontaneous hemobilia after LT, control group matched according to age (± 2 years) and sex with fourfold number of study group was randomly selected from LT patients without spontaneous hemobilia during the same period.
Results: Of the 53 patients, 33 patients were included to study group. The mean age of study patients was 52.4 ± 8.7 years and 24 (72.7%) patients were male. The indications for LT were hepatitis B virus-associated LC in 19 cases (57.6%), alcoholic LC in 7 cases (21.2%), fulminant hepatic failure in 5 cases (15.2%), and cryptogenic LC in 2 patients (6.0%). Endoscopic nasobiliary drainage (ENBD) was achieved in 33 cases (100%). Hemobilia was stopped in 29 of 33 patients (87.9%). The frequency of spontaneous hemobilia was 1.22% (33/2701). On multivariate analysis, United Network for Organ Sharing (UNOS) status I or IIa (OR 3.095, 95% CI 1.097–8.732, $P = 0.033$), alcoholic LC (OR 3.942, 95% CI 1.261–12.324, $P = 0.018$), and body mass index (BMI) < 24.5 kg/m^2 (OR 2.329, 95% CI 1.005–5.397, $P = 0.049$) were significant risk factors for spontaneous hemobilia after LT.
Conclusion: ENBD was feasible method for management of spontaneous hemobilia after LT. In patients with UNOS status I and IIa, alcoholic LC, or BMI < 24.5 kg/m^2, special attention should be paid to occurrence of spontaneous hemobilia after LT.

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Disclosure of Interest: None declared

P1441 DIRECT VISUALIZATION FOR THE ACCESSMENT OF PANCREATIC NEOPLASM WITH SPYGLASS DIRECT VISUALIZATION PROBE (SDVP) THROUGH UNEVEN DOUBLE LUMEN CANNULA IN ENDOSCOPIC RETROGRADE PANCREATOGRAPHY (ERCP)

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Introduction: Direct visualization of pancreatic ductal epithelium with peroral pancreatoscopy (POPS) could be useful for the diagnosis because most pancreatic neoplasms are derived from the epithelium. Insertion of POPS into the duct, however might be impossible in the cases with no ductal dilatation or existence of strong flexure part in it. If the insertion would be succeeded viscous liquid could disturb visualization of epithelium. Furthermore the POPS is not widely accepted for routine use for the diagnosis of pancreatic neoplasm in ERCP because of the fragility of the scope. Spyglass Direct Visualization Probe (Boston Scientific, MA, USA)(SDVP) is a very thin probe to visualize directly pancreatic ductal epithelium which is 1mm in diameter and go through one lumen in double lumen cannula in ERCP. Direct visualization of the epithelium with SDVP could be done while using the other lumen, inserting gidewire into it or washing it with saline, etc. That is why SDVP could have several advantages when it comes to user-friendness for routine use in ERCP compared to conventional POPS.
Aims & Methods: To evaluate the efficacy and the safety with SDVP in conjunction with an uneven double lumen ERCP cannula (Piolax, Yokohama, Japan) for direct visualization for the assessment of various pancreatic neoplasms. We reviewed our experience with 16 patients underwent this novel visualization, EUS, and/or intraductal ultrasonography (IDUS) for the assessment of pancreatic neoplasms at our institution from 2012 to 2014. The rate of the probe to reach the lesion, the mean time required for the examination, the breakage rate of the probe, and the complication were retrospectively evaluated.
Results: Among 16 patients, there were 10 patients with intraductal papillary neoplasm (IPMN). 2 patients had unexplained main pancreatic duct dilatation. Besides, pancreatic adenocarcinoma (PDAC), pancreatic neuroendocrine tumor (PNET), carcinoma of papilla Vater, and pancreatic cyst was one, respectively. The rate of the probe to reach the lesion was no less than 100% without need for papillotomy. Each of the main pancreatic duct diameter in 6 patients was within normal range. The orifices of papilla Vater in 7 patients were wide open but those in 9 patients showed normal orifices. In 14 patients a drainage tube was placed in MPD just before completion of the examination. Mild pancreatitis occurred in 2 patients (16%) in 16 patients after the examination. Both recovered with conservative treatment of fasting and infusion within 2 days. Any probe did not break during the examination. Stenosis and obstruction of the lumen in MPD was observed in PDAC. Invasion of the tumor into the MPD epithelium was recognized in PNET. Protruding lesion like granular type or fish-egg–like type was visualized by the SDVP in 5 patients, but it was not detected by other examinations in 3 patients of them. Double lumen cannula made washing viscous liquid, linearizing flexure in MPD by guide-wire and inserting the probe possible.
Conclusion: This novel method could be considered useful for the assessment of pancreatic neoplasm by routine use following ERCP.
Disclosure of Interest: None declared

P1442 TECHNICAL SUCCESS AND PATIENT-RELATED OUTCOMES IN AN ERCP TRAINING PROGRAM: RESULTS FROM A PROSPECTIVE SINGLE-CENTER STUDY

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Introduction: Endoscopic retrograde cholangiography (ERCP) has evolved from a diagnostic to a mainly therapeutic procedure, with a complication rate of about 10% and associated mortality below 1%. Current quality standards recommend a selective cannulation rate of above 85% and a technical success rate of 80-90% for biliary procedures.
The case-volume and experience of the endoscopist are key factors influencing technical success and complication at ERCP. An estimated 200 procedures are required before attaining competency in ERCP, but training programs vary widely across institutions. Furthermore, there is little data available concerning the impact of training programs on patient-related outcomes.
Aims & Methods: We evaluated the factors affecting technical success rate and procedure-related complications in an ERCP training program. We conducted a prospective observational study of all ERCPs performed in our unit over a 12 month period and analyzed single operator biliary procedures in native papilla cases.
Procedures were conducted under deep sedation; initial cannulation was attempted using the guidewire technique with subsequent alternative techniques at the operator's discretion. Trainees were supervised by an expert endoscopist. Patients received 100mg Diclofenac intrarectally after the procedure to prevent postERCP pancreatitis (PEP).
Relevant clinical and laboratory data, the indication of the procedure, cannulation method, technical success of planned intervention and complications up to 30 days were recorded using standard forms. The experience of the operator (trainee or expert) and the complexity of the procedure according to the ASGE difficulty scale were also noted.

We compared cannulation rate, technical success and complication rates between trainee and expert endoscopists and analyzed risk factors for postERCP complications.
Results: 581 ERCPs were performed in our service during 2014 by one expert endoscopist (>1000 ERCPs) and 4 trainees (<200 ERCPs). 411 cases (70.7%) fulfilled inclusion criteria; 218 (53%) patients were female and mean age was 64 (±14) years. 209 procedures were performed by trainees (50.5%) and 202 procedures by the expert endoscopist (49.5%).
Overall successful cannulation rate was 85.6%, with no statistically significant difference between the two groups (p = 0.57). Adjusting for reinterventions, the successful cannulation rate per patient was 92%, with a technical success rate of 87% in the trainee group versus 89% in the expert group (p = 0.86). Procedure-related complications occurred in 33 patients (8%); there were 27 cases of PEP (6.5%) and 4 cases of acute cholangitis (0.9%), with a 30-day mortality rate of 0.7% (3 cases).
On logistic regression only female gender and higher bilirubin levels were associated with an increased risk of developing procedure-related complications. There was no statistically significant difference between expert and trainees regarding complication rate and 30-day mortality on either univariate or multivariate analysis.
Conclusion: ERCP procedures carried out by supervised trainees have a high success rate and carry no additional risk of procedure-related complications, complying with current quality indicators.

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Disclosure of Interest: None declared

P1443 ENDOSCOPIC MANAGEMENT OF BENIGN BILIARY STRICTURES WITH 'KAFFESTM' FULLY COVERED SELF-EXPANDING METAL STENTS: A RETROSPECTIVE, MULTICENTER STUDY

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Introduction: Besides European guidelines(1) recommending endoscopic treatment for benign stricture calibration with multiple plastic stents, fully covered self expanding metal stent (FCSEMS) arise in this indication with equivalent success rates, lower rates of obstruction and less procedures. However, high rates of stent migration, leading to treatment failure, have been reported with FCSEMS(2.3). We aimed to report our experience of endoscopic management of BBS using Kaffes™(Taewoong©) FCSEMS(4) in two French university hospitals.
Aims & Methods: We analyzed retrospectively all patients who underwent a placement of Kaffes™ FCSEMS for the treatment of BBS from 2006 to 2014 in two French university hospitals. Kaffes™ stent have an antimigration system with a 2mm narrowered waist at mid portion of the stent, which allows the radial force of the metallic stent to be directed maximally to the center hence inhibiting stent migration. A retrieval string permits removal of the stent that may thus be placed in the upper common bile duct. The main evaluation criterion was stricture resolution and secondary were stent migration, adverse events and removal success.
Results: Eighteen patients had a placement of Kaffes™ stent for BBS, five post cholecystectomy, 12 after orthotopic liver transplantation and one after hepatectomy. Median stenting time was 161 days [IQR,105-193 days] for the first procedure. The median time of follow up was 9.5 months [IQR,3-12.2 Mo]. Stricture resolution was observed in 12/18(62%) patients after the first ERCP and in 15/18(83%) after the second ERCP procedure using Kaffes™, stent. Stent migration was observed in 3 patients (17%). Stent removal was always possible, 8(62%) without any complication. There were one impaction, requiring removal by stent-in-stent procedure (366 days after stenting), two obstructions (193 and 366 days), and two breaks of the removal string (259 and 366 days).Three(17%) post ERCP moderate acute pancreatitis were observed.
Conclusion: In the largest retrospective cohort, Kaffes™, stent is an effective and safe technique to treat BBS. The design of this stent is interesting for treatment of stricture located next to the biliary convergence and allows longstanding stenting and fewer procedures where only plastic stents were relevant before.

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Disclosure of Interest: None declared

P1444 LONG-TYPE SINGLE-BALLOON ENTEROSCOPE IS USEFUL IN RETROGRADE CHOLANGIOPANCREATOGRAPHY FOR PATIETNS WITH ALTERED GASTROINTESTINAL ANATOMY: A PILOT TRIAL

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Introduction: Several endoscopic retrograde cholangiopancreatography (ERCP)-related procedures have been performed for biliary tract diseases in patients with surgically reconstructed intestinal tracts using double- and single-balloon enteroscope (BE). Short-type BE with an effective length of 1520 mm has been useful for ERCP because most of ERCP-related devices are applicable for short-type BE. With recent advance in ERCP-related devices, ERCP with a long-type BE with an effective length of 2000 mm can be applicable for ERCP. The present pilot trial in Ureshino Medical Center aimed to demonstrate whether long-type BE was useful for ERCP for the patient with altered gastrointestinal anatomy by the surgical procedure.
Aims & Methods: Totally 10 patients (15 cases) who underwent ERCP with long-type single BE in Ureshino Medical Center were enrolled in the pilot study during the period from October 2013 to March 2015. The mean patient age was 71.4 years, and the male:female ratio was 8:2. The types of intestinal tract reconstruction were as follows: Roux-en-Y hepaticojejunostomy in 3 patients, Billroth II with Braun anastomosis in 2 patients, Roux-en-Y gastrectomy in 4 patients, and pancreaticoduodenectomy and modified Child method in 1 patient. The goals of treatment in a total of 15 cases were as follows: biliary stone removal in 6 cases, biliary drainage in 5 cases, collection of foreign bodies (pancreatic stents) in the bile tract in 3 cases, and dilatation of choledochojejunostomy site in 1 case. The usefulness of long-type BE was evaluated based on following criteria: the arrival rate at the blind end, time required for arrival, total time required for procedures, treatment completion rate, safety based on the incidence of adverse events.
Results: The arrival rate at the blind end in long-type BE was 15/15 (100%), the median time required for arrival was 28 min (range, 7-59 min), the median total time required for the procedures was 118 min (range, 43-173 min), and the treatment completion rate was 12/15 (80.0%). Regarding adverse events, acute cholangitis, which rapidly resolved with conservative therapy, occurred after treatment in 1 patient (6.7%). In patients with uncompleted treatment, percutaneous transhepatic treatment and surgery were subsequently performed.
Conclusion: Although many limitations with a scope length of 200 cm and a forceps diameter of 2.8 mm, the present pilot study, with high achieved rate and minimum adverse events, clearly suggested that ERCP with long-type BE might be a first line treatment in the patient with the surgically reconstructed intestinal tracts. This pilot trial warrant further examination to compare the availability for ERCP between the short- and long-type BEs.
Disclosure of Interest: None declared

P1445 FIRST CLINICAL EXPERIENCE WITH SINGLE OPERATOR VIDEO-CHOLANGIOSCOPY

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Introduction: Single-operator cholangioscopy (SOC) with the SpyGlass™ Direct Visualization System was introduced into clinical practice in 2007 by Boston Scientific (Natick, MA, USA). Since then its clinical application and benefits in different indications e.g. evaluation of indeterminate biliary strictures or cholangioscopic-guided removal of refractory bile duct stones were reported in several publications. Image-quality of the precursor generation was substantially limited by the number of optical fibres. The new fully integrated SpyGlass™DS System enables videoendoscopic image quality and an improved four way deflection of the scope, which is introduced over a standard duodenoscope.
Aims & Methods: Objective of the current registry of the first 21 consecutive clinical applications in Europe was to assess procedural and technical aspects of SOC with the new SpyGlass™DS-System. Data was collected prospectively, descriptive statistics were used for analysis. All procedures were conducted by experienced endoscopists (H.N., T.B., A.D., A.H., R.K.) at three tertiary referral centers with great experience in hepatobiliary interventions and cholangioscopy. SOC was conducted in n = 21 patients (male 15, female 6, age 18-94 years). Indications for cholangioscopy were indeterminate biliary strictures or irregularities (n = 16, 76%) and/or complex biliary stones or filling defects (n = 6, 29%) in fluoroscopy.
Results: Technical success (target site of the bile duct system reached) was achieved in 100% of the cases. In all patients biliary sphincterotomy was conducted before cholangioscopy for papillary access, in 3 cases (14%) with an additional balloon dilation. Direct introduction of the SpyScope was possible in 43% of the cases (9/21), in 57% (12/21) a wire-guided access was achieved. In 91% (19/21) of all cases the scope was advanced into intrahepatic bile ducts, in 2 cases (9%) to the upper CBD. Neoplasms were diagnosed in 8 cases (38%, cholangiocarcinoma 7, biliary IPMN 1), 6 strictures were found to be

inflammatory and/or benign (29%, PSC 3, scarring 3). Biliary stones were identified cholangioscopically in 6 patients and successfully fragmented by laserlithotripsy (n = 5, 24%) and removed completely in all cases (6/6). Cholangioscopic intervention was undertaken in 14/21 patients (biopsy 9, laser lithotripsy 4, both 1) and was successful in 100%. Cholangioscopic findings led to changes in overall treatment in 13 of 21 patients (62%). Mean duration of the procedure was 25.6 minutes (11-58). Image quality of the new system was rated excellent by all investigators in 100% of the cases. No complications related to the intervention occured.

Conclusion: Our first data of the new generation of the SpyGlass™-System suggest that it can further simplify and shorten the procedure of cholangioscopy. Simultanously, the high image quality and maneuverability of the scope improve the ability to evaluate biliary lesions and conduct intraluminal therapy even in intrahepatic bile ducts. It now combines the advantages of a catheter-based single-operator system with the superior image quality of a videoendoscopic system.

Disclosure of Interest: None declared

P1446 VALIDATION OF AN ALGORITHM FOR THE MANAGEMENT OF ERCP-RELATED DUODENAL PERFORATIONS

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Introduction: Duodenal perforation is a rare, but serious adverse event of ERCP. There is no consensus to guide the clinician on the management of ERCP-related perforations, with considerable controversy surrounding the immediate surgical management of duodenal perforation due to overextension of the sphincterotomy.

Aims & Methods

Aims: To assess patient outcomes using a predetermined algorithm based on managing ERCP-related duodenal perforations according to the mechanism of injury.

Methods: A retrospective single-center study of all consecutive patients with Stapfer type I and II perforations between 2000 and 2014 were included. Stapfer type I perforations were defined as luminal perforation by the endoscope (1). Stapfer type II perforations were defined as extension of a sphincterotomy incision beyond the intramural portion of the bile or pancreatic duct (1). Our institutional algorithm since 2000 mandated that Stapfer type I perforations were managed surgically unless prohibited by underlying comorbidities and Stapfer type II perforations were managed non-surgically and only preceded to surgery if their clinical status deteriorated.

Results: A total of 61 (mean age 51 years, female 80%) patients were analyzed with Stapfer type I perforations diagnosed in 7 (11.5%) and type II in 54 (88.5%) patients. Table 1 shows the characterisics of these perforations. There were only 4 (7.4%) patients with Stapfer type II perforations that failed medical management and underwent surgery. The mean length of stay in the entire cohort was 9.6 days with a low mortality rate of 3.3%. Systemic inflammatory response syndrome (SIRS) was observed in only 18 (33.3%) patients with Stapfer type II perforations and was not associated with the need for surgery. Concurrent post-ERCP pancreatitis was diagnosed in 26 (42.6%) patients and was associated with an increased length of stay. There were 17 (27.9%) patients that had a Stapfer type II perforation due to extentsion of a pre-existing sphincterotomy using electrocautery. [Table 1 N ± 61, *N ± 55]

Time point of diagnosis	
Intra-procedural	6 (9.8)
Post-procedural	55 (90.2)
Post-procedural modality of diagnosis	
CT	45 (81.8)*
X-ray	10 (18.2)*
Imaging characteristics	
Retroperitoneal collection	17 (31.5)*
Retroperitoneal gas only	20 (37.0)*
Retroperitoneal gas + pneumoperitoneum/ pneumomediastinum	12 (22.2)*
Oral contrast extravasation on imaging	6 (11.1)*
Additional adverse events	
Post ERCP pancreatitis	26 (42.6)
Mortality	2 (3.3)

Conclusion: This study validates a predefined treatment algorithm for the management of ERCP-related duodenal perforations. Our results suggest that Stapfer type II perforations have excellent outcomes when treated non-surgically, challenging the belief that these patients are best managed operatively.

Reference

1. Stapfer M, Selby RR and Stain SC, et al. Management of duodenal perforation after endoscopic retrograde cholangiopancreatography and sphincterotomy. *Ann Surg* 2000; 232: 191—8.

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P1447 ERCP-RELATED PERFORATIONS ARE RARE BUT ASSOCIATED WITH SEVERE COMPLICATIONS

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Introduction: Iatrogenic perforations in endoscopic retrograde cholangiopancreatography (ERCP)-related interventions are rare. Diagnosis and treatment of such perforations are difficult.

Aims & Methods: Aims of this retrospective study were to identify risk factors, to assess morbidity and mortality associated with perforation and to review management of these patients. Patients were retrospectively identified by a full-text search within the endocospic database (Endobase, Olympus) and by radiological reports of CT scans (Centricity PACS, GE Healthcare) demonstrating the perforation. All cases (2007-2015) were reviewed for clinical plausibility, all ERCP procedures were performed as therapeutic intervention.

Results: 44 perforations occurred (19 in women, 25 in men) during 5845 ERCPs (0.75%) with 23 symptomatic and 21 asymptomatic patients. The mean age of patients with perforation was 57.5 ± 15.2y and the mean hospitalisation was 16 days. Causes of perforation were guidewire associated (18), needle knife sphincterotomy (8), standard sphincterotomy (4), endoscope-related (3), and other mechanisms (6). In 5 cases the cause for perforation remained unclear. Only four patients had a perivaterian diverticulum. Following the classification of Stapfer et al. [1] there were 3 type 1, 15 type 2, 18 type 3 and 8 type 4 perforations. Eight patients underwent surgery, though a leakage could be identified only in patients with type 1 perforation (2). Patients receiving a stent during ERCP less often underwent surgery than patients who did not receive one (3 of 27 vs. 5 of 17). Most of the perforations were guidewire-related and were rarely associated with significant complications (1/18). In contrast, sphincterotomy-related perforations relevant complications occurred significantly more often (7/12; Fisher's exact test: $p < 0.003$). 14 patients suffered from post-procedural pancreatitis (32%). Nine patients died during their stay in hospital (two in the operative group, 7 under conservative treatment). Only one death seemed to be associated with the ERCP procedure. Interestingly, no correlation was found between endoscopists' experience and the likelihood of a perforation. Most perforations occurred between 350 and 700 performed ERCPs.

Conclusion: ERCP associated perforations remain a rare but severe complication. Experience of the endoscopist and the likelihood of a perforation were not correlated. Conservative treatment of perforations except for type 1 seems safe, as surgical intervention can rarely identify the perforation site. The placement of a biliary stent may have a protective effect in case of perforations.

Reference

1. Stapfer M, Selby RR and Stain SC, et al. Management of duodenal perforation after endoscopic retrograde cholangiopancreatography and sphincterotomy. *Ann Surg*. 2000 Aug; 232(2): 191—8.

Disclosure of Interest: None declared

P1448 BIPOLAR RADIOFREQUENCY ABLATION OF TISSUE INGROWTH IN SELF-EXPANDABLE METAL STENT INSERTED TO THE BILE DUCT: IN VITRO STUDY

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Introduction: Bipolar RFA catheters for endobiliary RFA of biliary malignancy have been introduced. Animal study using porcine model showed that there is a linear relationship between the power of bipolar RFA and the depth bile duct ablation. Bipolar RFA of the tissue ingrowth in self-expandable metal stents (SEMSs) might restore the stent patency. However, there is no in vivo model to simulate tissue ingrowth in SEMS.

Aims & Methods: The aim of this study was to simulate the bipolar RFA effect on tissue ingrowth that causes SEMS occlusion using polyacrylamide gel phantom model. In vitro simulation of RFA of tissue ingrowth in SEMS was done using polyacrylamide gel phantom model. In brief, the gel fluid was poured into 4-mL, cuboidal cuvettes (Ratiolab, Dreieich, Germany). For bipolar RFA, we used ELRA RFA catheter and VIVA RF generator (STARmed, Gyeonggi-do, Korea). The power was set at 10 W. The RFA setting that resulted in the optimal RFA depth of the model was determined in the plain gel phantoms (i.e., gel phantoms without SEMS embedded). Bipolar RFA was done to uncovered SEMS-embedded (n = 10) and damaged covered SEMS-embedded (n = 10) gel phantoms. The RFA effects were compared.

Results: The optimal RF setting for *in vitro* evaluation of bipolar RFA using the plain gel phantom was 10 W, temperature range of 65-75°C, with a duration of 30 seconds. This setting resulted in an ellipsoid coagulated area with mean short

axis of 9.1 ± 0.21 mm and long axis of 11.8 ± 1.1 mm (n = 10). The short axis of the coagulated area just reached the wall of the cuvette at this setting. The mean cross-sectional area of coagulation was 84.3 ± 7.4 mm^2. Bipolar RFA of the uncovered SEMS-embedded gel phantom model resulted in early termination of RF generation. In detail, during the early course of RFA, a rapid drop in the impedance of the circuit was observed when the coagulated area came into contact with the wire of the uncovered SEMS. Subsequently the generation of RF was terminated, and re-initiation of RF generation was not possible. This phenomenon was observed in all 10 uncovered SEMS-embedded gel phantoms. Only small areas of coagulation confined near to individual electrodes were observed. The mean cross-sectional area of coagulation was 16.2 ± 11.0 mm^2, which was significantly different when compared to that of the plain gel phantoms ($P < 0.001$). No damage to the SEMSs was noted in the gel phantom model. Bipolar RFA of the damaged covered SEMS-embedded gel phantom model resulted in an ellipsoid area of coagulation. No early termination of RF generation was observed. In 5 models, the coagulated area was confined within the SEMS lumen. In the other 5 models, the coagulated area expanded beyond the wall of SEMS. The mean cross-sectional area of coagulation of 10 gel phantoms was 73.0 ± 14.9 mm^2. There was statistically significant difference between the mean areas of coagulation of plain gel phantoms and damaged covered SEMS-embedded gel phantoms ($P = 0.047$).
Conclusion: Power shut-off of the generator resulted when the coagulated area became in contact with the metal wire. Bipolar RFA of tissue ingrowth in uncovered SEMS might be of limited efficacy, as the RFA effect is limited around the individual electrodes and cannot reach beyond the SEMS wall. Ablation of the tissue outside the SEMS is likely to be limited.
Disclosure of Interest: None declared

P1449 A NEW TECHNIQUE OF THE WIRE-GRASPING METHOD IN FORCEPS BIOPSY FOR BILIARY STRICTURES; A PROSPECTIVE RANDOMIZED CONTROLLED STUDY OF EFFECTIVENESS

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Introduction: Although transpapillary forceps biopsy is an effective diagnostic technique in patients with biliary stricture, forceps insertion into the bile duct without endoscopic sphincterotomy (EST) is difficult. The aim of this prospective randomized controlled study was to determine the usefulness of the wire-grasping method, a novel technique for performing forceps biopsy.
Aims & Methods: Consecutive patients with biliary stricture or irregularities of the bile duct wall were randomly allocated to either the direct or the wire-grasping method group. In the wire-grasping method, a guide-wire placed into the bile duct beforehand is grasped by forceps in the duodenum, and then the forceps are pushed through the papilla without EST. In the direct method, forceps are directly pushed into the bile duct alongside a guide-wire. The primary endpoint was the success rate of obtaining specimens suitable for adequate pathological examination.
Results: In total, 32 patients were enrolled, and 28 (14 in each group) were eligible for analysis. The success rate of obtaining adequate specimens for pathological examination was significantly higher using the wire-grasping method than the direct method (100% vs. 50%, $P = 0.016$). Sensitivity and accuracy for diagnosis of cancer were also higher in the wire-grasping method group (91% vs. 42%; $P = 0.019$, and 93% vs. 46%; $P = 0.011$, respectively). No procedure-specific complications were observed in the wire-grasping method group.
Conclusion: The wire-grasping method is useful for diagnosing patients with biliary stricture or irregularities of the bile duct wall.
Disclosure of Interest: None declared

P1450 NOVEL FLOWER-TYPE COVERED METAL STENT TO PREVENT CHOLECYSTITIS: EXPERIMENTAL STUDY IN A PIG MODEL

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Introduction: Covered self-expandable metal stents (CSEMS) has the risk of obstruction of the cystic duct, and the main and branch pancreatic ducts due to strong radial force and covering material, which results in cholecystitis and pancreatitis. A flower-type covered self-expandable metal stents (F-CSEMS) having a five-petal shaped design with side grooves was constructed to prevent the obstruction of the cystic duct orifice.
Aims & Methods: This study investigated the value of the F-CSEMS in protection for cholecystitis in a pig model. Fourteen pigs randomly underwent endoscopic placement of either F-CSEMS or conventional CSEMS (C-CSEMS). The stent was placed across the cystic duct orifice to impede bile drainage from the gallbladder. Drainage was checked at 24, 48, 120 and 168 hours after implantation. Blood was collected at baseline, on days 2 and 7 following implantation. The animals were sacrificed for histologic evaluation on day 7.
Results: All stents were successfully inserted into bile duct without any procedure-related complications. At 48 hours, the rate of contrast drainage from the gallbladder was higher in the F-CSEMS group than the C-CSEMS group without significant difference (71.4% vs. 28.6% p = 0.28). C-CSEMS was associated with higher levels of C-reactive protein (35.2 μg/dl vs. 20.5 μg/dl, p = 0.03) and histologic inflammatory scores of gallbladder (score 4 vs. 2; p = 0.03).
Conclusion: The F-CSEMS appears safe and helpful to prevent cholecystitis without disturbance of bile flow in a pig model.
Disclosure of Interest: None declared

P1451 DIAGNOSTIC APPROACH USING EUS-GUIDED FINE NEEDLE BIOPSY AND TRANSPAPILLARY BIOPSY IN PATIENTS WITH SUSPECTED MALIGNANT BILIARY OBSTRUCTION

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Introduction: Although tissue sampling on ERCP is an initial procedure for histologic diagnosis of malignant biliary obstruction (MBO), EUS-guided sampling is emerging as an accurate diagnostic procedure. However, the diagnostic yields of EUS and ERCP-guided sampling on MBO were reported variously.
Aims & Methods: The aim of this study was to evaluate the usefulness of the diagnostic approach using EUS-guided fine needle biopsy (EUS-FNB) and ERCP-guided transpapillary forceps biopsy (TPB) combined according to an origin of stricture in patients with suspected MBO. A total of 151 patients with suspected MBO underwent intraductal ultrasonography (IDUS) and TPB during ERCP at first. Based on the results of cross sectional imaging study and IDUS, all patients were classified as 72 patients (47.7%) with intrinsic type and 79 patients (52.3%) with extrinsic type of MBO. If the malignancy was not confirmed by initial TPB, 2nd endoscopic TPB for intrinsic type of MBO and EUS-FNB using a core biopsy needle for extrinsic type of MBO was performed, respectively.
Results: The overall diagnostic accuracy of 1st endoscopic TPB was 76.2%. The diagnostic accuracy of 1st endoscopic TPB in intrinsic type was significantly higher than in extrinsic type (84.7% vs 68.4%; $p = 0.022$). In 11 patients of intrinsic type with negative for malignancy by 1st TPB, 2nd endoscopic TPB was achieved a diagnostic accuracy with 72.7%. In 25 patients of extrinsic type with negative for malignancy by 1st TPB, the diagnostic accuracy of EUS-FNB was 88.0%. The overall diagnostic accuracy of 1st TPB combined with 2nd TPB in intrinsic type and EUS-FNB in extrinsic type was 96.0%.
Conclusion: The TPB appears still a useful initial tool to be able to diagnosis and treatment of patients with MBO at the same time on ERCP. In addition, the diagnostic approach using 2nd endoscopic TPB or EUS-FNB according to the origin of MBO is considered highly effective to improve a histologic diagnostic accuracy of MBO in patients with negative for malignancy by 1st trial of endoscopic TPB.
Disclosure of Interest: None declared

P1452 EX VIVO MAGNIFYING ENDOSCOPIC OBSERVATION OF BILE DUCT MUCOSA USING NARROW BAND IMAGING

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Introduction: The utility of peroral cholangioscopy (POCS) has been reported since a new video POCS was developed. However, endoscopic diagnosis of bile duct mucosa using POCS with narrow band imaging (NBI) has not yet been fully established. We investigated to assess the association between magnifying endoscopic findings and histopathological findings of the bile duct ex vivo.
Aims & Methods: 41 common bile ducts which were surgically resected were enrolled in this study. These specimens included non-neoplastic and neoplastic mucosa obtained from the patients who underwent pancreatoduodenectomy, bile duct resection, or hepatectomy. We cut each common bile duct open for ex vivo endoscopic observation of its mucosa. We used a magnifying endoscope (FH-260AZI or H-260Z; Olympus Medical Systems, Tokyo, Japan) commonly used for the gastrointestinal tract, and we utilized both conventional white light imaging (WLI) and NBI (CV-260SL processor, CVL-260SL light source; Olympus). After histological diagnosis, we assessed the association between the magnifying endoscopic findings (using WLI and NBI) and histopathology.
Results: 41 specimens consisted of 28 non-neoplastic mucosa and 13 neoplastic mucosa. In nine regions of 28 non-neoplastic mucosa, many oval-shaped, depressed areas and a fine, regular network were observed using magnifying endoscopy. These regions were histologically confirmed of non-inflammatory mucosa. In the 11 regions of 28 non-neoplastic mucosa, these oval-shaped, depressed areas and the network could not be clearly seen. These regions were confirmed by histology of inflamed mucosa. In eight regions of 28 non-neoplastic mucosa, the depressed areas and network could not be found, and just irregular mucosa and microvessels were observed. Additionally, in four of the eight regions, the endoscopic image of these mucosa mimicked neoplastic mucosa. These regions were histologically identified as severe inflammatory or regenerative mucosa. Dilated and tortuous microvessels could be detected in 10 regions of 28 non-neoplastic mucosa, which were histologically confirmed of inflamed mucosa. In eight regions of 13 neoplastic mucosa, tumor margin could be recognized. Tumor margin was obscured in five regions of 13 neoplastic mucosa. Especially in the case of tumor with severe inflammation, it was difficult to

distinguish the tumor margin. Dilated and tortuous microvessels could be observed on the tumor surface in 12 regions of 13 neoplastic mucosa. In all cases, these findings could be more clearly seen by magnifying endoscopy with NBI.
Conclusion: Oval-shaped, depressed areas and a fine, regular network of microvessels are the characteristic features of normal bile duct mucosa. Inflammation obscures these features. Especially in case with severe inflammation, distinguishing neoplasm from non-neoplasm may be difficult. Dilated and tortuous microvessels can be detected on both non-neoplastic and neoplastic mucosa, therefore it may be risky to distinguish neoplasm from non-neoplasm only by detecting these vessels. NBI can depict mucosal architecture and microvessels of the bile duct in minute detail.
Disclosure of Interest: None declared

P1453 AN INTERNATIONAL SURVEY ON EUS-GUIDED TISSUE SAMPLING; PREFERENCES FOR TISSUE ACQUISITION AND PROCESSING

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Introduction: Endoscopic ultrasound (EUS)-guided tissue sampling has become invaluable in the diagnostic work-up of lesions in and around the gastrointestinal tract. As a result, EUS is used all over the world. Unfortunately, practice guidelines are lacking and execution is based on local expertise and consensus.
Aims & Methods: This survey was performed to gain insight in current tissue sampling routines and to assess intercontinental differences. An online survey was conducted among 400 endosonographists from Europe, the United States (US), and Asia. It contained 60 multiple-choice questions regarding specifics on tissue acquisition and specimen processing. Questions concerned both fine needle aspiration (FNA) and fine needle biopsy (FNB) procedures.
Results: Hundred eighty-six surveys were returned (47%); 85 (46%) from Europe, 54 (29%) from the US, and 47 (25%) from Asia. The median age of the respondents was 46 (IQR 41-52) years. Most were male (90%), gastroenterologists (96%), working in an academic setting (79%), and performing >100 EUS-FNA procedures per year (68%). Overall, the 22G needle was most preferred (55%). For FNB of submucosal masses, a 19G needle was preferred (63%). The reported number of needle passes varied according to target lesion; single for cystic lesions (80%) and two to three for solid lesions (53%). Most respondents preferred fanning as a needle motion technique for FNA (64%), while for FNB, fanning and "to and fro" were equally favored (44% and 46%, respectively). To increase the yield, 134 respondents (73%) routinely looked for tissue cores after FNA, and 136 (73%) prepared a cytological sample after FNB. FNA specimens were preserved in Cytolit by 72 (52%) of the European and US respondents, whereas in Asia, a tied standing was reported for the use of saline (27%) and alcohol (38%, $p < 0.001$). Rapid on-site pathological evaluation (ROSE) was used by half (51%) of the respondents from Europe and Asia, while almost all American participants (98%) had ROSE at their disposal ($p < 0.001$). Limited pathology staffing was given as the primary reason to omit ROSE (n = 49, 74%).
Conclusion: For EUS-guided tissue sampling, the majority of respondents prefer a 22G needle, for all but submucosal lesions. Most endosonographers carry out 2-3 needle passes, except for cystic lesions, where a single pass is generally performed. Specimens are mostly preserved in Cytolit in Europe and the US, while alcohol and saline are preferred in Asia. On-site tissue evaluation is standard practice in the US, but not in Europe and Asia, because of shortage in manpower. The consequences of these differences on diagnostic accuracy have yet to be evaluated in prospective studies.
Disclosure of Interest: None declared

P1454 A GLOBAL SURVEY ON THE PERI-PROCEDURAL PRACTICE OF EUS-GUIDED TISSUE SAMPLING; USE OF ANTICOAGULANTS, ANTIBIOTICS, AND SEDATION

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Introduction: Although endoscopic ultrasound (EUS) guided tissue sampling is widely executed, guidelines are lacking and practice differs according to local expertise and consensus.
Aims & Methods: This survey was performed to gain insight in current routines regarding peri-procedural measures, and to evaluate intercontinental differences. Four hundred endosonographers from the United States (US), Europe, and Asia were approached to complete an online survey, consisting of 18 multiple-choice questions regarding the peri-procedural management of anticoagulants, antibiotics, and sedation.
Results: Hundred eighty-six surveys were returned (47%); 85 (46%) from Europe, 54 (29%) from the US, and 47 (25%) from Asia. The median age of the respondents was 46 (IQR 41-52) years. Most were male (90%), gastroenterologists (96%), working in an academic setting (79%), and performing >100 EUS-FNA procedures per year (68%). Acetylsalicylic acid was continued by 87% of European and 50% of Asian respondents, whereas in the US, all respondents continued it ($p < 0.001$, Table 1). Thienopyridines, heparin, coumarins, and new oral anticoagulants (NOACs) were discontinued by most respondents (>73%). In Europe, heparin was stopped by 75% of the respondents, compared to 94% and 100% in Asia and the US ($p = 0.022$). The coagulation status was routinely checked by 66% of European and 68% of Asian respondents, but only by 20% of the US respondents ($p < 0.001$). Although most (80%) respondents considered an INR <1.5 to be safe, discontinuation of coumarins differed between the three continents. Most (86%) European respondents reported temporary discontinuation, while only 59% and 46% of their Asian and US colleagues did ($p = 0.003$). Virtually all respondents prescribed antibiotic prophylaxis when sampling a cystic lesion (95%). A minority (<39%) used antibiotic prophylaxes for other indications, such as a prosthetic cardiac valve, vascular graft, previous infective endocarditis, or congenital heart disease. For these conditions, European and Asian physicians prescribed antibiotic prophylaxes significantly more often ($p < 0.045$). Conscious sedation was favored by 52% of European and 84% of Asian respondents, while Propofol was preferred by US respondents (83%, $p < 0.001$). On-site anesthesiological assistance was routinely available for all US respondents (100%), as compared to 66% of European and 50% of Asian respondents ($p < 0.001$).
Table 1: Discontinuation of anticoagulants according to continent

Anticoagulant -no.stopped (%)	Europen = 56	Asian = 32	USn = 11	Alln = 99	p-value*
Acetylsalicylic acid	7 (13)	16 (50)	0 (0)	23 (23)	<0.001
Thienopyridines	47 (84)	25 (78)	8 (73)	80 (81)	0.618
Heparin	42 (75)	30 (94)	11 (100)	83 (84)	0.022
Coumarins	48 (86)	19 (59)	5 (46)	72 (73)	0.003
NOAC's	49 (88)	21 (66)	10 (91)	80 (81)	0.029

NOAC, new oral anticoagulants. *A chi square test was used to compare the three continents.

Conclusion: Overall, peri-procedural management for EUS-guided tissue sampling in Europe and Asia differs notably from the US. First, the majority of European and Asian respondents routinely check the coagulation status and more often decide to discontinue acetylsalicylic acid. In addition, Europeans reported to use antibiotic prophylaxis more often. Finally, conscious sedation is preferred in Europe and Asia, while the use of Propofol and the presence of anesthesiological assistance is more common in the US.
Disclosure of Interest: None declared

P1455 EUS-GUIDED FNA FOR SUSPECTED TUBERCULOUS LYMPHADENITIS- YIELD OF FNA AND CULTURE- SCOPE FOR IMPROVEMENT?

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Introduction: The most common form of extrapulmonary tuberculosis is tuberculous lymphadenopathy and its diagnosis remains a challenge since granulomatous lymphadenopathy has an extensive differential diagnosis. Several conditions, including sarcoidosis, fungal infections, and other inflammatory conditions, can present the same cytology and histopathology as tuberculous lymphadenopathy.
Definitive and rapid diagnosis of extrapulmonary tuberculosis is challenging since conventional techniques have considerable limitations.
The main difficulty with extrapulmonary specimens is that they yield very few bacilli and consequently are associated with low sensitivity of acid-fast bacillus (AFB) smear and culture. Acid-fast staining was positive in fewer than 10% of patients in most reports.
In view of the prevalence of multi drug resistant tuberculosis (MDR TB) culture and sensitivity forms the cornerstone of current anti tuberculous therapy.
Aims & Methods: Our aim was to evaluate the EUS guided FNA cytology of patients with suspected TB lymphadenopathy and in particular yield of the culture.
We collected data of all patients from January 2013 to January 2014 who had EUS guided FNA for suspected TB lymphadenopathy.
We had a total of 64 patients with suspected peri luminal lymphadenopathy.
Results: 4 patients had reactive nodes, 2 were non diagnostic, and 4 had granulomatous inflammation which was not diagnostic of TB. 1 patient had subsequent tests confirming sarcoidosis whilst the other had fungal infection.
52 patients had FNA cytology suggestive of TB of which only 1 patient had positive Ziehl Neelsen staining and subsequent positive culture at 6 weeks. 2 other patients had positive culture at 6 weeks. The remaining patients were treated on the basis of history, cytology and clinical evaluation.
15 out of 52 patients were lost to long term follow up as they were only tertiary referrals for EUS FNA, 33(63%) have had good response to treatment so far whereas 4(10.81%) patients have had further progression and eventually been diagnosed with MDR TB.
Of the 64 patient's 3 had repeat EUS FNA due to inadequate sampling or non diagnostic cytology.
Conclusion: The diagnosis of extrapulmonary tuberculosis is challenging for a number of reasons: the lack of adequate sample amounts or volumes; the apportioning of the sample for various diagnostic tests (histology/cytology, biochemical analysis, microbiology, and PCR), resulting in non uniform distribution of microorganisms; the paucibacillary nature of the specimens; the presence of inhibitors that undermine the performance of nucleic acid amplification-based techniques(NAAT); and the lack of an efficient sample processing technique.
As in our case 10.81% patient's had a delayed diagnosis of MDR TB.

PCR based tests i.e. NAAT may be especially useful in certain patient groups such as persons infected with human immunodeficiency virus (HIV) and children, who are disproportionably affected by smear-negative and extrapulmonary disease and who are also most adversely affected by delays in TB diagnosis and treatment but the cost and availability is an issue.
With the increased incidence and prevalence of multi drug resistant TB in the Indian sub continent alternative means must be sought, not only to obtain definite diagnosis but also to attain positive mycobacterial culture results which can identify MDR TB patients early on.

Reference

1. WHO guidelines 2012.

Disclosure of Interest: None declared

P1456 ENDOSCOPIC ULTRASOUND (EUS) - A MUST FOR SUSPECTED CHOLEDOCHOLITHIASIS PRIOR TO ERCP?

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Introduction: Endoscopic retrograde cholangiography (ERCP) has long been considered the most accurate method to detect CBD calculi but several studies confirm a similar accuracy rate (> 90%) for EUS. Direct comparison between EUS and MR cholangiography shows EUS to be the more accurate test. The sensitivity of both modalities is equally impressive at 100% but EUS had a specificity of 95% as opposed to a figure of 73% reported for MRI.
Aims & Methods: In the clinical setting, however, to determine the presence of ductal calculi remains a significant dilemma; a balance must be struck between invasive ERCP, associated complications and potential inaccurate diagnosis. Hence we prefer EUS as the preferred investigation prior to ERCP during the same sedation regardless of the results of previous imaging studies.
Hence we evaluated all patients with EUS who were referred to our center for ERCP for suspected choledocholithiasis. Each patient had at least 1 additional modality of imaging other than US Abdomen with cholestatic liver function test.
Results: A total of 179 patients were referred for ERCP in the year 2014. Each patient had an Ultrasound with either CT scan or MRCP indicative of choledocholithiasis.
Of these 37 (20.67%) patients avoided unnecessary ERCP's of which 23 had presumed spontaneous passage of stones, 5 had type 1 Choledochal cyst wherein the treatment is surgical excision, 3 had perivaterian diverticulum with dilated CBD and no stones and 6 had stones stuck in the Hartman's pouch.
Of the 37 patients 31 had gall stones, 4 had imaging microliths and 2 had a normal gall bladder.
In the latter 2 patient's it was presumed spontaneous passage of stones as previous imaging had suggested CBD stones.
Conclusion: EUS has remarkable accuracy in detecting choledocholithiasis and avoids unnecessary ERCP's even in patients who have had US, CT scan or MRCP.
A total of 20.67% patients avoided unnecessary ERCP's at our institution and only needed definitive cholecystectomy except the 2 patients who had normal gall bladder.
A small caveat being that the imaging quality and reporting can vary vastly in the Indian sub continent hence perhaps a good quality EUS with an experienced operator is a must prior to ERCP.
In particular, EUS is more accurate when choledocholithiasis occurs in the presence of an undilated bile duct.
EUS is useful in picking up stones in the Hartman's pouch and for detection of small stones 2-3 mm which can be best seen on higher frequency scanning. These are often termed as imaging microliths (starry night gall bladder) and missed in patients with biliary colic and recurrent acute pancreatitis.
EUS-ERCP interface is more cost effective than performing CT, MRCPs in these patients.

Reference

1. Author: Steven Edmundowicz; Sreeni Jonnalagadda; Riad Azar.

Disclosure of Interest: None declared

P1457 DIAGNOSTIC EFFICACY OF LIQUID-BASED VERSUS SMEAR CYTOLOGY FOR PANCREATIC SOLID LESIONS OBTAINED BY ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION

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Introduction: Traditionally, conventional Papanicolaou smear (CPS) analysis was performed after endoscopic ultrasound-guided fine needle aspiration (EUS-FNA), but cytohistological diagnostic methods such as rapid on-site cytological evaluation (ROSE) and the cell-block method have been developed recently. Compared to CPS, liquid-based cytology (LBC) has diagnostic utility in cervical cancer. However, there is a paucity of data on the diagnostic efficacy of LBC for pancreatic tumor samples obtained by EUS-FNA. We retrospectively analyzed the additional diagnostic efficacy of LBC using the SurePath™ method compared with CPS for samples of solid pancreatic lesions obtained via EUS-FNA without ROSE.
Aims & Methods: There were 283 consecutive patients who underwent initial EUS-FNA for solid pancreatic lesions between January 2007 and August 2014 included in this study. CPS was used for cytology of EUS-FNA samples obtained by May 17, 2012 (130 patients). Subsequently, LBC was used for cytological analysis (153 patients). The cell-block method was used for histological analysis. Cytohistological results were based on the combination of cytological and histological results. The cytological and cytohistological diagnostic yields for malignancy of CPS and LBC were compared.
Results: Overall, the proportion of total malignancy diagnosed was 85% (CPS 82%, LBC 89%). The diagnostic sensitivity and accuracy of LBC were significantly higher than those of CPS (89.0% vs. 59.4%, $P < 0.01$ and 90.2% vs. 66.9%, $P < 0.01$) and cytohistological analysis (94.9% vs. 82.1%, $P < 0.01$ and 95.4% vs. 85.4%, $P < 0.01$). LBC had also higher sensitivity and accuracy for pancreatic head lesions than CPS (85.7% vs. 53.8%, $P < 0.01$ and 86.8% vs. 61.0%, $P < 0.01$) and cytohistological analysis (92.9% vs. 75.4%, $P < 0.01$ and 93.4% vs. 79.2%, $P = 0.01$). LBC had higher cytological sensitivity and accuracy for pancreatic body or tail lesions than CPS (92.4% vs. 68.3%, $P < 0.01$ and 93.5% vs. 75.4%, $P < 0.01$) whereas the cytohistological correlation was similar in both groups (97.0% vs. 92.7%, $P = 0.37$ and 97.4% vs. 94.3%, $P = 0.40$).
Conclusion: Compared to CPS, LBC of EUS-FNA samples contributes to the diagnosis of malignancy in solid pancreatic lesions, and was especially useful for confirming malignancy in lesions of the pancreatic head.
Disclosure of Interest: None declared

P1458 DOES NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY IN PANCREATIC CYST EVALUATION AFFECT MANAGEMENT?

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Introduction: Incidental detection of pancreatic cysts is increasing due to increased radiologic imaging, which poses a source of uncertainty among clinicians who must distinguish benign from pre-malignant/malignant lesions. Needle-based confocal laser endomicroscopy (nCLE) may aid in determining type of pancreatic cyst.
Aims & Methods: The aim of this study is to determine if use of nCLE during EUS-guided evaluation of pancreatic cysts impacted clinical management, particularly decision to proceed to surgery. This observational retrospective chart review included all patients undergoing EUS with nCLE for pancreatic cysts with pathologic specimen confirmation performed at Columbia University Medical Center (CUMC) from 3/2014-4/2015. Data regarding patient demographics, radiologic studies, EUS appearance of pancreatic lesion, nCLE appearance and diagnosis, fluid CEA/amylase levels, FNA cytology, and surgical pathology, if available, were extracted. Based upon this information, the clinician who performed the EUS with nCLE rendered a final clinical impression, defining the pancreatic lesion as serous cystadenoma (SCA), intraductal papillary mucinous neoplasm (IPMN), neuroendocrine tumor, or other.
Results: Fourteen patients were identified. 57% were female. Mean age was 69 years. The majority of pancreatic cysts were located in the body/tail region of the pancreas (57%). Mean size was 29 x 27 mm with range of 10 x 9 mm to 60 x 40 mm. Based upon all available clinical data, 8 pancreatic lesions were classified as SCA, 3 IPMN, 1 gastrointestinal stromal tumor (GIST), and two neuroendocrine tumor, which were consistent with the gold standard of cytology in 10/14 cases and further corroborated by surgical pathology in 1 of these 10 cases. In the remaining 4 instances, cytology was nondiagnostic. In the majority of cases, nCLE appearance correlated with cytology (7/10) and the final diagnosis (11/14) but failed to do so when image quality was poor or had characteristics of multiple types of cysts. In all 4 cases lacking cytologic confirmation, nCLE imaging features confirmed the overall clinical impression. With the exception of one of these subjects who was referred for other indication, these individuals did not undergo surgical resection due to low malignant potential.
Table 1: nCLE Diagnosis of Pancreatic Cysts

Number of Patients	nCLE Diagnosis	nCLE Features	Overall Clinical Impression
6	SCA	Superficial vascular network	SCA
3	IPMN	Band-like projections	Side branch IPMN
2	Neuroendocrine	Dark clumps with bands	Neuroendocrine
1	Neuroendocrine > IPMN	Few areas of dark clumps	SCA
1	Nondiagnostic	Debris, poor imaging	SCA
1	Indeterminate	Rings, thick white bands with flow, papillary projections	GIST

Conclusion: nCLE findings correlated with both the gold standard of cytology and the overall clinical impression of the pancreatic lesion in the majority of cases. In cases in which cytology was nondiagnostic, nCLE proved particularly useful in providing further clinical confidence to support the diagnosis that did not warrant surgery. nCLE appears to have an emerging role in distinguishing

different types of pancreatic lesions and provides useful and clinically relevant information that impacts further patient management.
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P1459 A 19-GAUGE HISTOLOGY NEEDLE VERSUS A 19-GAUGE STANDARD NEEDLE IN SINGLE-PASS OF EUS-FNA FOR SOLID LESIONS: A MULTI-CENTER RANDOMIZED CROSSOVER TRIAL

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Introduction: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is a safe, reliable, and widely used method for obtaining pathological specimens from lesions around the upper intestine. Evaluation of tissue architecture or immunostaining by using histological samples is essential for diagnosing certain diseases, such as lymphoma, gastrointestinal stromal tumor, and autoimmune pancreatitis; furthermore, it is important in deciding optimal chemotherapy regimens. A 19-gauge histology needle (PC19; EchoTip®ProCore™, Cook Medical) has recently been developed and showed a high single-pass core tissue acquisition rate and histological diagnostic yield in the initial pilot study.
Aims & Methods: The aim of this study was to compare the histological diagnostic yield in single-pass EUS-FNA for solid lesions by using PC19 and a standard 19-gauge needle (EC19, EchoTip®Ultra, Cook Medical).
Consecutive patients ($n = 115$) with solid lesions, measuring ≥ 20 mm and located around the upper intestine, were enrolled in the study from five tertiary hospitals between 11/2013 and 8/2014. The patients underwent one pass each of EUS-FNA using PC19 and EC19 with randomization in order of using FNA needles. The presences of histologic core as well as histologic and cytologic findings were evaluated by pathological analysis. The primary endpoint was the histologic diagnostic accuracy. The secondary endpoints were the feasibility of FNA, the rates of presence of histological core, the cytological and overall diagnostic accuracy, and adverse events.
Results: Of the 115 patients, 110 (median age = 69; interquartile range 61-77; 49 women) underwent EUS-FNA, and 5 were excluded from the study because of lesion size < 20 mm on EUS. Lesions were located in the pancreas (70), lymph nodes (30), liver (5), gastric subepithelial tumor (4) or retroperitoneal mass (1), and were of a median size of 35.5 mm. EUS-FNA was performed from the esophagus (4), stomach (80), or duodenum (26). The final diagnosis was 100 malignant cases and 10 benign cases. The feasibility of EUS-FNA was 98.2% and 97.3% with PC19 and EC19, respectively ($p = 1.0$). The rate of presence of histological core, and histological, cytological, and overall diagnostic accuracy for PC19 and EC19 were 84.6% and 80.9% ($p = 0.59$), 83.6% and 73.6% ($p = 0.10$), 63.6% and 56.4% ($p = 0.34$), and 90.0% and 79.1% ($p = 0.04$), respectively. Adverse events were observed in four patients; these were mild abdominal pain (1), intramural hematoma (1), self-limited bleeding (1), and mild bleeding (1).
Conclusion: Single-pass EUS-FNA with PC19 was feasible and showed significantly higher overall diagnostic accuracy, and higher tendency for the rate of histological core acquisition, histological, and cytological diagnostic accuracy, compared with EC19.
Disclosure of Interest: None declared

P1460 COMPRESSION ELASTOGRAPHY AT ENDOSONOGRAPHY: CLINICAL AND DIAGNOSTICAL VALUE IN COMPLEX ALGORITHM OF PATIENTS WITH PANCREAS DISEASES EXAMINATION

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Introduction: Nowadays there are too many patients, suffering from pancreas diseases. Compression elastography in combination with endosonography becomes widespread technique in diagnostic of acute pancreas inflammation, pseudotumor and tumor foci.
Aims & Methods: To determine clinical and diagnostical value of compression elastography at endosonography incomplex algorithm of patients with pancreas diseases examination 119 patients at the base of Smolensk City Clinical Hospital from December 2012 till April 2015 were examined. There were (67 (56.3%) - men and 52 (43.7%) - women in the age from 31 till 67 ($p > 0.05$)), diagnosis: acute pancreatitis–in 45 (37.8%) patients, pseudotumor pancreatitis - 51 (42.9%), malignant pancreas foci in 23 (19.3%) patients ($p \geq 0.05$). Compression elastography at endosonography was made at scan «HITACHI PREIRUS» with compression elastography regime «PENTAX EG 387OUTK». Convex sensor at endoscope with frequency 7,5 MHz– 15,0 MHz was used; water nozzle for ultrasound sensor was not used while the research. Parenchymal lay of right and left kidney was a control zone at semi-quantitative evaluation, if there were no opportunity to kidneys measurement, the retroperitoneal tissue or the parenchyma of spleen were used as the control zone. The pancreas biopsy (per cutaneous) under ultrasound control was the referent method at 92 (77,3%) patients, and spiral computer tomography of pancreas - at 54 (45,4%) patients
Results: Emiquantitative and qualitative evaluation of elastographic images results was hold. At qualitative evaluation of elastographic image of pancreas and foci: chronic pancreatitis - predominance of green color; pseudotumor pancreatitis -mix type of color; malignant changes - hard type of staining (blue hue); At semiquantitative evaluation there was a calculation of comparative SR-coefficient. Coefficient of SR difference at acute pancreatitis - till 2 conventional units (c.u.), at pseudotumor pancreatitis - from 3 till 5 c.u., at malignant lesion - more than 5 c.u. SR data coincidence at pseudotumor pancreatitis and malignant changes of pancreas indicates the neccessarity of additional qualitative evaluation, which is useful for the diagnosis elaboration. The coincidence of biopsy results and compression elastography at endosonography results were in 87 (94.7) patients ($p \leq 0.05$). The sensitivity of compression elastography at endosonography was 97.7%, specificity – 91.3%, accuracy - 94.8%
Conclusion: Compression elastography of pancreas at endosonography has clinical value for the correct diagnosis and important diagnostic value in complex algorithm of patients examination. Qualitative and quantitative evaluation are important additions for the diagnosis elaboration.
Disclosure of Interest: None declared

P1461 ENDOSCOPIC ULTRASOUND IN SUSPECT CHOLEDOCHOLITHIASIS – SHOULD IT BE EXTENDED TO HIGH LIKELIHOOD PATIENTS?

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Introduction: In patients with suspected choledocholithiasis, the American Society of Gastrointestinal Endoscopy (ASGE) guidelines recommend different approaches depending on the probability of common bile duct (CBD) stones, based on clinical predictors. Endoscopic retrograde cholangiopancreatography (ERCP) is suggested in patients with high probability.
Aims & Methods: We aimed to assess the benefit of endoscopic ultrasound (EUS) in suspected choledocholithiasis and the impact on ERCP burden, not only in patients with intermediate probability, but also in those with high probability. Patients undergoing EUS for suspected choledocholithiasis between June 2011 and June 2014 were retrospectively evaluated. According to clinical data, patients had been classified as high or intermediate probability of choledocholithiasis. ERCP was performed whenever EUS revealed CBD stones. The remaining patients were followed for at least six months.
Results: We included 42 patients (59.5% female, mean age $55.1 \pm 21,3$ years), 22 with high probability of choledocholithiasis and 20 with intermediate probability. In 22 (high probability = 14, intermediate = 8) EUS showed choledocholithiasis (21 truly positives) and ERCP was performed, mostly in the same session (66.7%). "High probability" had a specificity of 57.1% (42.9% false positives) for diagnosis of choledocholithiasis. Sensitivity, specificity, positive predictive value and negative predictive value of EUS were 100%, 95.2%, 95.5% and 100%, respectively. It was found that the diameter of CBD was higher in patients with choledocholithiasis (9.3 ± 6.9 vs $4.3\text{mm} \pm 3.0\text{mm}$, $p < 0.05$). There were no differences in the level of total bilirubin, alkaline phosphatase, gamma-glutamiltranspeptidade or transaminases.
Conclusion: This study demonstrates that the use of clinical criteria alone might not adequately predict the presence of choledocholithiasis. EUS had a high diagnostic accuracy in the detection of CBD stones, preventing ERCP in 36.4% of high probability patients. EUS should be considered prior to ERCP, regardless of the probability of choledocholithiasis.
Disclosure of Interest: None declared

P1462 ROLE OF EUS-GUIDED NEEDLE BASED CONFOCAL LASER ENDOMICROSCOPY IN ASSESSMENT OF PANCREATIC CYSTIC NEOPLASMS

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Introduction: The differential diagnosis of pancreatic cystic neoplasms (PCN) is still a challenge. Clinical tools used for this purpose are cross sectional imaging, endoscopic ultrasound (EUS), cytology and cyst fluid analysis. EUS-guided needle based confocal laser endomicroscopy (nCLE) enhances the diagnostic arsenal in the evaluation of PCN and seems to be promissing technique.
Aims & Methods: Aim: to improve diagnosis performing EUS –guided nCLE in patients with pancreatic cystic neoplasms.
Material and methods: 69 patients with pancreatic cystic neoplasms(M-15, F-54, mean age – $59,4 \pm 19,7$ yrs) underwent complete investigation including transabdominal ultrasound, CT, EUS. In 11 (16%) cases imaging characteristics were uncertain that required EUS-guided nCLE, FNA with cytology and cyst fluid analysis (CEA).
Results: Cross-sectional imaging, EUS of 69 patients established IPMN in 45 (65%) cases: MD –IPMN in 5, BD-IPMN- 36, IPMN invasive carcinoma – 4 cases, SCN in 10 (14.5%) patients, MCN in 2(3%) patients, SPN in 2(3%) case, pseudocyst (14.5%) in 10 patients. The size of cyst ranged from 5 to 110 mm. EUS-guided nCLE was performed in 11(16%) patients with cyst size above 2 cm and revealed IPMN in 3 cases, SCN - in 7, SPN in 1 case. Cyst fluid CEA

level in IPMN patients reached 83 ± 53.6, ng\ml, in SCN patients - 7.3 ± 3.2 ng\ml. In 3 cases the results of nCLE influenced on the diagnosis and management of cystic lesions. In 2 cases suspected to MCN and neuroendocrine tumor nCLE revealed superficial vascular network pattern typical to SCN, which is considered to be benign and requires follow-up. In 1 case of BD-IPMN with cyst size < 3cm nCLE revealed typical fingerlike papillary projections and focus of high-grade dysplasia that was confirmed by cytology and refer the patient to resection.
Conclusion: EUS-guided nCLE in combination with EUS FNA may improve diagnosis and management of pancreatic cystic neoplasms. In experienced hands it allows to avoid unnecessary intervention or observation and establish indications to well-timed surgery.
Disclosure of Interest: None declared

P1463 EFFICACY OF EUS-GUIDED ANTEGRADE TRANSPAPILLARY STENTING IN CASE OF FAILED ERCP: RETROSPECTIVE ANALYSIS IN TWO LARGE-VOLUME CENTRES

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Introduction: EUS-guided biliary drainage (EUS-BD) has evolved as a viable alternative for biliary drainage. Published studies about EUS-BD have shown a lower rate of post-procedure pancreatitis, presumably due to bile duct access being away from papilla. EUS-guided antegrade transpapillary stenting resembles ERCP or PTBD as the stent exits through papilla, and not trans-luminally. There are no major published studies of EUS-AG
Aims & Methods: Aims: To assess safety and efficacy of EUS-AG for biliary drainage.
Setting: Two tertiary care centres.
Patients: Patients with obstructive jaundice and failed ERCP or ERCP is not possible.
Study design: Retrospective analysis.
Methods: Left hepatic duct puncture was done from proximal stomach using a 19 gauge needle. Guidewire was manipulated across the hilum, and papilla in to duodenum. After track dilation with a biliary balloon or a cystotome, a stent was inserted and positioned across the papilla.
Results: There were 56 patients (median age 65 years, 24 females). Fifty four patients had a malignant distal obstruction (pancreatic 50, ampullary 3, bile duct 1), and two had a proximal obstruction (bile duct 1, nodal 1). Twenty one patients (37.5%) had normal duodenum, 26(41%), had duodenal stenosis, while 9(16%) had post operative anatomy (Whipples 6, Billroth II 2, total gastrectomy 1). The mean pre-procedure bilirubin was 14.6 mg%. Technical success was achieved in 53 patients (94.64%). Expandable metal stents were placed in 49 patients while 4 patients had plastic stents. Six patients (10.71%) developed 8 adverse events (14.28%). Adverse events were highest in the prior surgery group (2/9, 22.2%, followed by those with duodenal stenosis (3/26, 11.53%, and normal duodenum (1/21, 4.3%). The difference however was not statistically significant ($p = 0.6$). Adverse events included pancreatitis in 2 (3.57%), bleeding in 2 (3.57%) and cholangitis, perforation, and stent migration in one patient each(1.78%). There was no mortality. Both the patients with pancreatitis had not undergone a prior ERCP. One patient developed mild, and another moderate pancreatitis. Over a median follow up of 280 days, 3 patients (5.6%) had partial stent migrations, while stent block developed in 14 patients (26.41%). Sixteen patients(30.1%) died with stent in situ. Kaplan-Meier curves for stent patency show that median stent patency was > 210 days.
Conclusion: EUS-AG procedure has safety and efficacy profile similar to other EUS-BD procedures. However the post-procedure pancreatitis rates appear higher, and are equivalent to those reported for ERCP. This could be due to papillary manipulation during antegrade stent placement. Prospective study compared with conventional ERCP is warranted.
Disclosure of Interest: None declared

P1464 VISUALIZATION AND NEUROLYSIS OF CELIAC GANGLIA WITH ENDOSCOPIC ULTRASOUND: RESULTS OF A CLINICAL CROSS-SECTIONAL AND HUMAN CADAVER STUDY

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Introduction: Endoscopic ultrasound-guided celiac ganglia neurolysis (EUS-CGN) by injecting ethanol in individual celiac ganglia has recently been introduced as an alternative to celiac plexus neurolysis. However, there is little evidence that the structures targeted during EUS-CGN are indeed celiac ganglia and that selective ethanol injection into ganglia is feasible.
Aims & Methods: The aim of this study was to assess the proportion of patients in which ganglia can be visualized with EUS, to evaluate whether these structures are indeed celiac ganglia and to visualize the local spread of ethanol after EUS-CGN. In 100 consecutive patients (44 male [44%], median age 60, IQR 45-68) undergoing linear EUS, ganglia were identified and their characteristics recorded. Furthermore, a linear echo-endoscope was placed in the region next to the celiac trunk in a prosected human cadaver. A hypodermic needle was inserted into a ganglion after identification and the tissue surrounding the needle was removed, dissected to visualize the ganglion and subsequently sectioned and stained. Finally, EUS-CGN was performed with ethanol 96%, mixed with orange dye, in a nonembalmed human cadaver. Thereafter, the entire region around the celiac plexus was removed and consecutive transverse sections were obtained with a heavy duty cryomacrotome, whilst taking high-quality pictures every 75μm. Afterwards, a 3D-reconstruction was used to obtain sagittal and coronal images.
Results: In total, 211 ganglia were detected in 86/100 patients. Median number of ganglia was 2 (range 1-9), median sizes of the long and short axis were 6.2 mm (IQR 4.5-8.6 mm) and 2.8 mm (IQR 2.2-4.0 mm), respectively. The ganglia were most commonly located anteriorly (n = 65, 31%), left (n = 64, 30%) or anteriorly and left (n = 75, 36%) of the celiac trunk. Histology of the dissected region in the cadaver showed numerous nerve cell bodies around the needle and no other structures with comparable echogenic characteristics, such as lymph nodes. In total, two ganglia were visualized with EUS in the nonembalmed cadaver and both were injected with 1mL of ethanol under EUS-guidance using a 25G FNA-needle. More than 2,200 images were taken during transverse sectioning with the cryomacrotome. 3D-reconstruction showed spreading of the dye in the celiac region, well beyond the ganglia, with a total spread of 80 x 70 x 53 mm.
Conclusion: Using EUS, it is possible to visualize celiac ganglia in the majority of patients, most commonly anteriorly and to the left of the celiac trunk. Histology from a cadaver confirmed that the visualized structures are indeed celiac ganglia. As a low dose (1 ml) of ethanol already spreads well beyond the injected celiac ganglion after EUS-CGN, it is doubtful whether selective celiac ganglia neurolysis is feasible.
Disclosure of Interest: None declared

P1466 SUPERIORITY OF THE SPLIT-DOSE PEG REGIMEN FOR SMALL-BOWEL CAPSULE ENDOSCOPY. A SINGLE-CENTER PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: Over the last years, it has become apparent that fasting and clear fluids alone obtain inferior small-bowel visualization when compared to what it is achieved with purgatives use. PEG (polyethylene glycol) lavage solutions has accumulated evidence and is, therefore, recommended by the last ESGE guideline. Whether this regimen can be further improved by changing the timing of administration is unknown.
Aims & Methods: To evaluate small-bowel cleansing quality, diagnostic yield, transit time and patients' tolerability, comparing two different PEG administration schedules (single-dose vs split-dose). Fifty-seven patients were prospectively enrolled and randomized in two groups: Group 1 (n = 29) were administrated 2L of PEG in the day before SBCE, time between PEG administration and SBCE = 10 hours; and Group 2 (n = 28) were administrated 1L of PEG in the day before SBCE and 1L of PEG in the morning before SBCE, time between PEG administration and SBCE = 4 hours. Small-bowel cleansing was independently assessed by four experienced gastroenterologists and the cleansing quality of the small-bowel was evaluated according to the system described and validated by Brotz *et al*[1] using the quantitative index (QI). SBCE image quality, detection of any mucosal abnormality, clinically relevant lesion (according to Saurin classification), transit times and patients' tolerability during preparation and after SBCE ingestion were compared.
Results: Groups were age and sex-matched. The entire and distal half small-bowel cleansing scores were significantly higher among G2 (median score 8 points vs 10 points, $p = 0.012$; median score 6 points vs 8 points, $p = 0.05$, respectively). Despite an higher proportion of patients in G2 with an adequate preparation (≥ 8 points), there was no statistical difference regarding the entire and distal half of the small-bowel cleansing (66% vs 82%, $p = 0.230$; 41% vs 54%, $p = 0.431$, respectively). Regarding the elementary assessment of the entire small-bowel cleansing, G2 had a significantly higher proportion of patients with a maximum elementary score (2 points) in the percentage of mucosa visualized ($p = 0.045$) and fluid/debris ($p = 0.016$). Although not reaching statistical significance, a trend was noted regarding better scores in the bile/chyme staining ($p = 0.141$) and brightness ($p = 0.070$) scores among G2 in the entire small-bowel assessment. A clinically relevant lesion was observed in 58% of the examinations, without statistical difference between the two preparations (52% vs 64%, G1 and G2, respectively, $p = 0.424$). There were no significant differences in transit times among the two PEG regimens. Both schedules were fairly well tolerated, showing no differences regarding symptoms while ingesting the preparation or after SBCE ingestion.
Conclusion: Split-dose PEG regimen for SBCE preparation improved the small-bowel cleanliness, didn't interfere with transit times and was equally well tolerated by patients. No differences were observed regarding diagnostic yield.

Reference

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P1468 UTILITY OF THE SMALL INTESTINE CAPSULE ENDOSCOPE FOR DIAGNOSING OBSCURE GASTROINTESTINAL BLEEDING IN ELDERLY PEOPLE

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Introduction: Vascular lesions such as angioectasia and erosions are the main causes of unidentified hemorrhages in the digestive tract. However, the frequency of the primary disease varies according to patient age. Especially among people ≥65-years-old (elderly, according to the World Health Organization definition), multiple comorbidities are often present in those taking antithrombotic drugs, and the incidence of the small intestine lesions increases with the use of these drugs. We compared groups of people <65-years-old and ≥65-years-old relative to obscure gastrointestinal bleeding (OGIB) in our hospital.

Aims & Methods: We examined 446 patients using small intestine capsule endoscopy (CE) and balloon endoscopy (BAE) between December 2014 and April 2004. Their small intestinal lesions were examined to determine the underlying disease, and their oral medications and small intestine transit times were compared.

Results: Among the 239 individuals in the <65-years-old group, we found cases of occult OGIB (n = 25), overt OGIB (n = 87), disease of the small bowel (n = 78), and others (n = 49). Among the 207 patients in the ≥65-year-old group, we found occult OGIB (n = 31), overt OGIB (n = 104), disease of small bowel (n = 51), and others (n = 21). In the <65-years-old group, 9% (20/239 patients) were taking antithrombotic drug and/or anticoagulant drug, and 30% (6/20 patients) were associated with angioectasia and/or erosions. In the ≥65-years-old group, 22% (43/207 patients) were taking antithromobotic drug an/or anticoagulant drug internal use, and 49% (21/43 patients) were associated with antioectasia and/or erosions. The intestinal transit time was significantly longer in the ≥65-years-old group (313 min) than in the <65-years-old group (265 min).

Conclusion: In individuals ≥65-years-old, there were many individuals using antithrombotic and/or anticoagulant drugs, and many cases with angioectasia and/or erosions were observed using CE. The small intestine transit time was also longer in the ≥65-years-old group, suggesting that an increased risk of mucous membrane disorders with the use of drugs. CE searches in elderly people with suspected OGIB are thought to be necessary to confirm the diagnosis.

Disclosure of Interest: None declared

P1469 COMPARISON BETWEEN CAPSULE ENDOSCOPY AND BALLOON-ASSISTED ENTEROSCOPY FOR THE DIAGNOSIS OF OVERT OBSCURE GASTROINTESTINAL BLEEDING

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Introduction: Although overt obscure gastrointestinal bleeding (OGIB) is difficult to diagnose, capsule endoscopy (CE) and balloon-assisted enteroscopy (BAE) are effective and essential devices for diagnosing small intestinal bleeding. Despite great progress, some OGIB cases cannot be detected using CE and BAE. Based on our data, we compared the detection rates for both methods, and checked undetected cases with CE and BAE.

Aims & Methods: CE and BAE were performed on 433 patients (285 male, 148 female), between April 2005 and September 2014, at our institute. A total of 167 patients were diagnosed with OGIB. For diagnosing overt OGIB, CE (Pillcam SB2; Covidien, Mansfield, USA) was employed first; BAE (single balloon enteroscopy; Olympus Medical Systems, Tokyo, Japan) was also used for both diagnosis and treatment. If small intestine lesions were suspected, based on another modality, BAE was used, despite negative CE findings. CE results were independently checked by at least two doctors. BAE was performed using either an oral and/or anal approach, depending on the CE results. Prior to checking for small intestinal lesions, esophagogastroduodenoscopy and total colonoscopy were both performed to ensure the absence of gastrointestinal bleeding from areas other than the small intestine.

Results: The CE diagnoses of the 167 cases of overt OGIB cases included angiectasia (29%), erosion/ulcer (29%), carcinoma (6%), and Crohn's disease (1%). Active bleeding was observed in 47 (28%) patients using CE, and all cases were rechecked using BAE. BAE diagnosed 39 (83%) of the 47 cases of active bleeding, and some cases (such as those with angiectasia) were simultaneously treated with BAE; 17 (36%) of the 47 cases were not diagnosed using BAE. In the 167 cases of overt OGIB, the sites of active bleeding could not be determined using CE in 108 (65%) cases; 5 (3.0%) cases were diagnosed using other modalities, such as scintigraphy or BAE. These 5 cases included 3 cases of Meckel's diverticulum, 1 jejunal sarcoma, and 1 ileal angiectasia; CE images were not taken, precluding diagnosis using CE only.

Conclusion: Both CE and BAE are very useful for the detection and diagnosis of OGIB. However, there are some cases that cannot be detected using either methodology. Therefore, if bleeding points are not detected using CE, but bleeding recurs, other modalities, including BAE, should be used.

Disclosure of Interest: None declared

P1470 THE ESSENTIAL ROLE OF SMALL BOWEL CAPSULE ENDOSCOPY IN RECLASSIFICATION OF UNCLASSIFIED COLITIS

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Introduction: Unclassified colitis is defined as an inflammatory bowel disease limited to the colon, whose combination of clinical, imaging, endoscopic and histological elements does not allow a differential diagnosis between Crohn's disease (CD) and Ulcerative Colitis (UC).

Aims & Methods: The aim of this study was to evaluate the role of small bowel capsule endoscopy (SBCE) on the reclassification of unclassified colitis.

We performed a multicenter, retrospective study including patients with unclassified colitis undergoing SBCE, between 2002 and 2014. SBCE studies were reviewed and the inflammatory activity was evaluated by determining the Lewis Score (LS). Inflammatory activity was considered significant and consistent with CD when the LS ≥ 135. The definitive diagnosis during follow-up was based on the combination of clinical, imaging, endoscopic and histological elements.

Results: Thirty-six patients were included, 21 females (58%) with mean age at diagnosis of 34 ± 13 (15-64) years. The mean follow-up time after the SBCE was 52 ± 41 (12-156) months.

The SBCE revealed findings consistent with significant inflammatory activity (LS ≥ 135) in 9 patients (25%); in all of them the diagnosis of CD was confirmed during follow-up. In 27 patients (75%), the SBCE revealed no significant inflammatory activity (LS < 135); in these patients, the diagnosis of UC was established in 16 cases (59.3%), CD in 1 case (3.7%) and 10 patients (37%) maintained a diagnosis of unclassified colitis during follow-up. A LS ≥ 135 at SBCE had a sensitivity = 90%, specificity = 100%, Positive Predictive Value = 100% and Negative Predictive Value = 94% for the diagnosis of CD.

Conclusion: SBCE proved to be very important in the reclassification of patients with unclassified colitis. In this study, absence of significant inflammatory activity in the small intestine allowed exclusion of CD in 94% of cases.

Disclosure of Interest: None declared

P1471 PILLCAM SB2 AND SB3 SMALL BOWEL CAPSULE ENDOSCOPY –COMPARISONS AND IMPLICATIONS FOR PRACTICE

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Introduction: South Tyneside Hospital has been a referral centre for capsule endoscopy since 2005, performing over 1000 studies. We have previously shown that the diagnostic yield (DY) of the PillCam SB3 capsule (Given Imaging, Israel) is significantly higher than that of the PillCam SB2[1]. Here we present additional data on ''learning curve'' and offer suggestions for practice.

Aims & Methods: Previous work compared the DY of the last 100 SB2 capsules with the first 100 SB3s. To assess for a ''learning curve'' effect we reviewed our first 100 SB2 capsules (Oct 2007–Aug 2008). Indications, completion rates, small bowel recording times and pathology were recorded. Pathology was classed as significant if it related directly to indication.

Results: 46 of the first 100 SB2 capsules were abnormal, of which 31 had significant pathology; almost identical to the last 100 SB2s (45 abnormal, 30 significant). Most tests (255/300, 85%) were for unexplained anaemia or Crohn's disease assessment. More capsules are now done for acute GI bleeding; 4 of the first 100 SB2 capsules, 12 of the last 100 SB2s and 15 of the first 100 SB3s. There were 23 incomplete SB2 capsules (11.5%) of which 18 (9%) were in small bowel at the end of recording and 5 were held up by pathology (2.5%). Only 5 SB3 studies (5%) were incomplete, with 4 (4%) not entering the colon and 1 (1%) held up by pathology. On average SB3 capsules had a longer recording time of 9 hours and 24 minutes compared to 8 hours and 2 minutes for the SB2s.

Table 1: Pathology by capsule group

	Capsule Type		
First 100 SB2	**Last 100 SB2**	**First 100 SB3**	
Angioectasia	7	6	18
Blood	4	3	4
Coeliac changes	2	3	1
Polyp/Mass	1	1	4
Stricture	1	3	1
Ulcers/erosions	16	14	20
Other	0	0	1
Total	31	30	49

Conclusion: 219 capsules were reported before the SB2 was introduced. Between the first hundred and last hundred SB2 capsules there were 1003 SB2 studies. This suggests that the increased DY is not due to a ''learning curve'', supporting our finding of increased DY with the SB3. Any ''learning curve'' is likely to be from the first 200 studies. Most studies are for iron deficiency anaemia and Crohn's disease assessment but there is a trend towards using capsules as a diagnostic tool in overt GI bleeds. Fewer SB3 studies were incomplete compared to SB2s. Our unit is now more proactive in monitoring gastric transit and colonic entry using the real time viewer and this change in practice may have helped with this. Longer recording times due to increased battery life may also play a part. We recommend monitoring capsules in real time and leaving the recorder on for longer if gastric transit is delayed or colonic entry is not clear.

Reference

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Disclosure of Interest: None declared

P1472 DIAGNOSIS OF SMALL INTESTINAL LESIONS BY THE PILLCAM SB3-IS THE EFFICIENCY OF IMAGE READING IMPROVED IRRESPECTIVE OF EXPERIENCE?

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Introduction: The PillCam SB3 is a third-generation small intestinal capsule endoscope that features automatic conversion of the imaging frame rate and improvement of image resolution when used in combination with the DR3 recorder. In addition, the efficiency of lesion detection has been improved by advances in video processing when the PillCam SB3 is used in combination with RAPID Reader8 interpretation software. In the present study, we investigated whether the efficiency of image reading could be improved by using the PillCam SB3 irrespective of the experience of the reader.

Aims & Methods: Sixty-four patients underwent small intestinal capsule endoscopy around May 2014 when the PillCam SB3 was introduced to our hospital. Among them, 30 and 34 patients were assigned to the SB2 plus and SB3 groups, respectively, and 10 patients with an average small intestinal transit time were extracted from each group. Data obtained from these 20 patients were randomized and were assessed by 3 readers with different levels of experience (beginner: <20 images, intermediate: ≥ 50 images, expert: ≥ 600 images). Then the reading time and the findings were compared among these readers. RAPID Reader8 was used as the interpretation software. After preparation of a start-point thumbnail for each gastrointestinal tract, image reading was performed under the conditions of manual mode, 4 images, and 28× speed in the SB2 plus group, while the conditions were review mode, 4 images, and 28× speed in the SB3 group. The reading time was defined as the period required for image reading and preparation of the thumbnail comment.

Results: There were no significant differences of patient background factors between the two groups. The gastrointestinal transit times of the SB2 plus group and the SB3 group were as follows: the esophageal transit time was 3.7 ± 2.4 vs. 2.9 ± 1.8 seconds, the gastric transit time was 16 ± 17.9 vs. 16 ± 13.3 minutes, the small intestinal transit time was 244.5 ± 47.3 vs. 232.7 ± 30.7 minutes, the large intestinal transit time was 121.1 ± 52.4 vs. 135.4 ± 52.5 minutes, and the tota test time was 381.6 ± 46.3 vs. 384.1 ± 43.2 minutes. There were no significant differences between the two groups. The reading time up to the small intestine was shorter in the SB3 group for each reader (SB2 plus group vs. SB3 group: beginner, 40.2 ± 10.1 vs. 23.7 ± 6.7 ($p = 0.0009$); intermediate, 21.4 ± 4.9 vs. 10.3 ± 2.9 ($p = 0.0003$); expert, 23.2 ± 5.6 vs. 11.1 ± 2.9 ($p = 0.0002$)). The total reading time up to the large intestine was also shorter for each reader in the SB3 group (beginner: 49.9 ± 10.4 vs. 24.9 ± 6.7 ($p = 0.0002$), intermediate: 30.4 ± 6.4 vs. 11.4 ± 3.7 ($p = 0.0002$), expert: 31.7 ± 4.1 vs. 12.1 ± 3.4 ($p = 0.0002$)). The correspondence of findings with those obtained by the expert reader was 84.6% for the beginner and intermediate readers.

Conclusion: When the RAPID Reader8 and SB3/DR3 recorder were used in the SB3 group, the reading time was much shorter than in the SB2 plus group irrespective of the experience of the reader. It is concluded that examination using the PillCam SB3 can reduce the burden placed on readers.

Disclosure of Interest: None declared

P1473 COMPARISON BETWEEN SIDE VIEW (CAPSOCAM) AND FRONT VIEW (PILLCAM SB, MIROCAM) CAPSULE ENDOSCOPES IN CROHŃS DISEASE AND IRON-DEFICIENCY ANEMIA. A SINGLE-CENTER EXPERIENCE

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Introduction: Capsule endoscopy is an established method for the exploration of the small bowel with a high diagnostic yield.

Since 2012 we are using a new developed capsule system with 4 cameras (Capsocam; SV1, SV2, Capsovision, Saratoga, CA) for a 360° panorama lateral viewing and on board storage.

Aims & Methods: The aim of our clinical observation was to evaluate if there is a difference between relevant findings of front view systems and the new side view capsules. Relevant findings are defined as lesions that changed the patient's therapy (endoscopic treatment or medication).

We used Capsocam for 200 patients (102 female, 98 male, mean age 52.6), 812 for front view capsules (related distribution for gender and age).

Included are patients with suspected Crohn's disease or known crohńs disease with unknown lesions in the small bowel (57 Capsocam, 116 front view capsules) and patients with iron-deficiency anemia with negative upper and lower gastrointestinal endoscopy (61 Capsocam, 213 front view capsules).

Results: For the indication Crohn's disease or iron-deficiency anemia we have done 118 examinations.

In the Crohn's group with side view capsules we included 57 examinations, 28 with relevant pathological findings (49.1%); with front view capsules 116 examinations, 26 with relevant pathological findings (22.4%).

In the iron-deficiency anemia group with side view capsules we included 61 examinations, 36 with relevant pathological findings (59.0%); with front view capsules 213 examinations, 67 with relevant pathological findings (31.5%).

DIAGNOSTIC YIELD	side view	front view	Chi square	Chi square equal
Crohn's disease	49,1%	22,4%	$p < 0,001$	12,974
Iron-deficiency anemia	59%	31,5%	$p < 0,001$	15,354

In 200 examinations we found a complete small bowel passage in 96.8%, with a mean examination time of 974 min (374 - 1376 min). 7 patients lost the capsule (3.5%). No capsule retention occurred. In 3 capsules there was one of the four cameras defect. The duodenal papilla was detected in 78.9%.

Conclusion: In our series for Crohn's disease and iron-deficiency anemia the new side view capsule endoscope (Capsocam) shows significant better results in comparison to the established front view systems (PillCam SB, Mirocam).

Disclosure of Interest: None declared

P1474 GASTROGRAFIN AS AN ADJUNCT TO COLON CAPSULE ENDOSCOPY

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Introduction: Sodium phosphate (NaP) is a key component of the standard bowel preparation regimen for colon capsule endoscopy (CCE), particularly to cause excretion of the capsule endoscope while the battery is still functioning. However,

the use of NaP is limited due to the possibility of causing severe adverse events, e.g. acute phosphate nephropathy, acute renal failure, hypertension, or mineral imbalance. According to the latest report investigating the performance of CCE compared with CT colonography, Gastrografin (the water-soluble iodinated radiopaque oral contrast medium) was first used for the CCE regimen, because Gastrografin is generally used as part of the CT colonography regimen for "fecal tagging". In our experience, a CCE regimen using Gastrografin without NaP, achieved a very high capsule excretion rate.
Aims & Methods: The aim of this study is evaluate the use of Gastrografin in the bowel preparation regimen for CCE.
From June 2014 to March 2015, 37 patients (median age 65.2 years; 11 males, 26 females) underwent CCE. All had a history of laparotomy and/or previously incomplete colonoscopy. Bowel preparation started from breakfast the day before examination. Patients had low-residue meals at breakfast and lunch, and drank 1L of polyethylene glycol (PEG) plus ascorbic acid with 0.5L of water in the evening, and 10mL of sodium picosulfate hydrate at bedtime. On the morning of the examination, patients again drank 1L of PEG plus ascorbic acid with 0.5L of water. After capsule ingestion, 50mL of Gastrografin diluted with 0.9L of magnesium citrate was administered to facilitate capsule excretion. Gastrografin with magnesium citrate was given again after one hour. If the capsule was not expelled within four hours of ingestion, 50mL of Gastrografin with water and/or a bisacodyl suppository were added.
Results: The capsule excretion rate was 97% (36/37). The one patient who did not expel the capsule within the duration of battery life was a 51-year-old man with severe diverticular disease of the sigmoid colon. The median GI transit time was 4h 26 min (range 1h 9 min to 10h 11 min). The median colon transit time was 2h 43 min (range 16 min to 8h 34 min). GI transit time as well as colon transit time was lower than previously reported. Bowel cleansing was adequate (excellent/good) in 90% of patients. The polyp (≥6 mm) detection rate was 64.9% (24/37). Diluted Gastrografin was well tolerated by all patients. No adverse events occurred in this pilot study.
Conclusion: The use of Gastrografin in CCE bowel preparation regimen is promising. However, other modifications might influence the high excretion rate and short transit time. A clinical trial to compare regimens with and without Gastrografin is warranted.
Disclosure of Interest: None declared

P1475 UTILITY OF THE CAPSULE ENDOSCOPY IN THE DIAGNOSIS AND MONITORING OF CELIAC DISEASE

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Introduction: For its minimal invasiveness, capsule endoscopy is a useful tool in the exploration of the small intestine. It has been proposed to be useful in the diagnosis and management of patients with celiac disease, however, evidence that supports and enables a broad recommendation to use the capsule in this entity is still controversial and limited.
Aims & Methods: Aim. To determine the utility of capsule endoscopy (CE) in the diagnosis and monitoring of celiac disease (CD).
Methods. Single-center, retrospective and comparative study of patients with indication for CE study by suspected CD or disease monitoring. Were distributed according to the indications in two groups: patients previously diagnosed of CD with persistent symptoms despite gluten free diet (GFD) (Group A) and patients with clinical suspicion of CD (Group B). The parameters examined were: clinical findings, capsule-endoscopic findings (CEF), duodenal biopsy by Marsh scale and serology by anti-tissue transglutaminase antibodies (anti-tTG).
Results: 60 patients were included in this research (31F/29M; 48.95 ± 17.13 years). We included in Group A 8 patients previously diagnosed of CD with persistent symptoms and GFD, observed in all CEF with celiac pattern (villi-denuded, atrophy and/or intestinal scalloped) and one of them was observed ileal neoformation not stenosing that was resected 3 weeks after (T-cell lymphoma). In group B included 52 patients with clinical suspicion of CD [iron deficiency anemia (IDA) 17/52, chronic diarrhea (CrD) 16/52, CrD + IDA 12/52, vitamin B12 deficiency 3/52, chronic abdominal pain 2/52, IDA + osteopenia 1/52 and herpetiform dermatitis 1/52]. Of these 52 patients, 33 had positive anti-tTG and 19 anti-tTG negative. Of the 33 patients with positive serology, 22 had CEF positives and all biopsies were positives according to the Marsh scale (6/22 M1, 8/22 M2 y 8/22 M3). Eleven patients had CEF negatives and in 8 of them the biopses were negative too. On the other hand, of the 19 patients with negative serology, 10 had CEF positives and in 2 cases of them the biopsies were positives, as long as the other 9 patients had CEF negatives and in 8 of them the biopsies were negatives too. So, finally in 24 of the 32 patients with CEF positives was confirmed CD. The extraintestinal findings most frequently observed were: colonic diverticulum, polyps > 4mm and hemorrhoids.
Conclusion: CE in our experience is a useful tool in the diagnosis and monitoring of CD. In all patients with positive serology and CEF positives the diagnosis of CD was confirmed by biopsy, so it could arise in certain cases establish the diagnosis without performing gastroscopy and biopsy, however more studies are needed to confirm this.
Also, in accordance with the literature, it is useful to rule out complications in patients with persistent symptoms despite GFD. Finally, in our experience in cases of negative serology and CEF negatives yield gastroscopy and biopsy is low.
Disclosure of Interest: None declared

P1476 PER POLYP SENSITIVITY OF COLON CAPSULE ENDOSCOPY ACCORDING TO PATHOLOGICAL DIAGNOSIS

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Introduction: We previously reported that the sensitivity of colon capsule endoscopy (CCE) for clinically significant polyps in a Japanese multicenter trial was 94% when results of the first colonoscopy (CS) was set as the gold standard. The aim of this additional study is to clarify the per-polyp sensitivity according to the pathological diagnosis.
Aims & Methods: This multicenter trial was conducted from December 2011 to May 2012. Written informed consent was obtained from all patients prior to enrollment. Eligible patients with significant polyps detected by the first CS received CCE (PillCam® COLON 2) procedures in tertiary-care centers. Then, a second CS was conducted to remove the significant polyps. We retrospectively reviewed the endoscopic reports from the second CSs and the pathological diagnoses, and calculated the per-polyp sensitivity of CCE according to the diagnosis.
Results: After CCE, a second CS was performed in 66 subjects to remove lesions. In total, 268 lesions were confirmed by CCE and/or second CS in the 66 subjects. Among the 268 lesions, 111 lesions were detected only by CCE, 136 lesions were detected by both CCE and the second CS, and 21 lesions were detected only by the second CS. The 157 lesions that were detected by the second CS were resected endoscopically during the second CS, and the pathological diagnosis was confirmed. The per-polyp sensitivity was estimated as 87% (136/157). Regarding the pathological findings, the per-polyp sensitivities were 100% (7/7) in cancer, 86% (18/21) in high grade dysplasia, 85% (94/110) in low grade dysplasia, 86% (6/7) in hyperplastic polyp, and 92% (11/12) in sessile serrated adenoma/polyp (ns), respectively.
Conclusion: The per-polyp sensitivity was estimated as 87% in our analysis. There was no statistical significance in the per-polyp sensitivity of different pathological lesion types.
Disclosure of Interest: None declared

P1477 RISK FACTORS FOR REFRACTORINESS TO ESOPHAGEAL DILATION OF BENIGN ESOPHAGEAL STRICTURES

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Introduction: Benign esophageal strictures (BES) need repeated dilations to relieve dysphagia. Literature is scarce on risk factors for refractoriness of BES.
Aims & Methods: Assess risk factors for refractoriness of BES to esophageal dilatation (ED). Cross-sectional study of patients with BES referred to ED during a period of three years.
Results: Three hundred and twenty seven ED were performed in 103 patients. Thirty-seven percent of the patients reported dysphagia for solids. Forty-four percent of the patients had anastomotic strictures, 17% were peptic, 6% were caustic. Strictures were complex in 13% of the patients. After dilation, stenosis was transposed in 95% of patients. There was need for further dilations in 54% of patients, being more frequent in patients with dysphagia for solids (81% *vs* 66%, p = 0.003, OR 2.160), with caustic strictures (89% *vs* 70%, p = 0.007, OR 3.487) and with complex strictures (83% *vs* 70%, p = 0.047, OR 2.132). Dysphagia for solids and caustic strictures kept statistical significance in the multivariate analysis (respectively, p = 0.01 and 0.021). Time until subsequent dilations was lower in patients with dysphagia for solids (42 days *vs* 135 days, p < 0.001), in peptic strictures (49 days *vs* 98 days, p = 0.004), in caustic strictures (49 days *vs* 78 days, p = 0.005) and in complex strictures (47 days *vs* 80 days, p = 0.009). In multivariate analysis, further dilations occurred earlier when dysphagia for solids (HR 1.673, p < 0.001), in peptic strictures (HR 1.608, p = 0.003) and in caustic strictures (HR 1.685, p = 0.005). The median time between dilations was 42 days (IQR: 15 – 87).
Conclusion: Dysphagia for solids and caustic strictures are associated with a greater need for subsequent dilations; the time until subsequent dilatations is lower in patients with dysphagia for solids, caustic strictures and peptic strictures.
Disclosure of Interest: None declared

P1478 RISK FACTORS FOR COMPLICATIONS AFTER PLACEMENT OF SELF-EXPANDING METAL STENTS IN ADVANCED ESOPHAGEAL CANCER

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Introduction: Self-expanding metal stents (SEMS) are the treatment of choice for advanced esophageal cancers. Literature is scarce on risk factors predictors for the occurrence of complications after SEMS placement.
Aims & Methods: Assess risk factors predictors for the occurrence of complications after SEMS placement for advanced esophageal cancer. Cross-sectional study of patients with advanced esophageal cancer referred for SEMS placement, during a period of 3 years.
Results: Ninety-seven patients with advanced esophageal cancer placed SEMS. The tumor was located in the proximal/mid esophagus in 59% of the patients and in the distal esophagus/cardia in 41%. Dilation previous to SEMS placement was performed in 14% of the patients. Fluoroscopy was used in 36% of the patients. SEMS had < = 11cm of extension in 40% of the cases. Stent migration occurred in 21% of patients, obstruction in 7%, fistula in 3% and hemorrhage in 2%. Complications were more common in the tumors located at the level of the distal esophagus/cardia (47.5% *vs* 22.8%, p = 0.011), with statistical significance being kept in the multivariate analysis (OR 3.1, p = 0.018, $CI_{95\%}$ 1.2 – 7.8). Time until development of complications was lower in the tumors located at the level of the distal esophagus/cardia (p = 0.036). Fluoroscopy did not influence the occurrence of migration (22.9% *vs*19.4%, p = 0.682), fistula (2.9% *vs* 3.2%, p = 0.919), obstruction (2.9% *vs* 9.7%, p = 0.182) or bleeding (0% *vs* 3.2%, p = 0.178). The occurrence of complications was not influenced by dilation previous to SEMS placement (p = 0.404), kind of stent used (p = 0.644) nor stent extension (p = 0.611).
Conclusion: The occurrence of complications after SEMS placement for advanced esophageal cancer is not influenced by the use of fluoroscopy nor by the stent used. Tumors located at the level of the distal esophagus/cardia are associated with a greater number of complications, which also occur earlier.
Disclosure of Interest: None declared

P1479 ENDOSCOPIC TREATMENT OF POST-SURGICAL ESOPHAGEAL FISTULAS WITH SELF-EXPANDING METAL STENTS

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Introduction: Esophageal fistulas (EF) secondary to surgery have a high morbidity and mortality. Self-expanding metal stents (SEMS) have been used as an alternative to re-operation, however, there are no comparative studies of efficacy.
Aims & Methods: Assess clinical efficacy of SEMS in post-surgical EF. Cross-sectional study of patients with post-surgical EF referred for SEMS placement in a reference center during a period of 3 years. Clinical success was defined as closure of the EF in barium swallow at 15 days.
Results: Thirteen patients (11 male) with a mean age of 63 years (20 – 83) placed SEMS. EF had in median 20mm of size (8 – 40). The EF was secondary to Ivor-Lewis esophagectomy in 6 patients, total gastrectomy in 2, thoracic surgery in 2, Nissen fundoplication in 1, after cervical esophagostomy reconstruction in 1 and excision of esophageal diverticulum in 1. The median time between surgery and SEMS placement was 20 days (8 – 178). SEMS had < = 11cm of extension in 5 patients. One patient died 2 days after SEMS placement and one had worsening of the fistula after SEMS expansion. Four patients had migration of the SEMS, with placement of a second stent in 3 of them and repositioning of the first stent in the other one. Time till stent migration was 9 days (2 – 23). Clinical success was achieved in 8 of 11 patients, with removal of the stent without recurrence of EF in 4 patients (median: 46 days after placement). All fistulas with less than 20mm were solved endoscopically. In the 10 patients who died during follow-up, median survival was 59 days ($CI_{95\%}$: 45 – 73).
Conclusion: Clinical success of SEMS in EF is higher than 70%, however, due to high morbidity and mortality, only 36% of the patients have their stent removed, being removal more common when fistulas have less than 20mm.
Disclosure of Interest: None declared

P1480 CLINICAL OUTCOMES OF SELF-EXPANDABLE METAL STENTS FOR MALIGNANT RECTAL OBSTRUCTION, COMPARED WITH LEFT COLONIC OBSTRUCTION

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Introduction: The placement of self-expandable metal stents (SEMS) is widely used for treatment of malignant colorectal obstruction. However, SEMS placement is still considered unsuitable or contraindicated for patients with malignant rectal obstruction within 5cm of the anal verge because of anal pain and foreign body sensation.
Aims & Methods: The aim of this study was to investigate clinical outcomes and complications of SEMS in patients with malignant rectal obstruction including lower rectal obstruction. From January 2005 to December 2014, medical records of patients with malignant rectal or left colonic obstruction who were treated with SEMS were reviewed retrospectively. Technical and clinical success rates and complication rates including pain were evaluated.
Results: SEMS insertion was attempted in a total of 573 patients; 419 for left colon obstruction and 154 for rectal obstruction. Rates of extrinsic colonic malignancy and palliative intention was higher in patients with rectal obstruction than those with left colon obstruction. Technical success rates were similar between two groups (93.2% vs 93.1%, $p = 0.857$), however, clinical success rates were lower and complication rates were higher in patients with rectal obstruction (92.1% vs 85.4%, $p = 0.022$; 25.1% vs 36.6%, $p = 0.014$, respectively). Multivate analysis revealed that extrinsic colonic malignancy and covered stents were significant risk factors for clinical failure, and complete obstruction and palliative intention were associated with complications. Although overall complications were not different in patients with lower rectal obstruction (33.3% vs 27.7%, $p = 0.526$), patients with lower rectal obstruction complained pain due to SEMS placement (11.1% vs 1.5%, $p = 0.014$), two of whom required stent removal and surgical intervention.
Conclusion: SEMS placement in patients with rectal obstrcution including lower rectal obstruction is acceptable for decompression of obstructive symptoms. However, patients with rectal obstruction tended to have extrinsic colonic malignancy and place SEMS as a palliative intention which could influence clinical outcomes.
Disclosure of Interest: None declared

P1481 SELF-EXPANDABLE METALLIC STENT AS A BRIDGE CONTRAST EMERGENCY SURGERY FOR ACUTE MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: The efficacy and safety of self-expandable metallic stent (SEMS) for patients with acute malignant colorectal obstruction (AMCO) are still controversial.
Aims & Methods: We conducted this study to evaluate the safety and efficacy of SEMS for AMCOs. From January 2010 to July 2014, a total of 171 patients with AMCOs were retrospectively enrolled in this study: 120 patients received emergency stent placement followed by selective operation as stent group, and 51 patients received emergency operation as emergency-surgery group.
Results: The operation time and hospital stay were significantly shorter in stent group (114.51 ± 28.65 min vs 160.39 ± 58.94 min, $P < 0.001$; 8.00 ± 3.97 d vs 12.59 ± 9.07 d, $P < 0.001$). Stent placement also significantly reduce the intraoperative blood loss (61.00 ± 43.70 ml vs 121.18 ± 85.90 ml, $P < 0.001$). The incidence of postoperative complications in stent group was lower than emergency-surgery group (16.7% vs 37.3%, $P < 0.05$). In subgroup analyses, patients received laparoscopic surgery after stent placement had significantly shorter days to first flatus (3.37 ± 1.04d vs 4.47 ± 1.95d, P = 0.041) and postoperative hospital stay (7.10 ± 1.43d vs 8.47± 1.43d, P = 0.001) than open surgery. In stent group, 5-year overall survival (OS) values were significantly better than those in emergency group (47% vs 37%, P = 0.02).
Conclusion: Stent placement as a bridge followed by selective operation is a safe and feasible procedure, providing significant advantages of short-term outcomes and a favorable prognosis for patients with AMCOs. Laparoscopic surgery could be considered as an optimal treatment after stent placement.
Disclosure of Interest: None declared

P1482 LONG-TERM OUTCOME OF BALLOON DILATATION IN PATIENTS WITH GASTRIC OUTLET OBSTRUCTION RELATED TO PEPTIC ULCER DISEASE

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Introduction: Endoscopic balloon dilatation (EBD) is one of the methods among patients with benign gastric outlet obstruction (GOO). The prevalence and underlying etiologies of GOO in various populations are different.
Aims & Methods: This retrospective study evaluates the effectiveness, safety, long term outcomes of EBD and factors that would affect its success rate in patients with GOO related to peptic ulcer disease (PUD).
We reviewed the charts of 104 patients with GOO related to PUD. Only 62 patients required EBD after failure of medical treatment. The dilatation was performed using a hydrostatic balloon (through the scope) with a mean diameter of 15.9 mm (range 12-20 mm). Eradication of *Helicobacter pylori* (H. pylori) was associated to the endoscopy treatment. Endoscopic check-up examinations were carried out 4 to 6 weeks later, and in case of relapse. The mean follow-up period was 25.7 months (range 1-126).
Results: Eighty seven dilatations were performed in the 62 enrolled patients (51 men and 11 women). The mean age was 49.5 years (20-85 years). A reliable post-eradication *H. pylori* status was available in 40 and was negative in 29. Non steroidal anti-inflammatory drugs were stopped in all patients. Patients on aspirin for the prevention of atherosclerosis received concomitant antisecretory therapy (AST). Symptomatic relief was obtained immediately in 96%, at 6 weeks in 83.8%, at 12 months in 69%, at 24 months in 60% and at 30 months in 55%. The average number of dilatations was 1.4 per patient (1-4). Twenty patients had recurrent stenosis (22.9%) between 2 and 116 months after the first dilatation. Complications occurred in 3 cases (3.4%): perforation in 2 patients and bleeding in one case. Surgery was indicated in 16 patients. Factors predicting referral for surgery included smoking, need for multiple procedures, and dilatation of the stomach. Eradication of *H. pylori* was associated with successful relief of obstruction without surgery.
Conclusion: Balloon dilatation is an effective and safe treatment for GOO related to PUD, avoiding surgery in up to 70% of patients.
Disclosure of Interest: None declared

P1483 ONCOLOGICAL OUTCOMES OF COLONIC STENT AS "BRIDGE TO SURGERY" VS EMERGENCY SURGERY FOR OBSTRUCTIVE COLO-RECTAL CANCER: A COMPARATIVE STUDY

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Introduction: The short-term results of colonic stenting followed by elective surgery (bridge to surgery, BTS) for malignant large-bowel obstruction (MLBO) have been well described. However long-term oncological outcomes are still debated and international endoscopy societies have recently not recomended it as a first-line approach.

Aims & Methods: A comparative observational cohort study was performed based on clinical data review from patients treated in our center between 2006 and 2012 (6 years). We analysed overall survival (OS), disease-free survival (DFS) and recurrence as primary end-points. We also reviewed demographic data, disease staging and peri-operatory morbility and mortality (Clavien-Dindo Classification).

Results: A total of 126 patients were included: 79 (62.7%) were treated with a BTS strategy (group 1) and 47 (37.3%) underwent an emergent surgery (group 2). The distribution by sex, age (70.9 ± 11.4 years) and TNM stage was similiar. The median follow-up was 43.2 ± 3.6 months. There was no significant difference in peri-operatory complications ($p = 0.23$) and adjuvant chemotherapy ($p = 0.53$). The need for a definite stoma was higher in group 2 ($p < 0.001$). The recurrence did not differ significantly between the two groups, although it was superior in group 2 (34.5% vs. 42.5%, $p = 0.492$). DFS (22.2 vs 19.7 months; $p = 0.652$) and OS (43.2 vs. 31.9 months, $p = 0.096$) also did not differ signficantly between the two groups, being slightly longer in group 1.

Conclusion: Results of our study on oncological outcomes, as stated in most recent meta-analysis, as well as well-described short-term outcomes, suggest that BTS could be a promising alternative strategy for MLBO. Larger prospective studies and randomized clinical trials are definetely needed.

Disclosure of Interest: None declared

P1484 SELF-EXPANDABLE METAL STENTS FOR COLORECTAL CANCER – FROM GUIDELINES TO CLINICAL PRATICE

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Introduction: Colonic self-expandable metal stent (SEMS) placement is recommended and widely used for palliation of obstructive colorectal cancer (CRC). However, the role of SEMS in CRC as a bridge to elective surgery remains unclear.

Aims & Methods: The aim of this study is to evaluate the efficacy and safety of SEMS placement in obstructive CRC and discuss current recommendations in this procedure. Patients with CRC who underwent endoscopic stent placement between January 2012 and January 2015 were retrospectively analysed. Statistical analysis was performed with SPSSv22.

Results: We included 28 patients, 17 (61%) women, mean age 71 ± 11.9 years. Obstructive CRC demanding urgent stent placement occurred in 96% ($n = 27$) of patients. Stent placement as a bridge to elective surgery was performed in 82% ($n = 23$) and as a palliation treatment in 18% ($n = 5$). In 96% ($n = 27$) of procedures, technical and clinical success was achieved. No procedure-related death was recorded. Three (11%) complications were observed: 2 migrations and 1 perforation. When SEMS were placed as a bridge to surgery, average time between endoscopic procedure and surgery was 3 ± 9.7 days (excluding patients who underwent neoadjuvant chemotherapy). Five perforations were registered: 3 during surgery and 2 only after histological review. All patients underwent adjuvant chemotherapy. During the follow-up period (15.6 ± 9.3 months) no recurrence was recorded.

Conclusion: In this study, SEMS placement was an effective procedure in obstructive CRC. It was mainly used as a bridge to elective surgery. However, a significant (20%) rate of macro and microscopic perforation was observed, which might increase recurrence rate and decrease overall survival in potentially curable patients. In this study, stent placement followed current recommendations in 64% of patients.

Disclosure of Interest: None declared

P1485 PALLIATION OF INOPERABLE MALIGNANT COLORECTAL OBSTRUCTIONS BY STENTING IS EFFECTIVE FOR HOME CARE

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Introduction: Although self-expandable metal stents (SEMS) is useful to palliation of inoperable malignant colorectal obstructions[1)], long time prognosis is unclear. The present study examined the long time benefits of SEMS for palliation of inoperable malignant colorectal obstructions.

Aims & Methods: Between 2008 and 2013, a total of 57 patients underwent colorectal CEMS placement in Okayama Saiseikai General Hospital. We reviewed 20 patients who were treated in order to palliation of inoperable malignant colorectal obstructions. We examined prognosis of the 20 patients. The mean age of the patients (12 males, 8 females) was 69 (range 37 to 94). Their primary disease were gastric cancer ($n = 6$), pancreas cancer ($n = 2$), and colorectal cancer ($n = 12$). We used WallFlex stent or Niti-S stent.

Results: We experienced no severe complication by stenting. Three gastric cancer patients (15%) needed another stenting in stomach or jejunum. Two patients (10%) needed second colorectal CEMS placement, and two patients needed ileostomy due to stent obstruction. After first placement, they survived a median of 210 days (range 5 to 728 days). Sixteen patients (80%) could stay at home. They were able to stay at home for a median of 54 days (range 1 to 572 days). One patient (5%) could receive end-of life care at home. Others died in hospital. We treated 13 patients (65%) with chemotherapy. One gastric cancer patient treated with S-1-CDDP-PTX-DTX and CPT-11 could stay at home for over 500 days. The patients with chemotherapy stayed at home for a median of 33 days (range 0 to 572 days), without chemotherapy stayed at home for a median of 25 days (range 0 to 372 days) ($p = 0.38$).

Conclusion: Palliation of inoperable malignant colorectal obstructions by stenting is effective for home care. Some patients can stay long time at home with additional chemotherapy.

Reference

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Disclosure of Interest: None declared

P1486 CLINICAL LONG-TERM OUTCOME OF PATIENTS TREATED WITH ENDOSCOPIC RENDEZ-VOUS DILATATION OF COMPLETE OBLITERATIONS IN THE PROXIMAL OESOPHAGUS

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Introduction: Complete obliteration in the proximal oesophagus is a rare scenario, for instance after radiotherapy in patients with head and neck cancers. Antegrade dilatation is often unsuccessful but retrograde endoscopic rendez-vous dilatation can be a treatment option to restore oesophageal patency and to to resolve patients from PEG tubes.

Aims & Methods: We aimed to describe the technical feasibility and long-term clinical outcome of this technique, as the data in theliteratue is scarce.
This single-centre case series included all patients in a tertiary referral centre 7/2005 -2/2015 with complete obliteration in the proximal oesophagus, who were unable to swallow and were treated by retrograde endoscopic rendez-vous dilatation by endoscopists and ENT surgeons in general anaesthesia. Technical success was defined as achievement of a retrograde puncture and passage with the endoscope to apply a nasogastric tube. The long-term clinical success was defined as either independency from PEG-tube and/or ability of oral food intake. Follow-up was assessed by the validated Functional Oral Intake Scale (FIOS).

Results: Between 7/2005 and 2/2015 six patients (5 males; mean age 71 years [range 54-74]) underwent retrograde endoscopic rendez-vous dilatation(all nasal endoscopes). Apart from one patient with complete occlusion of sinus piriformis after Lyell syndrome, the remaining had undergone radiotherapy due to head &neck cancer (median interval fromradiotherapy to dilatation: 16 months, [range 14-90]). Technical success was achieved in 5 out of 6 patients (Table 1). During follow-up (mean 27 months, range 2-115) half of the patients stayed dependent on the PEG-tube, the other half achieved freedom from PEG-tube and were able to eat oral food. No major complications happened.

Table 1: Technical details and long-term clinical success of endoscopic rendez-vous dilatation in patients with complete obliteration of the proximal oesophagus or hypopharynx

Number and sex of patients (m:f)	6 (5:1)
Antegrade endoscopy, rigid, flexible	4, 2
Puncture with VisiGlide guidewire, Argon beamer	4, 1
Size of first dilatation (balloon and bougie)	median 10 mm (range 6 - 10 mm)
Success Technical success Need for recurrent dilatations or stent after discharge Long-term clinical success (f/u): median (range), months Need for long-term PEG tube Oral food intake without PEG	5/6 (83%)5/6 (83%) 27 months (2-115)3/63/6
Subsequent dilatations before dischargewith balloon, with bougie (range, in mm)	3, 2 patients (15-16.5 mm, 12-15 mm)
Complications: Death, Mediastinal emphysema	01/6

Conclusion: Endoscopic retrograde rendez-vous dilatation offers a safe and viable alternative to high-risk blind dilatation of the proximal oesophagus

and hypopharynx or surgical approaches in patients with complete proximal oesophageal obliteration. We found that technical success was fairly high. However in long-term follow-up only half of the patients remained independent from PEG-tube.
Disclosure of Interest: None declared

P1487 ENDOSCOPIC BALLOON DILATION OF STENOSIS AFTER LOW ANTERIOR RESECTION OF RECTUM IS EFFECTIVE

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Introduction: Symptomatic stenosis of colorectal anastomosis after low anterior resection of rectum (LAR) is observed in 4–10% of patients. Purpose of our study was to evaluate endoscopic dilation treatment of anastomotic stenosis with through the scope (TTS) endoscopic balloons.
Aims & Methods: Retrospective analysis of all patients with symptomatic anastomotic stenosis after LAR from 2011 to 2014 was performed. We analyzed time interval from LAR to symptomatic stenosis development, number of dilations, size of balloons and X-ray control during dilation. Dilations were performed in 4 week intervals. Successful treatment was defined as ability to pass standard colonoscope through the anastomosis 3 months after dilation and resolution of patients symptoms. All patients were evaluated for anastomotic recurrence of primary tumor with endoscopic biopsies and CT scan.
Results: Our group consists of 5 patients (4 males, 1 female). Mean age was 71 (range 64-80) years. In three patients LAR was performed for colorectal cancer, in one for GIST and in one for benign condition. Mean interval from operation to development of symptomatic stenosis was 10 (range 2-20) months. In one male patient colostomy had to be performed for ileus before dilation. We have performed 31 balloon dilations (2-18 in one patient) in total. For initial dilation 15mm balloons and combined endoscopic and X-ray control were used. Subsequent treatment was performed with 20mm ballon and endoscopic control only. We have achieved successful treatment in all of our patients. There was no recurrence of primary tumor in anastomosis. Complications: There were no perforation or bleeding complication in our group of patient. One patient had symptomatic hypotension after dilation that was treated with i.v. fluids. In one patient with stenosis resistant to treatment series of 10 dilations in one week interval was performed with good endoscopic and clinical effect.
Conclusion: Endoscopic dilation treatment of colorectal anastomotic stenosis after low anterior resection with TTS balloons is safe and effective. We have achieved treatment goals in all patients. Multiple dilations with increasing baloon diameter are often neccessary. We recommend X-ray control for initial dilation of tight stenosis.
Disclosure of Interest: None declared

P1488 LONG-TERM CLINICAL OUTCOMES OF PALLIATIVE DUAL ENDOSCOPIC STENTING IN PATIENTS WITH CONCURRENT BILIARY AND GASTRIC OUTLET OBSTRUCTION

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Introduction: Dual endoscopic stenting (DES) for palliation of concurrent biliary and gastric outlet obstruction (BGOO) caused by unresectable malignancy is not always possible. Endoscopic ultrasound (EUS) may help overcome limitations of ERCP in this difficult setting by allowing transmural biliary drainage where cannulation is hampered by duodenal strictures.
Aims & Methods: To define the need for EUS-guided biliary drainage (EUSBD) in the setting of BGOO and to assess long-term clinical outcomes of endoscopic palliation of BGOO. Consecutive patients with BGOO in whom DES was attempted at a tertiary Unit between 2010 and 2014 were prospectively identified. Baseline patient and stricture features, chronology of BGOO, endoscopic method of stent insertion, postprocedure adverse events and stent dysfunction rates were retrospectively assessed. Adverse events were defined and graded according to consensus. Follow-up data were obtained from clinical records and/or telephone contact. Length of follow-up was determined from DES until death or last recorded clinical evaluation. Chi-squared test was used for comparisons.
Results: DES was attempted in 61 patients (42 male, mean [range] age = 77 [30-92] years). Background malignancies were pancreas (55.7%), gastric (13.1%) and other (31.1%). Time sequence of BGOO was synchronous in 44.3%, first biliary then GOO in 41%, and first GOO in 14.1%. Location of strictures was duodenal bulb in 26 patients, second duodenum in 34, and third duodenum in 1. Biliary stents were successfully placed in 100% and duodenal stents in 98%. Method of biliary stent placement was ERCP in 60.7% and EUSBD in 39.3%. There were 4 immediate post-procedure adverse events, 2 mild (pancreatitis, bile leakage) and 2 severe (perforations resulting in death). Long-term follow-up data were available for 50 patients. Symptom recurrence leading to repeat hospital admission developed in 68.9% (cholangitis in 15, jaundice without cholangitis in 8, GOO in 9). Overall, 39 patientes experienced any stent dysfunction. Biliary stent dysfunction developed in 48.7%, duodenal in 41%, and combined in 10.3%. 67.4% were single-episode stent dysfunction and 32.6% relapsing episodes. All single-episode dysfunctions were managed endoscopically. 46/50 patients were dead at the end of follow-up, with a mean (SD) survival after DES of 21.5 (9.2) weeks. There were no significant differences in survival or stent dysfunction rate according to clinical presentation or transmural vs transpapillary biliary stent placement.
Conclusion: EUS-guided biliary drainage is required in 40% of patients undergoing endoscopic palliation of BGOO. Even if virtually all patients with BGOO can be palliated endoscopically avoiding percutaneous access by the combined use of ERCP and EUS, stent dysfunction leading to symptom recurrence is an issue in two thirds of patients, even if it can be solved by repeat endoscopy.
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P1489 STENT FIXATION USING ENDOSCOPIC SUTURES IS SAFE AND EFFECTIVE AT PREVENTING STENT MIGRATION IN BENIGN UPPER GASTROINTESTINAL CONDITIONS: A COMPARATIVE MULTICENTER STUDY

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Introduction: Fully covered self-expandable metal stents (FCSEMSs) have increasingly been used in benign conditions. Stent migration is the major limitation and occurs in 50% of cases. Endoscopic suture fixation (ES) of FCSEMS can potentially decrease migration risk and improve outcomes. The efficacy of this practice is currently unknown.
Aims & Methods: The aims of this study were to 1) evaluate the effect of ES on FCSEMS migration rate and clinical successand 2) compare outcomes of patients who received ES to those who did not receive stent fixation (NS group). This was a retrospective review of consecutive patients who underwent FCSEMS placement for benign UGI diseases (strictures, leaks, perforations or fistulae) at seven tertiary care centers. Patients were divided into either the NS group or the ES group. Outcome variables, including stent migration, clinical success (resolution of underlying pathology), and adverse events, were compared.
Results: A total of 125 (ES 44, NS 81) patients (males 53%, mean age 53 yr) underwent 224 stenting procedures. Stent placement was performed for benign strictures in 56 (45%) cases and leaks/fistulae/perforations in 69 (55%) cases. Stent migration was significantly more common in the NS group as compared with the ES group (33% vs. 16%, $p = 0.03$). In addition, time to stent migration was significantly longer in the ES group ($p = 0.02$). ES was significantly associated with a higher rate of clinical success (60% vs. 38%, $p = 0.03$). Rate of adverse events was similar between the two groups (19% vs 20%, $p = 0.84$). There were no adverse events directly related to the suturing procedure.
Conclusion: ES for stent fixation is safe and associated with decreased migration rate. It may also improve clinical response, likely due to reduction of stent migration.
Disclosure of Interest: S. Ngamruengphong: None declared, R. Sharaiha: None declared, A. Sethi Consultancy: Boston Scientific and Xlumena, A. Siddiqui: None declared, C. DiMaio: None declared, S. Gonzalez: None declared, J. Rogart: None declared, S. Jagroop: None declared, J. Widmer: None declared, J. Im: None declared, R. Hasan: None declared, S. Laique: None declared, T. Gonda: None declared, J. Poneros Consultancy: Boston Scientific, A. Desai: None declared, M. Kahaleh Financial support for research: Gore, MI Tech, and Pinnacle and Mauna Kea Technologies., Consultancy: Boston Scientific and Xlumena, A. Tyberg: None declared, V. Kumbhari: None declared, M. El Zein: None declared, A. Abdelgelil: None declared, S. Besharati: None declared, P. Okolo: None declared, M. Khashab Consultancy: Boston Scientific, Olympus America and Xlumena

P1490 THE EFFICACY OF AN ENDOSCOPIC SELF-EXPANDABLE METAL STENT FOR GASTRIC OUTLET OBSTRUCTION BY MALIGNANCIES

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Introduction: Gastric Outlet Obstruction (GOO) may be caused by malignant diseases of the stomach, pancreas and duodenum or by lymphonodal metastasis. GOO causes intractable nausea and vomiting, abdominal distention and deficient oral intake, resulting in progressive deterioration of the patient's quality of life (QOL). Advances in chemotherapeutic treatment have improved the prognoses of these types of cancer and the incidence of malignant GOO has increased both at the time of diagnosis and during the course of anticancer treatment.
The main goal of treatment in these patients is palliation of obstructive symptoms, thereby improving the QOL. Most patients at such a highly advanced stage of malignancy cannot tolerate surgical procedures. In Japan, the use of a self-expandable metal stent (SEMS) was approved for clinical application in April 2010, and before this, esophageal stent was used. Endoscopic placement of a SEMS into the narrowed portion of the duodenum has emerged as an alternative, minimally invasive procedure in cases of GOO and also has a high clinical success

rate. The purpose of this study was to review the clinical efficacy, safety and patency rate of placement of a SEMS and its overall clinical prognosis.
Aims & Methods: A total of 33 patients were retrospectively enrolled from April 2005 to March 2015. All patients had malignant GOO and also symptoms such as nausea, vomiting or reduced oral intake. Main outcome measurements were the type of stent, technical success, clinical response, early complications, patency and clinical course. We evaluated clinical response by using the four-point Gastric Outlet Obstruction Scoring System (GOOSS).
Results: The mean age of the patients was 66.8 years old. Of the 33 patients, 18 were male and 15 were female. The most frequent cause of GOO was pancreatic cancer, followed by gastric cancer. A SEMS was placed between the pylorus and the horizontal portion of the duodenum in most cases, and multiple SEMSs were used in 7 cases for initial therapy. 7 covered stents and 26 uncovered stents were used. There were no complications during procedures and the technical and clinical success rates were 100% and 94.0% respectively. The GOOSS was significantly improved from 0.48 to 2.55 by duodenal stenting. The major complication was stent occlusion which occurred in 5 cases (15.2%); stent dislocation which occurred in 4 cases (12.1%); and perforation which occurred in 2 cases (6.1%). Eight patients reached initiation of chemotherapy after stenting, and the mean period from stenting to chemotherapy was 13.4 days.
Conclusion: Stent dislocation occurred most commonly as a complication of covered SEMS, whereas tumor ingrowth became a problem in uncovered SEMS. However, duodenal stent placement contributed in a significant way to the management of malignant GOO. Not only did it result in improvement of quality of life in patients with limited life expectancy, but also lead to prolongation of overall survival by early resumption of chemotherapy, as evidenced in some cases.

Reference

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2. Japanese multicenter estimation of wallflex duodenal stent for unresectable malignant gastric outlet obstruction.

Disclosure of Interest: None declared

P1491 ENDOSCOPIC GASTROINTESTINAL BYPASS PERFORMED UNDER X-RAY CONTROL USING AIR AS A CONTRAST

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Introduction: Surgical complications like high-grade stenosis, fistulas and obstructions in the digestive tract often required open or laparoscopic surgical repair. Novel less invasive endoscopic techniques that allow the creation of fistulas in the gastrointestinal tract used to avoid surgery and were described as an alternative treatment for selected patients.
Aims & Methods: All endoscopic procedures were based in the same endoscopic technique: the use of air to distend an enteric segment followed by a fluoroscopy guided puncture using a FNA needle and wire advancement. Over the wire a balloon with 8 to 10 mm in diameter was inserted for dilation followed by stent placement. A gastrointestinal lumen-to-lumen communication was then created. Four patients with post surgical complications were treated with the same technique.
The first case is a high-grade ischemic stenosis of the colon after a partial colectomy for colon cancer treatment. A fully covered self expandable metal stent was deployed. A fistula of the distal colon to the ileum was created allowing the surgical closure of a protective ileostomy.
In second case, a patient with biliary-enteric anastomosis and Roux en Y anatomy performed for treatment of a cross-section of the common bile duct during an open cholecystectomy. She presented one year after the surgery with repeated acute cholangitis due to stenosis of the biliary-enteric anastomosis. Prior attempts to access the afferent limb with double ballon enteroscopy were unssuccessful. A fistula was created from the stomach to the jejunal loop, to access the biliary-enteric anastomosis at the afferent limb with a duodenoscope to treat the stenosis with the placement of plastic stents.
The third case is a stenosis in the esophagojejunal anastomosis after multiple procedures to treat dehiscences of a total gastrectomy procedure for treatment of a gastric adenocarcinoma. A fistula was created from the esophagus to jejunal loop to allow oral feeding.
The last case had a wide gastrocutaneous fistula in the gastric stump after gastric bypass for obesity treatment, that failed prior endoscopic treatment attempts. A neofistula was created from gastric stump to the jejunal loop to decrease the pressure in the gastric stump. After that, the gastrocutaneous fistula closed.
Results: All the procedures were successful. Follow-up of at least 3 years demonstrated a successfully bypass in all patients.
Conclusion: Creation of a lumen-to-lumen bypass by endoscopic means is feasible and safe in selected patients for treatment of post surgical complications.
Disclosure of Interest: None declared

P1492 EFFICACY AND SAFETY OF NON-EXPOSED ENDOSCOPIC WALL-INVERSION SURGERY (NEWS) AS AN ADVANCED METHOD OF FULL-THICKNESS RESECTION TECHNIQUE FOR GASTRIC TUMOR

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Introduction: Endoscopic submucosal dissection (ESD) has been widely accepted as an effective treatment for gastrointestinal tumors. However, ESD for early gastric cancer (EGC) with ulcer scarring is still technically difficult. Non-exposed endoscopic wall-inversion surgery (NEWS) is an advanced method of endoscopic full-thickness resection (EFTR) without transluminal communication, applying ESD technique.
Aims & Methods: The aim of this study is to evaluate the clinical efficacy and safety of NEWS for gastric tumors. Between July 2011 and April 2015, 19 patients (7 females, 12 males; mean age 66.4 years, range 49-79 years) underwent NEWS for gastric tumors. After marking around a tumor on both the mucosal and serosal surfaces and submucosal injection of sodium hyaluronate, circumferential seromyotomy and sero-muscular suturing were made laparoscopically, followed by circumferential muco-submucosal incision endoscopically. The resected specimen was perorally retrieved. Clinical data was analyzed to identify factors that impact the NEWS procedure.
Results: The mean tumor size and resected specimen were 23.3 mm (range, 7-45 mm) and 33.6 mm (range, 20-50 mm), respectively. All lesions were successfully resected in an en-bloc fashion. The mean operation time was 213.5 minutes (range, 140-397 minutes), and the median estimated blood loss was 0 g (range, 0-250 g). Patients started oral intake on mean postoperative day 2 (range, 2-3), and the mean length of postoperative hospital stay was 8 days (range, 6-13 days). There were no severe postoperative complications (hemorrhage, anastomosis insufficiency, or infection). Histopathological examination of the tumors showed 17 GISTs, 1 schwannoma and 1 early gastric cancer. No tumor residual or recurrences was confirmed by performing gastroscopy during follow-up (range, 0-34 months). Resected size ($P = 0.0599$) and blood loss ($P = 0.0474$) were associated with the duration of procedure time.
Conclusion: NEWS is an effective and safe full-thickness resection with minimum possible margin without contamination and tumor dissemination into the peritoneal cavity. Although the procedure is somewhat complex because of the subtlety of the technique, NEWS could be utilized as a novel treatment option especially for node-negative EGC difficult to resect by ESD, or EGC with possible lymph node metastasis with a combination of sentinel node navigation surgery.
Disclosure of Interest: None declared

P1493 EFFECT OF CERVICAL ANASTOMOSIS ON QUALITY OF LIFE OF LONG-TERM SURVIVOR AFTER ESOPHAGECTOMY FOR CANCER

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Introduction: Esophageal cancer still remain nowadays burdened by poor outcome despite recent advances in neoadjuvant therapies and surgery still plays a key role in the treatment. Therefore very few information are known about health-related quality of life (HRQL) in long-term survivor after surgery and more in detail if the anastomosis site can affect it.
Aims & Methods: This multicentric study is aimed to analyze how performing a cervical anastomosis could impact on HRQL of long-term disease-free survivor (>36 months). 54 patients who underwent esophagectomy for esophageal cancer from 2007 to 2011 in two different tertiary referral hospitals have been enrolled during the outpatient clinic follow up from October 2014 and March 2015. 29 patients from the Academic Medical Center of the Amsterdam University (Netherlands) and 25 patients from the Veneto Institute of Oncology in Padova (Italy) filled the validated Dutch and Italian version respectively of the European Organization for Research and Treatment of Cancer (EORTC) questionnaires QLQ-C30 and OG25. Global quality of life and symptoms perceived were the primary endpoints. Data about patients characteristics, cancer and anastomosis site and stage were retrieved. Non parametric statistics was performed.
Results: 54 patients underwent esophagectomy for esophageal cancer, 24 patients (44.4%) underwent cervical esophagogastric anastomosis following esophagectomy and 30 (65.6%) thoracic anastomosis.
Cervical anastomosis showed to be associated with worse dry mouth perception ($p = 0.033$), trouble with taste ($p = 0.032$), swallowing ($p = 0.029$) and coughing ($p = 0.018$). Moreover, the presence of cervical anastomosis was correlated with troubles with nausea and vomiting ($Tau = 0.375$, $p = 0.0003$) and decreased role function scale (RF2) of the QLQ-C30 ($Tau = -0.260$, $p =$ -level 0.011) while the Global Quality of Life scale (QL2) showed no significant differences.
Conclusion: Cervical anastomosis is associated with a higher perception of troubles in coughing, swallowing, taste and dry mouth perception that could be well explained with the gastric tube transposition near to the oropharynx. Despite these findings, no differences were observed in the QL2 scale pointing

out how surviving a cancer and its treatment is the most important predictor of HRQL even on long term survivors and can be well described by the "hedonic adaptation" paradox.
Disclosure of Interest: None declared

P1494 THE PROGNOSTIC VALUE OF A MODIFIED TUMOUR REGRESSION GRADE AFTER NEOADJUVANT CHEMORADIOTHERAPY AND RESECTION OF OESOPHAGEAL CARCINOMA

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Introduction: The tumour regression grade (TRG) is used to define the response to preoperative chemoradiotherapy for oesophageal carcinoma. The objective of this study was to determine whether inclusion of the postoperative pathological nodal status could improve the prognostic value of TRG.
Aims & Methods: All patients who underwent an oesophagectomy after chemoradiotherapy between 2003 and 2013 were included in this retrospective study. Patients were classified according to a modified TRG consisting of the TRG by Mandard et al (TRG 1 = complete response in the oesophagus; TRG > 1 = incomplete/no response) and the postoperative lymph node category (N0 = no lymph node metastases; N+ = at least 1 lymph node metastasis). Based on the TRG by Mandard and this modified TRG Kaplan-Meier survival analyses were performed and compared.
Results: 411 patients underwent neoadjuvant chemoradiotherapy followed by oesophagectomy. After exclusion due to non-specific histology (n = 2), unknown TRG (n = 3), intraoperative detection of distant metastases (n = 3), salvage procedures (n = 17) and in-hospital mortality (n = 15) 371 patients were analysed (289 adenocarcinoma, 82 squamous cell carcinoma). A significantly improved median disease free survival was observed in patients with TRG 1 compared to patients with TRG > 1 (90.3 vs. 30.8 months, P = 0.004). After implementation of the modified TRG significant differences in median disease-free survival were found between the four categories: TRG 1-N0 (n = 76) 90.3 months; TRG 1-N+ (n = 10) 20.8 months; TRG > 1-N0 (n = 146) 81.3 months; TRG > 1-N+ (n = 139) 18.1 months (P < 0.001).
Conclusion: The TRG, determined in the primary tumour, provides insufficient information about the prognosis after chemoradiotherapy followed by resection of oesophageal cancer. It is advisable to use a modified classification in which the postoperative pathological nodal status is considered.
Disclosure of Interest: None declared

P1495 POSSIBILITIES FOR PYLORODUODENAL STENOSIS DIAGNOSTICS AFTER SEALING OF PERFORATED DUODENAL ULCER

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Introduction: Disorders of gastric and duodenal motility are present in 10.0-56.3% of patients with ulcer and in up to 65% cases after its surgical treatment, which makes the issue of timely diagnostics and prevention of post-operational motility disorders very actual.
Aims & Methods: Aims. Improvement of early diagnostics of motor-evacuator disorders after organ-preserving operations on perforated duodenal ulcer (PDU).
Methods: Study subject - 227 patients with PDU operated in the period from 2008 till 2013. First group consisted of 189 (83.2%) patients after PDU sealing and second group consisted of 38 patients (16.7%), who underwent duodenoplasty. Control group consisted of 54 healthy volunteers.
Study method involved peripheral electrogastroenterography (PEGEG) using apparatus Gastroscan-GEM in accordance with the standard method. Statistical processing involved discriminatory analysis (DA) of PEGEG parameters with creation of mathematical models on its base. For automated screening diagnostics of electrophysiological signs of PDS and determination of the degree of its compensation on the basis of the created PDS mathematical model we used original computer software "System for Decision Making Support in Determination of the Degree of Pyloroduodenal Stenosis Compensation".
Results: In the 1st group in 63.4% of cases the patients after sealing the PDU were classified into the group of subcompensated PDS, which was caused by the presence of stenosis in the PU sealing area with the disrupted peristalsis activity and initial signs of decompensated gastric motorics.
Post-operational radiological and endoscopic studies have confirmed the presence of the changes typical for the subcompensated stenosis in form of the narrowing of duodenum and enlargement of the stomach (27%), presence of moderate amount of liquid in fasting state (34%) and deformity of duodenal bulb (69.2%).
Signs of severe gastric stasis in this group of the patients manifested in 15.4% of patients and signs of moderately severe gastric stasis manifested in 23.1% of patients.
The performance of intraduodenal revision significantly increased the number of detected combined ulcerative complications and lesions. For example, in 2nd group of the patients pyloroduodenal stenosis was detected during the surgery in 26.3% of cases, "mirror" and circular ulcers of duodenum were detected in 18.4% of cases.
After duodenoplasty with correction of stenosis detected during the operation in 26.3% of cases we noted completely opposite distribution of patients with compensated type of motorics of stomach and other gastrointestinal sections with physiological response to stimulation and timely or residual accelerated evacuation of food stimulant from the stomach into the duodenum. This group of patients did not have any clinical manifestations of stenosis and needed no repeated surgical interventions due to stenosis.
Conclusion: Conclusion. The software "System for Decision Making Support in Determination of the Degree of Pyloroduodenal Stenosis Compensation" created on the basis of DA of PEGEG parameters and their mathematical models allows us to perform the automated computer screening diagnostics of PDS and to determine the degree of its compensation.
Disclosure of Interest: None declared

P1496 THE SAFETY PROFILE OF DEEP SEDATION WITH THE COMBINATION OF PROPOFOL AND DEXMEDETOMIDINE HYDROCHLORIDE DURING ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: ESD is accepted as a standard treatment for early-stage gastrointestinal neoplasias, however, the most effective and safest sedatives and sedation protocol for ESD have not yet been clearly established. In our hospital, the sedation with the combination of propofol (PF) and dexmedetomidine hydrochloride (DEX) under the charge of anesthesiologists have been introduced as new sedation for gastric and esophageal ESD since August 2013.
Aims & Methods: The aim of this study was to clarify the safety profile of the sedation with the combination of PF and DEX during ESD, and to evaluate the acceptability of the sedation on the elderly patients.
Design: Retrospective cross-sectional study.
Setting: Single tertiary referral center.
Subjects: The present study included consecutive 120 patients undergone ESD for early gastric carcinomas or superficial esophageal carcinomas under the sedation with the combination of PF and DEX at the Yokohama City University Hospital between August 2013 and March 2015. Patients in ASA physical status more than II or patients with a tracheotomy were excluded in this study. The subjects were divided into 2 groups, namely, younger than 80 years patients (younger group) and 80 years or older patients (elderly group).
Interventions: We reviewed medical records of subjects, and compared retrospectively the parameters of the safety of the sedation in the elderly group to those in the younger group.
Outcome Measurements: The clinical patient characteristics (including age, gender, body mass index, underlying disease and ASA physical status), endoscopic findings for gastrointestinal neoplasias (including the lesion localized site and macroscopic type) and histopathological findings after ESD (including invasion depth of the lesion and the resected specimen size) were reviewed. Minimum value of blood oxygen saturation (SpO_2), minimum value of systolic blood pressure (sBP), and minimum value of pulse rate (PR) during ESD were investigated as the safety parameters of the sedation. Furthermore, the safety of the sedation during ESD was also evaluated on the basis of the presence or absence of hypoxemia ($SpO_2 \leq 94\%$), hypotension (sBP ≤80 mmHg), bradycardia (PR ≤50 bpm) and serious adverse events defined as cardiopulmonary instability forcing discontinuation of ESD.
Results: During ESD, minimum value of SpO_2 was 97 (median, range 79-100) %, minimum value of sBP was 86.5 (median, range 47-150) mmHg and minimum value of PR was 50 (median, range 32-82) bpm in all cases. The incidence of hypoxemia, hypotension and bradycardia were 14.5%, 35.5% and 60.9%, respectively. There was no incidence of severe adverse events necessitating discontinuance of the procedure. Regarding the comparison between the elderly group and the younger group, there was no statistically significant difference in the safety parameters of the sedation between the two groups.
Conclusion: When using the sedation with a combination of PF and DEX during ESD, it is necessary to pay attention to the occurrence of hypotension and bradycardia. However, those were successfully treated with drugs such as ephedrine or atropine, and no serious adverse event necessitating discontinuation of the procedure was encountered.
Disclosure of Interest: None declared

P1497 OUTCOME OF OVER 220 INSERTIONS OF "PUSH" PERCUTANEOUS ENDOSCOPIC GASTROSTOMY

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Introduction: As the Department of General and Visceral Surgery of the Sisters of Charity Hospital Linz, Austria, is focused on oncology there is a need of supportive care. Especially patients with head and neck cancer, or cancer of the esophagus benefit from permanent or temporary push-PEG. Also patients with chronic ileus due to peritoneal carcinosis benefit from this technique. Our department already studied the difference of pull-through- and push-PEG (1). Aim of this study was to compare the outcome of patients before and after standardization of the push-PEG-intervention.
Aims & Methods: Between 2009 and 2012 a first series of retrospective analysis of all patients (n = 100) who underwent percutaneous endoscopic gastrostomy was performed at our department. A second series of retrospective analysis (n = 123) was done between 2013-2/2015 after standardization of the procedure of push-PEG insertion. Data collection included patients' demographics, comorbidities,

complications graded according to the Clavien Dindo classification, indication, peri-interventional radio- and/or chemotherapy, tube diameter, morbidity and mortality. Further the complications of both series were compared. No antibiotic prophylaxis was used.
Results: All in all there were 223 push-PEGs inserted in our department between 2009-2012 and 2013-2/2015. In 96.4% (215/223) the patients suffered from malignant disease. We studied 45 (20.2%) female and 178 (79.8%) male patients, average age was 62.5 years. Nearly two third (138/223, 61.9%) of our patients received radio- or/and chemotherapy within 4 weeks after the push-PEG insertion. Altogether we noticed complications in 82/223 (36.8%) and classified them according to Clavien Dindo. We documented 26.9% (60/223) Clavien Dindo 1 events, where no further treatment was required. 5.8% of patients (13/223) suffered from Clavien Dindo 3a and higher. Surgical site infections which had to be treated pharmacologically occurred in 0.4% (1/223). In 11/223 cases (4.9%) a reoperation was needed. There were no statistically significant differences regarding the overall complications after standardization (39% vs 33.1%) inclusively dislocation but occlusions occurred significantly more often in series 1 (9% vs 1.6%) and surgical site irritations had a higher incidence in series 2 (9% vs 18.7%). Dilatation of gastrotomy (5/123) in series 2 was related with more complications than the cutting trocar technique (80% vs 33.1%).
Conclusion: After standardization of push-PEG insertion and comparing the two series we will use antibiotic prophylaxis in our next series of push PEG insertions due to the higher surgical site irritation rate, although we noticed only a small number of surgical site infections which had to be treated medically. Complications such as dislocation, leakage and occlusion, is often seen in non compliant patients and so sufficient education of patients is required. Push-PEGs of charriere 18 to 24 and dilation technique are connected with higher leakage, surgical site infection and patient discomfort.

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Disclosure of Interest: None declared

P1498 NOVEL EFFECTS OF SURGICAL FIELD EXPOSURE AND LYMPH NODE DISSECTION ON RECURRENT NERVE PALSY IN PRONE POSITION THORACOSCOPIC ESOPHAGECTOMY

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Introduction: Since July 2011, we experienced more than 200 cases of thoracoscopic esophagectomy in the prone position (TEPP). The indication for TEPP was initially limited to cases of early-stage esophageal cancer; however, it has now expanded to cases of advanced stage esophageal cancer. While expanding the indication for TEPP, the prolonged operative time and high incidence of recurrent laryngeal nerve (RLN) palsy are important factors. The incidence of RLN palsy was $<10\%$ in cases of open esophagectomy at our institution, but approximately 20% in cases of thoracoscopic surgery after the expansion of the indication. In most cases, RLN palsy occurs on the left side. RLN palsy after surgery for cases of esophageal cancer can cause dysphagia and difficulty in expectoration, followed by pneumonia as the most serious postoperative complication. Furthermore, RLN palsy may affect the quality of life, causing complications such as difficulty in ingestion.
Aims & Methods: In the present study, we focused on and evaluated the standardization of the exposure of the surgical field and lymph node dissection for shortening the operative time and avoiding left RLN palsy. The control of bleeding and upward/downward traction on the esophagus with rolling of the trachea is important for lymph node dissection around the left RLN. After the tracheal branches of the left tracheoesophageal artery were carefully coagulated and cut, the lymphatic chain around the left RLN was detached from the trachea. Moreover, the esophagus was transected at the aortic arch level in a relatively early stage. After the oral end of the esophagus was isolated upward as high as possible and pushed behind the right subclavian artery, the anal end of the esophagus was pulled downward with forceps by the surgical assistant with rotation of the trachea to the right side (T-shape exclusion). This exposure created by the assistant facilitated lymph node dissection around the left RLN with a stable and wide surgical field in the left upper mediastinum and adequate nerve tension. In this procedure, we avoided the use of energy devices as much as possible and strived to perform a sharp dissection using surgical scissors.
Results: After the expansion of the indication for TEPP, the operative time and incidence of left RLN palsy increased. However, the standardized lymph node dissection around the left RLN shortened the thoracic operative time (from 280.9 min to 255.0 min, $p < 0.001$) and decreased the incidence of left RLN palsy (from 20.0% to 13.0%).
Conclusion: These clinical outcomes are because of an improved technical stability, owing to the achieved standardized operative field, regardless of the patient's body type.
Disclosure of Interest: None declared

P1500 THE REALITIES OF VIRTUAL COLONOSCOPY IN RECOGNITION OF CONSTIPATION SYNDROME

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Introduction: During many years, a barium enema was the principal diagnostic tool in establishing structure and location of colon abnormalities within the abdominal cavity in patients with chronic constipation. Virtual colonoscopy (VC) is worthy of a consideration among the modern diagnostic methods. In the past decade, this method initially introduced by D.J. Vining et al. (1994) for a non-invasive diagnostics of colon and rectum diseases became very popular among clinicians and radiologists as a result of rapid advances in information processing technologies and image analysis. VC produces three-dimensional digital images of the colon. The method is based on a plain VC scan of the abdomen without contrast after inflating colon with air.
Aims & Methods: To evaluate an application of VC in diagnostics of colon related forms of chronic costiveness.
To analyse colonic architectonics, twelve patients with decompensated forms of chronic constipation were evaluated with VC scans using Phillips Brilliance 64 Slice VC (collimation -1,5 mm; 50 mAs, 120 kV, total duration of procedure - 5 minutes, equivalent dose - 14mSv). Barium enema was used as control. After retrograde inflation of colon by 1500-2000 ml of air, plain abdominal VC scans were performed in patients in supine position. Colons were inspected for position and structural abnormalities followed by post-processing information handling and 3D rendering using VC software of Extended Brilliance Workspace (Phillips).
Specifics of position and structure of colon, length and width of different colon parts, presence or absence of haustration were studied.
Results: Using VC technology, we were able to diagnose the cases of dolichocolon, dolichosigma and Payr's syndrome. In one clinical observation, VC allowed us to establish a dilatation of the right side of the colon with a reduction of haustraion in it. However in this case, Payr's syndrome was diagnosed only by a barium enema under an erect position of the patient.
Conclusion: VC objectively reflects structural features of the colon, anatomical-topographical relations of its different parts and inflammatory changes in its wall.
Disclosure of Interest: None declared

P1501 INITIAL EXPERIENCE WITH AN INNOVATIVE NEW MODULAR TRAINING MODEL FOR PROCTOLOGY SUITABLE ALSO FOR FLEXIBLE ENDOSCOPY

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Introduction: Proctological examination is a challenging procedure which requires profound knowledge of anatomy and pathology as well as optimal diagnostic and therapeutic experience in handling of the equipment as well as a good manual dexterity. The usual learning on the patient by ''trial and error'' is not optimal from an ethical point of view, but yet there is a lack of standardized reality-like human training options.
Aims & Methods: A novel hands-on model has been developed for the learning and training of proctology which is designed for a modern didactic concept. Constructed from synthetic materials and animal-free artificial tissues and based on patient data, the phantom matches human anatomy exactly and offers realistic haptics.
Results: Our newly developed simulator enables now a complete interactive proctology examination including colorectal endoscopy. It is based on the animal-free Tuebingen training phantoms for flexible endoscopy with new modular insets but considers the special requirements for procotogical examination. These insets have to be optimized for a reality-like phantom, especially the optical and tactile aspects (elastic pelvic floor, functional and variable sphincter, uterus/prostate etc.).
The trainees of our workshops have the opportunity to perform a complete proctological examination (from digital rectal examination to colonoscopy) in a reality-like clinical setting. The colon of the phantoms consists of several segments, so that in colonoscopy also variations of standard anatomy can be shown. For visual inspection the mucosal vessels in the rectum are shown anatomically correct. For a differentiated training the phantom can be adjusted individually and various pathologies are palpable, visible and comparable.
A specially developed sphincter simulates the different intensities of tonuses from insufficiencies up to stenoses of the anal canal continuously and accurately reproducible. The phantom can be switched easily between male and female phenotype. A replacement of this module allows the presentation of various pathologies within a few minutes (e.g. hemorrhoids, polyps, adenomas, prostate tumors, uterine fibroids). On the basis of pressure sensors, the participant receives an objective acoustic feedback on the tactile methodology of his digital rectal examination.
Conclusion: This innovative model represents an important step towards a reality-like phantom for diagnosis and intervention. It will enable the simulation of a complete proctologic examination, and will enable an effective medical education and training in this previously neglected area.
Disclosure of Interest: None declared

P1502 A SYSTEMATIC REVIEW OF SEGMENTAL VS SUBTOTAL COLECTOMY AND SUBTOTAL COLECTOMY VS TOTAL PROCTOCOLECTOMY FOR COLONIC CROHN'S DISEASE

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Introduction: Surgical management of colonic Crohn's disease (CD) is still unclear since different procedures can be adopted. The choice of operation is clearly dependent on the extent of colonic disease but the advantage and the disadvantages of increasing the removed colonic portion are still debated since no prospective randomised study has been undertaken yet [1].
Aims & Methods: The aim of the present study is to evaluate the differences in short-term and long-term outcomes of adult patients with colonic CD who underwent either subtotal colectomy and ileorectal anastomosis (STC) or segmental colectomy (SC) or total proctocolectomy and end ileostomy (TPC). Comparative studies published between 1984 and 2012, of STC vs SC and of STC vs TPC were selected. The study end points were overall and surgical recurrence, postoperative morbidity and incidence of permanent stoma. Fixed effect models were used to evaluate the study outcomes.
Results: Eleven studies, consisting of a total of 1412 patients (496 STC, 455 SC and 374 TPC) were included. Analysis of the data suggested that there was no significant difference between STC and SC in term of overall and surgical recurrence of CD. On the contrary, STC showed a higher risk of overall and surgical recurrence of CD than TPC (OR = 3.54 [95%CI: 2.45-5.1], $p < 0.001$; OR = 3.52 [95%CI: 2.27-5.44], $p < 0.001$, respectively). Moreover, SC had a higher risk of postoperative complicationns compared to STC that also had a lower risk of complication than TPC (OR = 2.84 [95%CI: 1.16-6.96, $p < 0.001$; OR = 0.19 [95%CI: 0.09-0.38], $p < 0.001$, respectively). SC resulted to have a lower risk of permanent stoma than STC (OR = 0.46, 95% CI 0.30-0.70).
Conclusion: All the three procedures were equally effective as treatment options for colonic Crohn's disease and the choice of operation remains intrinsecally dependent on the extent of colonic disease. However, patients in the TPC group showed a lower recurrence risk than those in the STC group. Moreover Sc had a higher risk of postoperative complication but a lower risk of permanent stoma. These data should be taken in account when deciding surgical strategies and when informing patients about postoperative risks.

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P1503 PATIENT PERCEPTIONS OF PHYSICIAN PERFORMING THE DIGITAL RECTAL EXAMINATION

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Introduction: The sex of the physician performing the digital rectal examination (DRE) procedure is one of the parameters influencing patients' comfort and satisfaction. It is postulated that the stress related to DRE during admission to the surgical ward may affect the compliance.
Aims & Methods: The aim of our study was to characterize patients' preferences according to their sex, age, socioeconomic status, and religious beliefs and according to DRE-related variables. All patients admitted to the Department of General and Colorectal Surgery at Medical University of Lodz between January 2015 and April 2015 were asked to complete a questionnaire regarding their sex, age, ethnic background, socioeconomic status, religious practice, and preference for a physician performing the DRE during admission to the surgical ward. The questionnaire was comprised of 2 open and 15 closed questions. Only fully completed questionnaires were included for fruther analysis.
Results: The study involved 300 patients, who agreed to complete the questionnaires - 52% (n = 156) women and 48% (n = 144) men. The most common reason of admission to the hospital was colorectal cancer, reported in 39% (n = 117) patients. Most patients (81%, n = 244) expressed no preference for sex of the physician performing the DRE during admission, while 12% (n = 36) preferred a same-sex physician. Stepwise logistic regression analysis showed that the age (OR 0.96; 95% CI 0.92-0.99), female sex (OR 0.27; 95% CI 0.09-0.81), higher education (OR 14.02; 95% CI 5.01-39.19), comorbidities (OR 16.48; 95% CI 3.75-72.34), and previous DRE experience (OR 18.94; 95% CI 3.52-101.90) were all associated with preference fore a same-sex physician. 41% (n = 124) of patients prefer to be examined by a mature doctor (30-60 year old), 3% (n = 8) by a young doctor (resident), 1% (n = 4) by an elderly physician (over 60 year old), while 55% (n = 164) of patients had no preference for that age of a physician. Physician's sexual preference as important variable was reported by 27% (n = 80) of patients. Different skin color of physician as a problematic factor was noted in 12% (n = 36) of patients.
Conclusion: In our study most patients expressed no preference for sex of the physician performing the DRE during admission to the surgical ward. However, over one-tenth of patients reported such preferences. Most of these patients preferred a same-sex physician. Female sex, lower level of education, no comorbidities, young age of patient, and no previous DRE are all associated with a physcian sex preference. It is important to offer these patients the choice of physcian performing the DRE. Addressing patients' preferences may improve the atmosphere in the clinical environment, reduce stress, and facilitate better treatment.
Disclosure of Interest: None declared

P1504 LAPAROSCOPIC OR OPEN TOTAL MESORECTAL EXCISION FOR RECTAL CANCER: 10-YEAR ONCOLOGIC OUTCOMES OF A PROSPECTIVE COMPARATIVE STUDY

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Introduction: Only few data from studies comparing laparoscopic total mesorectal excision (LTME) and open total mesorectal excision (OTME) for rectal cancer with follow-up longer than 5 years are available.
Aims & Methods: The aim of this study was to compare 10-year oncologic outcomes after LTME and OTME for non-metastatic rectal cancer. This is a single-institution prospective non-randomized study comparing LTME and OTME for rectal cancer. Statistical analyses were performed on an ''intention-to-treat'' basis and by actual treatment. Overall survival (OS) and disease-free survival (DFS) were compared by using the Kaplan-Meier method. A multivariate analysis was performed to identify predictors of poor survival.
Results: Similar 10-year OS and DFS after LTME and OTME were observed: 72.1% vs. 69.1% (P = 0.491) and 64.7% vs. 68.1% (P = 0.784), respectively. Conversion to OTME did not adversely affect OS and DFS. Stage-by-stage comparison showed no significant differences between LTME and OTME. No significant differences were observed in local recurrence rates between the two groups (6.1% vs. 14.1%, P = 0.155). Median time until local recurrence was 21.5 (range, 12-56) months after LTME and 20 (6-64) months after OTME (P = 0.499). Poor tumor differentiation, lymphovascular invasion and a lymph node ratio of 0.25 or more were the independent predictors of poorer OS and DFS. A distal margin ≤1 cm and lymphovascular invasion were associated with higher risk of local recurrence in patients undergoing anterior resection.
Conclusion: LTME has similar 10-year long-term oncologic outcomes to OTME in non-metastatic rectal cancer patients.

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Disclosure of Interest: None declared

P1505 NEW TECHNIQUE OF BALLOON-OVERTUBE- AND FLUOROSCOPY-ASSISTED DIRECT PERCUTANEOUS ENDOSCOPIC JEJUNOSTOMY FOR PATIENTS WITH SURGICALLY ALTERED UPPER GI TRACT ANATOMY

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Introduction: Experience using direct percutaneous endoscopic jejunostomy (DPEJ) in patients with surgically altered upper gastrointestinal (GI) tract anatomy is limited to case reports and small series. By using the pull-through method of jejunostomy placement, perforation of the small bowel at the various anastomoses or strictures may occur. The present study describes a new method of DPEJ in patients with surgically-altered upper GI tract.
Aims & Methods: The aim was to report on the efficacy and safety of a novel overtube- and fluoroscopy-assisted DPEJ technique in patients with surgically deranged upper GI tract anatomy.
This was an observational, retrospective, single-arm study conducted at a tertiary care hospital during a 24-month period. Technique: Deep enteroscopy was performed by using the standard push-pull-technique with the patient under general anesthesia and in supine position. Careful attention was paid to clearly define the efferent jejunal limb. The new DPEJ technique focuses on three key components: (i) use of balloon-assisted overtube; (ii) use of fluoroscopy; (iii) leaving the overtube in place during the entire procedure (and also for subsequent DPEJ removal). After a suitable site was identified, DPEJ placement was performed using the Ponsky-method (pull-type-percutaneous gastrostomy tube technique) using a 20 Fr PEG-kit. The overtube was left in place during the entire

procedure, in order to safely allow for the passage of the PEG through the anastomoses, kinks and potential stenosis of the altered anatomy. Leaving the overtube in place also allowed for post-insertion inspection of the PEG-button.
Results: The study included 24 patients with complex post-surgical anatomy (13 female, 11 male, mean age 53 years, age range 28-78). In 14 patients previous endoscopic or radiologic attempts at providing enteral feedings had failed. The patient's upper GI anatomy was the following: gastric bypass (n = 4), Whipple's (n = 5), Billroth II (n = 7), Ivor-Lewis (n = 3), gastric sleeve with leak (n = 3), several anastomosis with undefined, complex post-surgical status (n = 2). The technical success was 90%. In two patients transillumination was not obtainable and placement failed. The mean distance of DPEJ was 75 cm (range 45 to 120 cm) past the gastrojejunal anastomosis. The mean procedure time was 36 minutes (range 20-115). There were no major adverse events associated with the procedure.
Conclusion: DBE-DPEJ using fluoroscopic assistance seems an efficacious, safe and successful approach for patients requiring jejunal enteral feeding. To the best of our knowledge this is the largest study using DPEJ in patients with complex surgically altered upper GI tract anatomy. The novel technique using overtube- and fluoroscopy was efficacious, safe and successful. Future comparative studies are now warranted.
Disclosure of Interest: None declared

P1506 ASSESSMENT OF MMP-2/-9 EXPRESSION BY FLUORESCENCE ENDOSCOPY FOR EVALUATION OF WOUND HEALING IN A MURINE MODEL OF INTESTINAL ANASTOMOSIS

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Introduction: Disturbance of intestinal mucosal wound-closure leads to insufficient anastomotic healing and is associated with considerable morbidity following colorectal resections. Matrix-metalloproteinases play a crucial role in regulation of mucosal wound closure. Especially in the early phase, they can be used as markers for evaluation of the healing process.
Aims & Methods: Evaluation of fluorescence endoscopy for detection of MMP-2/-9 during intestinal anastomotic healing. Correlation of the MMP-2/-9 expression with an endosopic healing score for prediction of anastomotic healing.
A total of 24 Balb/c mice have been used as a model of intestinal anastomotic healing. Following incision of the upper rectum an end-end anastomosis has been performed and endoscopically analyzed on postoperative days 1, 3, and 5 (POD1, POD3, POD5). Mucosal healing was assessed by conventional white-light endoscopy (WLE). For detection of MMP-2/-9 in the anastomotic tissue fluorescence endoscopy was used (FE) following *i.v.*-administration of a Cy5.5-labeled MMP-2/-9 specific tracer 24h prior to endoscopy. Endoscopic analysis was complemented by *ex vivo* quantification of the fluorescent signal using the *MS-FX PRO Optical Imaging System* following removal of the anastomosis.
Results: The use of WLE/FE allowed evaluation of anastomotic healing and visialization of mucosal MMP *in vivo*. In 14 of 24 cases disturbed anastomotic healing was detected. During the healing process the content of mucosal MMP gradually increased from POD1 to POD3 (SNR: $16,3 \pm 2,2$ vs. $24,8 \pm 8,5$, $P = 0.021$) as well as from POD3 to POD5 (SNR: $24,8 \pm 8,5$ vs. $51,8 \pm 13,7$, $P = 0.002$). Areas with defective anastomotic healing showed significantly higher uptake of the tracer *in vivo* as well as *ex vivo* (SNR (Signal-to-noise ratio): $19,9 \pm 8,2$ vs. $40,8 \pm 18,9$, $P = 0,004$).
Conclusion: During disturbed anastomotic healing increased expression of MMP-2/-9 was observed in the anastomotic tissue. Fluorescence endoscopy for detection of MMP-2/-9 during the healing process can be a promising tool for early identification of anastomoses at risk.
Disclosure of Interest: None declared

P1507 SURGICAL MANAGEMENT OF RECTOVAGINAL FISTULAS – TEN YEARS' EXPERIENCE IN TERTIARY REFERRAL CENTER

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Introduction: Rectovaginal fistula (RVF) is chronic and serious condition with significant influence on patient's quality of life. Due to difficult surgical techniques and various etiologies, treatment of RVF remains a challenge and demands individual approach to the patient. Thus, low rates of long-term positive outcomes are reported and recurrences are frequent.
Aims & Methods: The study aimed at evaluating the outcomes of surgical treatment of RVF depending on the etiology. A retrospective analysis was performed on 94 females who underwent surgical treatment of RVF and related complications at our institution from January 2003 to December 2014. 82 of them were available for follow-up. The study data were retrieved from the hospital medical records, surgical protocols, laboratory test results, and imaging examinations. Data from patients who underwent follow-up in outpatient clinic were also included.
Results: The causes of fistula included: radiation induced (63 patients), inflammatory bowel diseases (IBD) (6), obstetric injury (5), trauma (2), cancer (8) and other (10). Median patients' age varied significantly between groups (obstetric – 31 years; radiation induced – 60 years; IBD – 44 years; trauma – 35 years; cancer – 63 years; others – 38 years). Median follow-up was 3 years. The best surgical outcomes were achieved in the group of patients after obstetric injury (80% healing rate). Satisfactory results were achieved in trauma and others group (75% healing rate). In the group of radiation induced RVF, nearly all patients were managed by fecal diversion and this enabled healing in 10 patients (15,9%) among which 5 undergone restoration of gastrointestinal continuity. In cancer group 2 fistulas were healed (healing rate 25%). In multivariate analysis, patients age below 60, presence of high fistula, no cancer history were independent predictors of fistula healing.
Conclusion: Treatment outcomes depend significantly on RVF etiology and patient-related factors (age, comorbidities). In management of RVF complex approach to the patient is crucial in order to achieve optimal outcomes.
Disclosure of Interest: None declared

P1508 IS EARLY APPENDECTOMY ASSOCIATED WITH BETTER OUTCOMES IN THE TREATMENT OF ACUTE APPENDICITIS?

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Introduction: Historically appendicitis is tend to be operated as soon as possible in order to prevent future complications, but recent discussions shows, that urgent operation does not always reduce the rate of postoperative complications. Immediate appendectomy can be delayed in some cases.
Aims & Methods: Retrospective, non-randomized, single center, cohort study was performed. During one year period 167 consecutive patients diagnosed with acute appendicitis in which operation was performed and who met the inclusion criteria were included in the study. The study population was divided into two groups according to the time from the onset of the symptoms to the operation. Group I (time to the operation ≤ 24 hours) consisted of 74 patients and Group II (time to the operation ≥ 24 hours) – 93 patients. Primary (postoperative complications) and secondary (length of operation, length of hospital stay and perforation rate at the final pathology report) endpoints were evaluated and compared.
Results: There were no statistically significant difference in the rate of postoperative complications (Clavien-Dindo grading system for the classification of surgical complications) when comparing both groups. In Group I – 21.9% patients (87.5% Grade I) and in Group II – 25.8% patients (83% Grade I) had postoperative complications. Length of operation (in minutes) was similar between the groups (72.97 ± 29.1 (Group I) vs 79.95 ± 35.4 (Group II)). Length of hospital stay (days) was longer in Group II, but no statistically significant difference was found (2.85 ± 2.3 vs 3.34 ± 4.88 accordingly). Perforation rate at the final pathology report was twice higher in Group II (8 (10.8%) vs 17 (18.3%)), but no statistically significant difference was found. Additional analysis comparing different timing (time to the operation $\leq$48 hours vs $\geq$48 hours) in the same patient's cohort was performed. Statistically significant better outcome was found in "$\leq$48 hours" group (complications rate, length of operation and length of stay, perforation rate at the final pathology report).
Conclusion: This study showed shorter length of operation and length of hospital stay, lower rate of perforations in early appendectomy group (≤ 24 hours), but no statistically significance was found. These findings supports earlier reports showing that delayed appendectomy is safe surgical procedure without higher rate of postoperative complications. The appendectomy should be performed as fast as possible ($\leq$48 hours), but the timing of operation can be chosen by responsible surgeon depending on the available personnel and hospital resource.
Disclosure of Interest: None declared

P1509 TRANSANAL ENDOSCOPIC MICROSURGERY UNDER SPINAL ANESTHESIA: PRELIMINARY RESULTS OF A PILOT STUDY

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Introduction: Transanal Endoscopic Microsurgery (TEM) allows a full thickness excision of rectal benign lesions and early rectal cancer with excellent oncologic outcomes compared to Endoscopic Submucosal Dissection (ESD). Today the major advantage advocated by flexible endoscopists is the avoidance of general anesthesia. Combining a minimal-access operation with segmental anesthesia may further enhance the advantages of a real surgical dissection provided by TEM, over ESD that forces to long lasting sedations.
Aims & Methods: The purpose of the study is to assess the feasibility and safety of TEM under epidural anesthesia.
A prospective observational study was conducted with the aim to collect data of patients who underwent TEM under spinal anesthesia. Primary end-points were feasibility and safety; secondary endpoints were post operative pain, heart rate (HR) and non invasive blood pressure (NIBP) at 4, 8, 24 and 48 hours after surgery measured by Visual Analogue Scale (VAS), need of opioids (during and after the operation), post operative nausea or vomiting (PONV) and urinary retention (UR) rate.
Results: 48 patients were included. Median age was 70.5 years and male/female ratio 28/20. No intraoperative complication occurred and median operative time was 60 minutes (range 20-120). 5/48 patients (10,4%) required opioids in the operatory room (fentanyl 50 mcg) and 8/48 (16,7%) in the postoperative time (a single dose of 100 mg tramadol). Median postoperative pain assessed by VAS was 0 (range, 0–3) at 4 h, 0 (range, 0–2) at 8 h, 0 (range, 0–2) at 24 h and 0 (range, 0–1) at 48 h. Median HR was 70, 70, 72,5, 71 bpm and median NIBP

was 130/72,5, 130/75, 125/70, 130/75 at 4, 8, 24 and 48 hours. PONV occurred only in 1/48 patient (2,1%), while 5/48 patients (10,4%) developed urinary retention.
Conclusion: The study proves feasibility and safety of TEM under spinal anesthesia, with reduced impact of side effects. The possibility to avoid general anesthesia opens new opportunities for TEM against flexible endoscopic techniques such as ESD.
Disclosure of Interest: None declared

P1510 A PROSPECTIVE MULTICENTER STUDY OF SELF-EXPANDABLE METALLIC STENT PLACEMENT AS A BRIDGE TO SURGERY FOR MALIGNANT COLORECTAL OBSTRUCTION IN JAPAN: FEASIBILITY IN 112 CASES

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Introduction: Endoscopic stenting with a self-expandable metallic stent (SEMS) as a bridge to surgery (BTS) is widely used for acute malignant colonic obstruction (MCO), but recent European Society of Gastrointestinal Endoscopy guidelines discourage this procedure in curable patients. To clarify SEMS feasibility, we conducted a prospective, observational, single-arm, multicenter clinical trial (UMIN000011304) using standardized SEMS placement methods among participating facilities in Japan.
Aims & Methods: Our objective was to estimate the feasibility of SEMS placement as a BTS for MCO. This study was conducted in October 2013. Before start-up, stenting methods considered adequate and standard were discussed and shared among 32 participating facilities. Each patient was treated with a Niti-S Enteral Colonic Uncovered Stent, D-type. Patients with SEMS as BTS were followed up until discharge post-surgery. BTS clinical success was defined as having adequate passage of stool until surgery without stent-related complications and without the need for endoscopic re-intervention or emergency surgery.
Results: A total of 205 consecutive patients were enrolled in this study; 6 were excluded because of loose stenosis, inability to visualize the tumor, respiratory failure, fistula, or benign stricture. The remaining 199 patients comprised the per-protocol cohort. Treatment intent was BTS in 112 patients (56.3%) and palliative in 87 patients (43.7%). 76.8% of the BTS patients had no distant metastasis. Stenting was successful in 99.1% patients (111/112). The clinical success rate was 96.4% (108/112), with 3 persistent colonic obstructions causing failure. The overall preoperative complication rate was 4.5% (5/111). No perforation or stent migration was observed. No emergency surgery was performed for management of complications, and all technical success patients received elective surgery. Median time from SEMS placement to surgery was 20 days (range, 6-159). Open surgery and laparoscopic surgery were performed in 42 (37.8%) and 69 (62.2%) patients, including 7 cases of conversion to open surgery (10.1%), respectively. The tumor was resected in 110 patients. The primary anastomosis rate was 96.4% (107/111). The rate of anastomotic leakage was 2.8% (3/107). The overall stoma creation rate was 4.5% (5/111), including 3 Hartmann operations, 1 diverting stoma, and 1 colostomy without tumor resection. Median duration of hospitalization after surgery was 13 days (range, 6-114). The overall postoperative morbidity rate was 16.2% (18/111). The in-hospital postoperative mortality rate was 0%.
Conclusion: The current study has demonstrated the feasibility of SEMS placement as a BTS for MCO. SEMS placement using shared, standard methods is a safe and effective BTS with acceptable stoma creation and complication rates, allowing elective surgery with a primary anastomosis in most patients.
Disclosure of Interest: None declared

P1511 INTESTINAL ELONGATION USING SMALL INTESTINAL TISSUE ENGINEERING IN COMBINATION WITH BIANCHI'S PROCEDURE

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Introduction: Bianchi's operation, which lengthens intestinal loops while decreasing the luminal diameter to decelerate the intestinal transit time, is sometimes performed in patients with short bowel syndrome with severely dilated bowel loops. We conceived an innovative design concept in which the absorptive area of the small intestine could be increased without changing the caliber of the lumen if a bioscaffold, which might be expected to induce local intestinal regeneration, was interposed longitudinally instead of using staples as in the classic Bianchi's procedure. Small intestinal submucosa (SIS) is a biodegradable, acellular, collagen-rich matrix containing functional growth factors.
Aims & Methods: We investigated SIS-induced small intestine and evaluated it in terms of muscle contractility and other tissue characteristics in the SIS-grafted area when the blood supply was delivered as in the classic Bianchi's procedure. In nine micro-mini-pigs with non-dilated small intestines, the mesentery was separated based on the bifurcated vessels, and the bowel was divided and discontinued as described by Bianchi [1] without the use of surgical staplers. Rather than sewing the edges of the bowel to itself to form two separate loops, the temporary defect that was caused by unstapling was patched by the 3.5×2.0-cm SIS, sutured to the edges of the defect. Next, the two separate conduits that were integrated with SIS were moved in the opposite direction with the mesentery (which contained a single blood supply from one of the bifurcated vessels), and were reconnected in series with the rest of the small intestine as in Bianchi's operation. A muscle strip was obtained and an organ bath technique with electrical field stimulation was applied at the 6-month evaluation. Native small intestine and grafts were investigated morphologically using histology and immunohistochemistry. The enzyme activity of alkaline phosphatase was also measured by absorption spectrometry.
Results: All pigs survived and thrived, and were healthy at the time of functional evaluation. The *in vitro* study revealed that the tissue contracted in response to an acetylcholine agonist and electrical field stimulation. The mucosa was covered with normal epithelium, and regeneration of neural and smooth muscle cells had occurred. The alkaline phosphatase activity in the regenerated area was the same as for the normal tissue.
Conclusion: We obtained good outcomes using the above-described surgical technique with an SIS graft, which may represent a beneficial treatment for patients with short bowel syndrome regardless of their small intestinal diameter. Further investigation in clinical settings is now warranted.

Reference

1. Bianchi A. Intestinal loop lengthening – A technique for increasing small intestinal length. *J Pediatr Surg* 1980; 15: 145—151.

Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 09:00–14:00
IBD III – HALL 7

P1512 MUCOSAL INNATE IMMUNITY IS DYSREGULATED IN CIGARETTE SMOKERS - IMPLICATIONS FOR CROHN'S DISEASE?

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Introduction: Crohn's disease (CD) is a chronic inflammatory disease characterized by defective handling of intestinal bacteria, particularly by the innate immune compartment. Although the underlying cause is unknown, genetic and environmental factors are important. One of the most recognized environmental risk factors is cigarette smoking, which impacts disease risk, prognosis and treatment response. Insight into how cigarette smoking influences innate immunity and gut physiology are now needed.
Aims & Methods: We investigated mucosal immune changes and gastrointestinal (GI) symptoms (using validated GI symptom questionnaires) in non-health care seeking smokers and non-smokers identified in three population-based endoscopy studies, comprising 2554 participants, including a population who had undergone ileocolonoscopy and mucosal biopsy. Tissues were stained with Haematoxylin and Eosin (H&E), and specific immunostains (e.g. CD117). To determine whether smoking was causally linked to mucosal changes and susceptibility to intestinal inflammation we employed a preclinical model of smoke exposure and 2,4,6-Trinitrobenzenesulfonic acid (TNBS)-induced colitis.
Results: Significant changes in the frequency of cells implicated in mucosal defence were observed in the gut of individuals who smoke, most notably in the terminal ileum (TI) and caecum. These changes included expansion of Paneth cells in the terminal ileum ($P < 0.04$), depletion of mast cells in the TI (median count 231 in smokers vs 324 in non-smokers, $P < 0.03$) and depletion of mast cells in the caecum (median count 116 in smokers vs 170 in non-smokers, $P < 0.002$). No significant changes were observed in the transverse or left hemicolon. Smoking was also associated with significantly increased GI symptoms. In particular, there was increased diarrhoea in smokers in comparison with non-smokers (OR = 2.04,1.29-3.21, $P < 0.002$). In preclinical studies mast cells were also depleted in the TI and colon of smoke exposed mice, consistent with the likelihood that the mucosal changes observed in human smokers were causally linked to smoking. Crucially, smoke exposed mice with dysregulated mast cell numbers exhibited heightened susceptibility to experimental colitis induced by TNBS.
Conclusion: Cigarette smoking was associated with altered frequencies of mucosal dwelling cells implicated in host innate immunity, and changes were most apparent in the TI and right hemicolon – the most commonly affected sites in CD. Similar changes were observed in the gut of smoke exposed mice – which was associated with heightened susceptibility to experimentally induced colitis. Together these data provide new insight into the links between smoking, innate immunity and CD.
Disclosure of Interest: None declared

P1513 CHROMOGRANIN-A REGULATES ANTI-INFLAMMATORY MARKERS IN THE CONTEXT OF EXPERIMENTAL COLITIS AND HUMAN RECTAL SAMPLES

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Introduction: The pathophysiology of inflammatory bowel disease (IBD) can result from altered communications between nervous, immune and endocrine systems through chemical messengers. Enterochromaffin (EC) cells are the predominant neuroendocrine cell type in the gut and the main source of Chromogranin A (CgA). CgA is a neuropeptide, which facilitates the neuroendocrine immune communication and has been reported to be increased in IBD patients. Mucosal changes in IBD are characterized by a downregulation of T-regulatory cells (Forkhead Box P3: *FOXP3*), interleukin (*IL*)-10 & transforming growth factor (*TGF*)-β as anti-inflammatory mediators and loss of mucosal healing. Krüppel-like factor 5 (*KLF-5*) has been implicated in mucosal healing in a model of experimental colitis.
Aims & Methods: The aim of this study was to investigate the effect of the lack of CgA using an experimental model of ulcerative colitis (UC) and the correlation between CgA and anti-inflammatory regulators and healing mediators in rectal biopsies from IBD and healthy individuals.
Colitis was induced in CgA-C57BL/6-deficient ($CgA^{-/-}$) mice and wild type ($CgA^{+/+}$) mice by administrating dextran sulfate sodium (DSS 5%) in drinking water for 5 days. Disease activity index (DAI) was evaluated daily and mice were sacrificed on day 5 post-DSS induction to assess the extent of colitis. At sacrifice composite macro- and microscopic scores were evaluated. Myeloperoxidase (*MPO*) activity, *FOXP3*, *IL-10*, *TGF-β*, and *KLF-5*, were quantified in colon and spleen using ELISA or RT-qPCR. Rectal human biopsies were collected from healthy and IBD patients, the correlations between mRNA expression levels of CgA and *FOXP3*, *IL-10*, *KLF-5* were determined.
Results: Delayed onset and DAI were observed in $CgA^{-/-}$ mice as compared to $CgA^{+/+}$ mice after induction of colitis. Macroscopic and histological damage scores and colonic *MPO* activity were significantly decreased in $CgA^{-/-}$ mice as compared to $CgA^{+/+}$ mice. This was correlated with a significant up-regulation of *FOXP3*, *IL-10* and *KLF-5* of mRNA expression levels in the spleen and colonic tissue. However, *TGF-β* mRNA expression levels were not modified. In control mice the mutation did not affect any inflammatory markers studied. Using the mRNA expression levels, in human rectal biopsies, CgA showed a moderately strong negative linear association with *FOXP3* ($r = -0.66$, $P = 0.01$), *KLF-5* ($r = -0.67$, $P = 0.009$) and negative linear relationship with *IL-10* ($r = -0.34$, $P = 0.21$).
Conclusion: These observations suggest that lack of C*g*A in C*g*A-deficient mice reduced the severity of DSS-induced colitis and that C*g*A is critical in the pathogenesis of inflammation in that model of experimental colitis. In human clinical cases, the relationship between C*g*A and anti-inflammatory markers corroborated this observation. These findings reveal new insights into the mechanisms of colonic inflammation, which may ultimately lead to novel therapeutic strategies in human IBD.
Disclosure of Interest: None declared

P1514 THE PERSISTENCE OF CROHN'S ANAL FISTULAE COULD BE DUE TO THE INTERACTION BETWEEN THE GUT MICROBIOME AND THE IMMUNE SYSTEM

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Introduction: An interaction between genetic, microbiological and immunological factors drives Crohn's disease. Bacterial infection probably initiates idiopathic anal fistulae but does not maintain them. There is no evidence that bacterial infection causes the persistence of idiopathic anal fistulae. The aetiological factors behind Crohn's anal fistulae remain unclear. Perhaps an interaction between the gut microbiome and the immune system is implicated. Dendritic cells (DC) express Toll-Like receptors (TLR), which are pattern recognition receptors that are activated by bacterial ligands.
Aims & Methods: We aimed to compare the expression of TLRs and microbiota profiles of Crohn's and idiopathic fistulae. Biopsies were taken from 35 Crohn's and 25 idiopathic fistulae at the time of surgery. DC were identified as HLA-DR-positive and lineage-negative, and characterized by flow cytometry using fresh samples. The expression of TLR2 and 4 was determined. Immunohistochemical techniques determined the expression of TLR2, TLR4 and TLR9 on paraffin-imbedded anal fistula biopsies. DNA was extracted from frozen samples and bacterial 16S rRNA genes were sequenced using a MiSeq sequencer.
Results: TLR2 and 4 were expressed on DC from both Crohn's and idiopathic perianal fistulae using flow cytomtery. There was no significant difference in TLR2 ($p = 0.27$) or TLR4 ($p = 0.45$) expression on CD and idiopathic fistulae. Immunohistochemistry showed equal expression of TLR2 ($p = 0.42$) and TLR4 ($p = 0.11$) on lymphocytes. TLR9 expression was significantly higher in CD fistulae ($p = 0.01$).
Microbiota were classified as common and abundant, infrequent, and rare. The total number of operational taxonomic units (OTUs) observed and the number of species identified in Crohn's fistulae was significantly higher than idiopathic ($p = 0.02$). The most abundant species in the Crohn's group were *Bradyrhizobium pachyrhizi* followed by *Pseudomonas azotoformans* and *Prevotella oris*.
Conclusion: Bacterial products and the local immune response to them are present in perianal fistula tracts. Crohn's anal fistula persistence may be driven by bacterial products rather than live bacteria. This could provide therapeutic treatment targets for Crohn's anal fistulae.
Disclosure of Interest: None declared

P1515 INFLIXIMAB RESTORES THE BARRIER TO E. COLI IN ACTIVE CROHN'S COLITIS VIA EFFECTS ON LIPID RAFTS

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Introduction: Crohn's disease (CD) is characterized by chronic inflammation in the gastrointestinal tract with increased amounts of the pro-inflammatory cytokine TNF-α. Treatment with anti-TNF-α antibodies, e.g. infliximab, is established as an important part of the therapeutic arsenal in severe CD, working, at least in part, via cytotoxic effects on T cells. TNF-a can decrease epithelial barrier function by apoptosis or changes at the tight junctions, however, it is unclear if part of the beneficial effect of anti-TNF-a therapy is due to prevention of this barrier dysfunction.
Aims & Methods: To investigate how infliximab affects uptake of adherent invasive *E. coli* across the colonic mucosa in CD and study mechanisms of transepithelial transport of the adherent invasive *E. coli* HM427 across monolayers of the human Caco-2 epithelial cell line treated with TNF-α ±infliximab.
Methods: Biopsies from macroscopically non-inflamed colon were obtained from CD colitis patients ($n = 6$) before and after a 4-week infliximab treatment. Biopsies from healthy volunteers ($n = 4$) and patients undergoing colon cancer screening ($n = 4$) served as controls. Biopsies were mounted in Ussing chambers, and the radioactivity labeled paracellular probe ^{51}Cr-EDTA and live GFP-incorporated *E. coli* HM427 were added to the mucosal sides of the tissues and passage into the serosal buffer was assessed by g-counting and flow cytometry, respectively. Caco-2 cells were cultured on transwell filters (bacteria transport assay) or 12-well plates (internalization assay) and exposed to either HM427 or the non-invasive *E. coli* HB101 with TNF-α ±infliximab for 24 h. Some monolayers were pre-treated with colchicine or methyl-β-cyclodextrin to stabilize microtubules and disrupt lipid rafts.
Results: Prior to infliximab, transcytosis of HM427 (CD: 2475 bacteria (450-3000) vs controls 1163 (225-1950), $p < 0.05$) and ^{51}Cr-EDTA passage (CD: 2.31 cm/s x 10^{-6} (1.70-6.67) vs controls 1.07 (0.62-1.55 x10^{-6}), $p < 0.05$) was increased in CD colitis. Treatment with infliximab restored transcytosis of HM427 to control group level (CD: 150 (18.8-1069)) and ^{51}Cr-EDTA (CD: 1.82 (0.64-2.95)). Data are presented as median ± IQR. *In vitro* studies demonstrated that infliximab reduced the TNFα-induced increase in bacterial transcytosis. The TNF-a-induced bacterial transcytosis was decreased by methyl-β-cyclodextrin but not colchicine.
Conclusion: Patients with active CD colitis showed a defect in the barrier to adherent *E. coli*, which was restored by a 4-week treatment with infliximab. The results suggest that TNF-α plays an important role in the barrier dysfunction in CD colitis, facilitating the transcytosis of commensal and pathogenic bacteria that is dependent on lipid rafts. The ability of infliximab to block these effects of TNF-a on epithelial permeability likely contributes to the clinical efficacy of this drug.
Disclosure of Interest: None declared

P1516 RELATIONSHIP BETWEEN HISTOLOGICAL AND ENDOSCOPIC ACTIVITY AND ANGIOGENIC AND LYMPHANGIOGENIC FACTORS EXPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Angiogenic and lymphangiogenic factors may play an important role in inflammatory bowel disease.
Aims & Methods: To correlate the main angiogenic and lymphangiogenic factors expression in colonic mucosa biopsies with the endoscopic and histological activity in patients with inflammatory bowel disease (IBD).
Prospective study in patients with IBD that underwent a colonoscopy because of medical criteria. Samples of colonic tissue biopsies for histological analyses were obtained. In patients where activity was observed during colonoscopy, samples from affected and non-affected mucosa were also taken. Endoscopic activity was assessed by endoscopic Mayo subscore for ulcerative colitis (UC) and SES-CD for Crohn's disease (CD). Considering histological findings, patients were classified into four groups: Quiescent IBD, mild, moderate and severe lesion. VEGFA, -C, -D, -R1, -R2, -R3 and PlGF expression results were

graded as follows: (++) over 50% of the tissue cells were stained, (+) below 50%, and (-) completely negative. Ang1, Ang2 and Tie2 were assessed as the average density of five hot spots at a magnification of x40. Protein expression was determined by immunohistochemistry.
Results: 82 biopsies from 58 patients with IBD (36 UC and 22 CD) were included. 64% of the patients did not have endoscopic activity, 16% had moderate, 14% mild and 6% severe activity. There were significant ($p < 0.01$) differences in the mean count of Ang1 and Ang2 depending on endoscopic activity. Higher expression of Ang1 and Ang2 was found when the endoscopic activity was severe compared to inactive disease. According to histology, 60% of the patients had quiescent IBD, 20% had moderate lesions, 15% mild and 5% severe lesions. Expression of VEGFD ($p < 0.05$), PlGF ($p < 0.05$) and VEGFR3 ($p < 0.01$), and mean count of Ang1 ($p < 0.05$) and Ang2 ($p < 0.01$) were also significantly different depending on the histological activity. These expressions were increased in parallel with the severity of histological lesions excepting for VEGFD, that was decreased with the severity of the activity. Positive correlations ($p < 0.05$) between histological activity and expression of Ang1 ($r = 0.4$), Ang2 ($r = 0.5$), PlGF ($r = 0.4$), VEGFC ($r = 0.3$), and VEGFR3 ($r = 0.3$), and negative for VEGFD ($r = -0.3$), were demonstrated. On the other hand, positive correlations ($p < 0.05$) between endoscopic activity and expression of Ang1($r = 0.4$), Ang2 ($r = 0.5$), PlGF ($r = 0.4$), and negative for VEGFD ($r = -0.3$), were found. The best area under the Receiver Operator Characteristic (ROC) curve for the diagnosis of histological activity was 0.73 for Ang1 (cut-off at 39.8: 89% sensitivity and 56% specificity).
Conclusion: The expression of VEGFA, -D, -R3, PlGF, and Ang1 and -2 in mucosal biopsies correlates with the histological activity of IBD. Ang-1 and -2 expressions in mucosal samples are markers of histological and endoscopic activity.
Disclosure of Interest: None declared

P1517 CHARACTERIZATION OF ENTEROCHROMAFFIN CELLS IN POUCHITIS AFTER PROCTOCOLECTOMY WITH ILEAL POUCH-ANAL ANASTOMOSIS FOR ULCERATIVE COLITIS

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Introduction: Several immune-mediated gastrointestinal disorders, including inflammatory bowel disease (IBD), are associated with neuroendocrine cell hyperplasia.
Aims & Methods: We here studied neuroendocrine cells in patients with pouchitis after proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis (UC). Serial sections from 17 patients with pouchitis and from ileum of 13 IBD patients (5 Crohn's ileitis and 8 UC backwash ileitis) and 11 control subjects were processed for the immunohistochemical detection of CgA and serotonin. Mucosal tryptophan hydroxylase (TpH)-1 and serotonin-selective reuptake transporter (SERT) transcripts were measured by quantitative RT-PCR. We also detected TpH-1 and SERT transcripts in pouchitis biopsies cultured with infliximab or its isotype-matched control human IgG1, while interleukin (IL)-6 and IL-8 were measured by ELISA in culture supernatants.
Results: We observed an increase in CgA-positive cells in both patients affected by pouchitis and those with IBD ileitis compared to control subjects, with no difference between pouchitis and IBD ileitis. No change was found for serotonin-positive enterochromaffin (EC) cells amongst pouchitis and the other two groups, whereas IBD ileitis have higher EC cells than control subjects. we detected an increase in CgA-positive and serotonin-negative cells, calculated by subtracting the number of CgA-positive cells from the number of EC cells, in pouchitis in comparison to IBD ileitis and control subjects. Raised transcripts of mucosal TpH-1, but not SERT, were found in IBD ileitis in comparison to control subjects, without significant difference amongst pouchitis and the other two groups. Although infliximab down-regulated the *ex vivo* production of IL-8, but not IL-6, compared to IgG1, it did not change the expression of TpH-1 and SERT in pouchitis biopsies.
Conclusion: We show hyperplasia of neuroendocrine cells in the mucosa of both pouchitis and IBD ileitis. EC cells and TpH-1 transcripts are increased in the mucosa of IBD ileitis, but not in pouchitis. Hyperplasia of neuroendocrine cells seems to be due to other cell types in pouchitis.
Disclosure of Interest: None declared

P1518 ISOLATION AND CHARACTERIZATION OF ADHERENT-INVASIVE ESCHERICHIA COLI IN CROHN'S DISEASE PATIENTS IN BRAZIL

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Introduction: Crohn's disease (CD) is an inflammatory bowel disease (IBD) characterized by chronic inflammation of the intestine in humans. The etiology of CD remains unknown, however, the most common hypothesis is that chronic inflammation results from an abnormal inflammatory response against intestinal microbiota in a genetically susceptible host. Several studies have demonstrated that the intestinal mucosa of CD patients is abnormally colonized by adherent-invasive *Escherichia coli* (AIEC) strains. However, to date, no studies have focused on the involvement of such *E. coli* strains in CD patients in Brazil.
Aims & Methods: The aim of this study was to isolate and characterize the *E. coli* strains associated from intestinal mucosa in CD patients in Brazil. Biopsies were performed on 35 subjects: 10 CD patients in active phase, 15 CD patients in remission phase and 10 controls (without intestinal disease).
Results: Although the difference was not significant, the colonization level of the ileal mucosa by adherent bacteria is higher in CD patients than in the control group. Among 270 isolates strains, 241 were identified as *E. coli* strains. Mark from different phylogenetic groups of *E. coli* was carried out by PCR. In controls patients, 47.9% of the strains belong to group A, 2.1% in the B1 group, 6.3% in the B2 group and 43.7% in group D. In CD patients, 36.8% of the strains belong to group A, 30% in the B1 group, 10.9% in the B2 group and 22.3% in group D. In CD patients, a difference between the classification of *E. coli* strains was observed related to disease activity, especially among groups B2 and D. CD patients in active phase (20.2%) harboured 10-fold more *E. coli* belonging to the B2 group compared to CD patients in remission (2.0%) and 2.4-fold less strains of group D (12.8% CD active vs 31.3% CD remission). The adhesion and invasion ability of *E. coli* strains isolated were determined using human intestinal epithelial cells (I-407) and we observed that 26.9% of the isolated strains from CD patients are invasive. For each patient, the *E. coli* strain with the greater capacity of invasion was selected to analyze its ability to survive and multiply in human macrophages (THP-1), and we observed that 76.19% of the selected strains can survive and multiply within human macrophages.
Conclusion: This preliminary study on a small cohort of Brazilian CD patients suggests that the ileal mucosa of CD patients in Brazil is also colonized by *E. coli* strains having adherent and invasive properties.
Disclosure of Interest: None declared

P1519 THE ROLE FOR T-CELL DERIVED CYTOKINES IN THE PATHOGENESIS OF CROHN'S DISEASE ASSOCIATED FISTULAE

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Introduction: Fistulae represent a frequent complication in Crohn's disease (CD). Surgical resection is often required, as medical treatment outcome with conventional drugs is often insufficient. We have previously demonstrated that epithelial-to-mesenchymal transition (EMT) plays a critical role for fistula development. The T-cell cytokines tumor necrosis factor (TNF), interleukin (IL)-13, IL-17A and IL-22 are highly expressed in transitional cells along fistula tracts in CD patients. Similar to transforming growth factor (TGF) β, TNF is able to induce EMT and the expression of molecules being associated with cell invasiveness and migration. IL-13 has no impact on epithelial cell morphology, but also induces expression of genes being associated with invasive cell growth, such as *SLUG* transcription factor and *β6-integrin*. Here, we analyzed whether the T-cell derived cytokines interferon (IFN) γ, IL-10, IL-17A and IL-22 might be associated with the onset of EMT suggesting a possible role in the pathogenesis of CD-associated fistulae.
Aims & Methods: The effects of IFNγ, IL-17A and IL-22 on EMT development were investigated by stimulating HT29 intestinal epithelial cells (IECs), seeded as hanging drops as an *in vitro* model for EMT (spheroids), for one and seven days, followed by analysis of mRNA expression levels of EMT-associated genes, as well as morphological evaluation. Further, immunohistochemistry visualizing IL-10 was performed using human perianal fistula tissue from seven patients.
Results: Treatment of the HT29 spheroids with IFNγ (100 ng/ml) resulted in a loss of the well-defined globular spheroid shape after day 7. We observed a clear separation of IECs, suggesting the initiation of EMT. This observation was supported by the up-regulation of mRNA levels of the EMT-related transcription factors *SNAIL-1* and *ETS-1*. IL-17A (100 ng/ml) had no effect on cell morphology suggesting that it does not induce EMT in our cell model. On a molecular level, IL-17A had no effect on the mRNA expression of EMT-associated genes, but prevented the TGFβ-induced up-regulation of *SNAIL-1* and *ETS-1*. Similar to IL-17A, treatment with IL-22 (50 ng/ml) did not induce EMT in our spheroid model and did not exert significant effects on the expression of EMT-associated genes. Immunohistochemistry of fistulae tissue derived from CD patients did not reveal a considerable staining for IL-10.
Conclusion: Our data demonstrate that T-cell derived cytokines may play a crucial role in the pathogenesis of CD-associated fistulae. Th1 cell derived IFNγ may be involved in the onset of EMT in IECs, however Th17 cell derived cytokines IL-17A and IL-22 are likely not implicated, and may prevent EMT-associated effects of TGFβ. This observation supports the hypothesis that Th17 cell derived cytokines exert a pivotal role for maintaining intestinal homeostasis. We demonstrated only poor expression of IL-10 in fistulae tissue of CD patients. IL-10 is an antagonist of TNF as well as IL-13, which were previously shown to be highly expressed in the fistula regions. Thus, IL-10 may represent a promising therapeutic agent against fistulae development.
Disclosure of Interest: None declared

P1520 FARNESOID X RECEPTOR AGONISM MODULATES GUT EPITHELIAL INNATE IMMUNE RESPONSE

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Introduction: Disruption to the epithelial barrier is central to the pathophysiology of IBD (Zeissig et al., 2007, Su et al., 2009). A variety of innate immune mechanisms contribute to the maintenance of the epithelial barrier. When stressed, either by pathogens or by inflammatory cytokine, gut epithelial cells produce IL-8, which acts as a chemo-attractant to circulating polymorphonucleocytes (Eckmann et al., 1993). Farnesoid X receptor (FXR) is a bile acid receptor which promotes gut homeostasis by maintaining the epithelial barrier and exerting anti-inflammatory effects (Gadaleta et al., 2011). The mechanism by which FXR maintains the epithelial barrier is not known.

Aims & Methods: The aim of this study was to assay the effect of FXR agonism on the production of IL-8 by human, gut-derived epithelial cells in response to cytokine stress. HT29 cells were cultured with media containing an FXR agonist (GW4064) or control (DMSO) with or without an FXR antagonist (guggulsterone). Following exposure to the FXR agonist +/- guggulsterone, HT29 cells were stimulated with media containing TNFα. IL-8 was measured both at a protein level, by ELISA, and transcriptional level by RT-PCR.

Results: In the control group, gut epithelial cells produced high levels of IL-8 when exposed to TNFα (6,316 +/- 870 pg/mg). Concomitant treatment with FXR agonist at high dose (GW4064 10μM) completely attenuated this IL-8 response ($p = 0.0004$). Lower doses of FXR agonist (0.1μM and 1μM) had no significant effect on the concentration of IL-8. Guggulsterone was able to reverse the attenuating effect of high dose FXR agonist, with significantly more TNFα-induced IL-8 detected ($p = 0.0005$). Measurement of relative IL-8 gene expression confirmed the findings measured at a protein level (TNFα alone – fold increase ~640 +/- 20, TNFα + FXR agonist – fold change ~0.08 +/- 0.02).

Conclusion: These experiments demonstrate that FXR agonism decreased the IL-8 response of human, gut-derived epithelial cells to TNFα. Gut epithelial IL-8 production is an important innate immune mechanism and this data is in keeping with other studies in demonstrating an immuno-modulatory role for FXR (Vavassori et al., 2009, Haselow et al., 2013). This is a potential mechanism by which FXR may act to maintain epithelial homeostasis.

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P1521 EFFECT OF ANTI TNF-ALPHA THERAPY ON INTESTINAL EPITELIAL CELLS APOPTOSIS

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Introduction: Research of intimate mechanism of anti TNF-alpha led to emphasis on the involvement of this therapy in intestinal epitelial cells apoptosis.

Aims & Methods: We aim to investigate the modifiation of apoptotic ratio after the anti TNF-alpha induction therapy and to correlate the magnitude of that modifiation with the endoscopic response. 27 patients with ulcerative colitis with the indication of anti TNF-alpha therapy admitted consecutively in the Institute of Gastroenterology and Hepatology Insititute Cluj-Napoca was included in the study. We evaluated the apoptotic ratio of intestinal epitelial cells by using TUNNEL method on the biopsy specimens taken before and after the adminstration of anti TNF-alpha therapy. We evaluated at the same time the presence of mucosal healing after the induction therapy.

Results: Determination intestinal epithelium apoptotic rate was performed before and after induction therapy. There is a clear decrease in the rate of intestinal cell apoptosis after the induction therapy compared with biopsies taken before. Thus, the mean apoptotic before initiating TB rate was 74.67% (44-94%), and after initiation of TB was 24.33% (5-45%). The difference between these two values was significant: OR: 50.33 (CI95%: 43.29-57.38), $p < 0.001$. The decrease in apoptotic rate was significantly higher in patients who achieved mucosal healing (median, 62%) compared with those without mucosal healing (median - 39.5%), $p < 0.001$.

Conclusion: Anti TNF-alpha therapy induces apoptosis of intestinal epithelial cells with a significant decrease in the apoptotic ratio at the end of induction therapy, witch correlates very well with the presence of mucosal healing.

Disclosure of Interest: None declared

P1522 CEREBRAL MAGNETIC RESONANCE IMAGING IN QUIESCENT CROHN'S DISEASE PATIENTS WITH FATIGUE – A PILOT STUDY

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Introduction: Crohn's disease (CD) is characterized by an increased level of pro-inflammatory cytokines, which is called systemic inflammation. Previous studies suggest that systemic inflammation can contribute and accelerate brain diseases, and thereby hypothesized that systemic inflammation possibly have effects on the brain. Although in other chronic diseases such as Rheumatoid Arthritis (RA) structural brain changes have been shown, no research have been performed to evaluate the effect of systemic inflammation on the cerebral mechanism in CD patients.

Aims & Methods: The aim of our study was to assess brain involvement in quiescent CD patients with fatigue using quantitative Magnetic Resonance Imaging (MRI) and relate these data to neuropsychological scores. Multiple MRI acquisitions were used to assess cerebral abnormalities in 20 quiescent CD patients with fatigue (defined with at least 6 points out of an 11-point numeric rating scale (NRS)) compared with 17 healthy age and gender matched controls. Furthermore, neuropsychological data was obtained by conducting the Hospital Anxiety and Depression Scale (HADS) and Neuropsychological Inventory (NPI), including the Mini-Mental State Examination (MMSE), the Wechsler Memory Scale (WMS) and a revised form of the Wechsler Adult Intelligence Scale (WAIS-R).

Results: CD patients encountered significantly more depressive symptoms ($p < 0.001$). Results of the NPI showed a reduction of the total score on the WMS ($p = 0.04$), the WAIS-R ($p = 0.001$) and the MMSE ($p = 0.08$) in CD patients compared with healthy controls. Generally, CD patients made more mistakes and more time was needed to complete the tests. Subcortical atrophy was found in the Amygdala, Accumbens, Putamen, Thalamus and the right Caudate, right Hippocampus and right Pallidus ($p < 0.01$). Reduced Glutamate + Glutamine units ($p = 0.02$) and ratios to total Creatine ($p = 0.02$) were found compared with controls. Furthermore significant increased Cerebral Blood Flow (CBF) values ($p < 0.05$) were found in CD patients (53.08 ± 6.14 ml/100g/min) compared with controls (47.60 ± 8.62 ml/100g/min).

Conclusion: To our knowledge, this pilot study is the first one that investigates the changes in the brain due to CD with multiple MRI techniques. Preliminary evidence for structural brain changes is shown, enhancing the hypothesis that systemic inflammation could influence the brain and the association with cognitive tests results. This is the first step in the understanding of the brain involvement in CD patients.

Disclosure of Interest: None declared

P1523 REDUCED MUCOSA-ASSOCIATED BUTYRICICOCCUS ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS CORRELATES WITH ABERRANT CLAUDIN-1 EXPRESSION

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Introduction: *Butyricicoccus* is a butyrate-producing clostridial cluster IV genus whose numbers are reduced in the stool of patients with ulcerative colitis (UC). Conditioned medium of *Butyricicoccus pullicaecorum* 25-3^T (*B. pullicaecorum*) prevents TNFα-induced increase in epithelial permeability *in vitro*.

Aims & Methods: Since butyrate is one of the parameters affecting intestinal epithelial barrier integrity, we further investigated the relationship between the presence of *Butyricicoccus* in colonic mucosa and the expression of tight junction (TJ) complex genes that are partly regulated by butyrate.

Expression of tight junction protein 1 (TJP1), occludin (OCLN), claudin-1 (CLDN1) and *Butyricicoccus* 16S rRNA was analyzed by quantitative real-time PCR in a collection of colonic mucosal biopsies of healthy controls and UC patients with active disease (both $N \pm 10$). CLDN1 expression was also evaluated in ileal lysates of TNF$^{\Delta ARE/WT}$ mice ($N \pm 8$). The effect of butyrate and *B. pullicaecorum* conditioned medium on tight junction gene expression and CLDN1-dependent Notch signalling was investigated *in vitro* in TNFα-stimulated CaCo-2 monolayers and *ex vivo* in inflamed mucosal biopsies of UC patients ($N \pm 5$).

Results: Compared to healthy controls, transcription of TJP1 and OCLN was significantly decreased in inflamed colonic biopsies of UC patients ($P = 0.004$ and 0.041, respectively), whereas CLDN1 mRNA levels were increased ($P < 0.001$). This counterintuitive upregulation of CLDN1 was also observed in TNF$^{\Delta ARE/WT}$ mice compared to their TNF$^{WT/WT}$ littermate controls ($P < 0.001$). *Butyricicoccus* bacteria were present in colonic mucosal biopsies and the number of 16S rRNA transcripts was decreased in active UC patients compared to healthy controls. Interestingly, mucosa-associated *Butyricicoccus* activity negatively correlated with CLDN1 expression (Spearman R = -0.528,

P = 0.0017). In addition, inflammation-induced increase of both CLDN1 protein levels and CLDN1-associated Notch activation could be reversed *in vitro* by butyrate (P = 0.0016). *Ex vivo* stimulation of inflamed UC biopsies with *B. pullicaecorum* conditioned medium normalized CLDN1 mRNA levels and Notch-regulated transcription of HES1 and ATOH1.
Conclusion: *Butyricicoccus* is a mucosa-associated bacterial genus underrepresented in colonic mucosa of patients with active UC whose activity inversely correlates with CLDN1 expression. Butyrate and *B. pullicaecorum* conditioned medium reduce CLDN1 and associated Notch activation, supporting the use of *Butyricicoccus* as a pharmabiotic preserving epithelial TJ integrity.
Disclosure of Interest: None declared

P1524 ROLE OF CD24 IN THE PATHOGENESIS OF DSS-INDUCED EXPERIMENTAL COLITIS IN MICE

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Introduction: CD24, a cell surface glycoprotein, is expressed on immune and intestinal epithelial cells. We have shown that CD24 is important in CRC carcinogenesis (Sagiv, 2008; Shapira, 2011), and that *CD24* SNPs are associated with a late IBD onset and considered protective (Lisiansky, 2014). We hypothesize that CD24 is important in IBD pathogenesis through a combination of immune regulation and alteration of the enteric microbiota composition.
Aims & Methods: Aim: Investigate the role of CD24 in acute and chronic dextran sulphate sodium (DSS)-induced colitis.
Methods: Acute model: *CD24* knockout (KO) and wild-type (WT) C57BL/6J mice were given 2.5-4% DSS in their drinking water for 5 days, followed by 2 days of water. Each group (n = 12) was compared to control animals, which received only water. Mice were sacrificed on day 7 and scored for their disease activity index (DAI). Chronic model: Mice (n = 5/group) were exposed to 3 one-week DSS cycles. Between cycles, mice received water for 2 weeks. The optimal DSS concentration for chronic colitis was determined following various DSS doses (1.5-2.0-2.5%). Colitis severity was assessed clinically and pathologically. High-throughput sequencing of stool 16S rRNA genes was performed (Illumina, Miseq) and enteric microbial populations were characterized using the QIIME software. Specific cytokines were assayed by ELISA.
Results: *CD24* KO mice were more resistant to DSS-induced acute colitis compared to WT even at high DSS concentrations (4%). Colon length of the WT (2.5% DSS) was significantly shorter than the KO mice (6.9 ± 0.4 vs. 4.9 ± 0.2cm, respectively) ($p < 0.001$). DAI scores in the WT were significantly elevated on day 7 (DAI = 9.4 ± 1.2) while no changes were seen in the KO mice. In WT DSS-treated mice (4%), colitis appeared already on day 4 (DAI = 5.1 ± 3.3) with a high (17%) mortality rate (DAI on day 7 = 11.4 ± 1.07) ($p < 0.05$). The optimal DSS concentration in the chronic model was 1.5% (mild inflammation with no death). *CD24* KO mice were significantly less sensitive than the WT. DAI scores at the end of the experiment were 1.0 (KO) and 2.7 (WT) ($p < 0.05$). Colon lengths were reduced by 28.4% in the WT vs. 4.6% in the KO mice ($p < 0.001$). High-throughput sequencing of stool 16S rRNA showed significant differences between the enteric microbial populations. IL-12 levels in the colon were significantly elevated in DSS-treated KO mice compared to WT ($p = 0.02$). Changes in other cytokines, though not significant, were also detected, supporting the involvement of CD24 in the inflammatory response.
Conclusion: 1. *CD24* deficiency protects against colitis induced by acute and chronic exposure to DSS; 2. Microbiota may play a role in this protection; 3. CD24 may be an important player in IBD pathogenesis and serve as a novel target therapy.

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P1525 INTESTINAL EPITHELIAL RESPONSE TO FUNGI: IMPLICATIONS FOR THE PATHOGENESIS OF CROHN'S DISEASE

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Introduction: Antibodies directed against fungal cell-wall glycans are associated with Crohn's disease (CD) and may represent loss of tolerance towards intestinal microorganisms. The potential role of fungi and their cell wall glycans in modulating human intestinal immune responses and the cells and receptors recognizing them are still unclear. Intestinal epithelial cells (IECs) are the first to encounter luminal antigens and may play an active role in intestinal immune responses. We recently reported that β-glucans induced chemokine secretion by IEC lines in a Dectin-1 and spleen tyrosine kinase (Syk)-dependent manner.
Aims & Methods: To assess the effects of fungi and fungal glycans on activation of the intestinal mucosa, specifically IECs. IECs were freshly isolated from surgical specimens and mucosal samples were obtained from IBD patients and healthy controls. C-type lectin receptors (CLRs) were detected by immunohistochemistry, flow cytometry, real-time PCR (rt-PCR), Western-blot (WB) and immunofluorescence (IF). Human IEC lines (HT-29 and SW480) were activated by *Candida albicans* and *Saccharomyces cerevisiae*. Chemokine secretion was assessed by ELISA. Syk phosphorylation and microtubule-associated protein 1A/1B-light chain 3 (LC3) activation were assessed by WB and IF.
Results: Expression of the CLRs Dectin-1, Dectin-2, Mincle and DC-SIGN was detected in primary IECs as well as IEC lines. Expression of Dectin-1, Dectin-2 and Mincle was significantly increased in inflamed mucosa from the colon and small bowel of CD patients compared to normal controls [e.g. 18 ± 8 fold increase of Mincle mRNA expression in inflamed colon of CD (n = 7) vs. normal controls (n = 9) p = 0.001]. While IEC lines responded to β-glucan (zymosan or curdlan) activation by pronounced IL-8 and CCL2 secretion (e.g. 8.1 ± 0.6 vs. 0.3 ± 0.01 ng/ml IL-8 in zymosan-treated vs. control HT-29 cells, respectively), their activation by commensal fungal particles of heat-killed (HK)-*S. cerevisiae*, live, HK- or UV-inactivated wild-type *C. albicans*, or live non-hyphal forming *efg1*ΔΔ, *cph1*ΔΔ mutant did not yield significant IL-8 or CCL2 secretion. In contrast, Syk phosophorylation in IECs was similarly induced by β-glucans and fungal particles. Interestingly, exposure of IECs to β-glucans or fungal particles induced activation of the autophagy protein LC3. Furthermore, LC3 activation by HK *C. albicans* was sensitive to Syk inhibitor.
Conclusion: CD-related inflammation is characterized by increased expression of fungi-recognizing receptors. IECs express these receptors and can recognize luminal fungi and the cell wall component β-glucan leading to Syk mediated signaling. The Syk- dependent LC3 activation suggests that autophagy may be involved in IECs' response to fungi and β-glucans. The discordant chemokine secretion in response to commensal fungi and to β-glucans suggests common signaling mediated by receptors additional to Dectin-1. Thus, IECs' response to fungi may play a role in mucosal homeostasis that may be distorted in CD. Defining the mechanisms underlying intestinal immune responses to fungal glycans may enable therapeutic intervention, e.g., inhibition of key signaling mediators such as Syk.
Disclosure of Interest: None declared

P1526 EXPRESSION OF CLAUDINS IN METAPLASTIC GLANDS IN IBD

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Introduction: One of the characteristics of inflammatory bowel disease (IBD) is gland metaplasia. The aim of the study was to describe changes in claudin expression pattern by metaplastic epithelial cells in patients suffering from Crohn disease (CD) and ulcerative colitis (UC) in comparison to healthy controls.
Aims & Methods: Immunohistochemistry (IHC) for claudins 1, 2, 3, 4 and 8 on formalin-fixed paraffin-embedded (FFPE) tissue samples from resected intestine of IBD patients (8 patients with CD, 5 patients with UC and 7 controls) was performed. The following primary antibodies were used: claudin-1 (AbCam, ab56417, 1:250), claudin-2 (AbCam, ab125293, 1:75), claudin-3 (GeneTex, GTX15102, 1:50), claudin-4 (AbCam, ab53156, 1:1000), claudin-8 (AbCam, ab183738, 1:1000) followed by DAKO EnVision Detection System (Cat.No. K5007). TNFa, IFNg, claudin-1, claudin-2, claudin-3, claudin-4 and claudin-8 mRNA analysis were performed using the same sample tissue as for IHC. RNA was reverse transcribed using random hexamers and a SuperScript III First-Strand synthesis system. RT-qPCR was performed using the TaqMan method and glycerin-aldehyde-3-phosphate (GAPDH) as a housekeeping control.
Results: TNFa and IFNg were increased both in CD and UC samples confirming an inflamed environment. Expression of measured sealing claudins (1, 3, 4, 8) was absent or decreased in metaplastic epithelium. Claudin-1 expression by epithelial cells lining non-metaplastic glands was increased in both patient groups, comparing to healthy mucosa. In contrast, epithelial cells of metaplastic glands did not express claudin-1. Expression of claudin-3 by metaplastic epithelial cells was decreased in comparison to both, glandular epithelium in healthy mucosa and non-metaplastic glands in IBD mucosa. Claudin-4 was expressed along membranes of epithelial cells in healthy mucosa, as well as by epithelial cells of non-metaplastic glands in IBD, whereas epithelial cells of metaplastic glands did not express claudin-4. Claudin-8 in healthy mucosa was expressed mainly by differentiated epithelial cells. Its expression was increased in non-metaplastic epithelium in IBD samples, but was not expressed by epithelial cells of metaplastic glands. In contrast to examined sealing claudins, pore-forming claudin-2, not present along membranes of epithelial cells in healthy colon, was expressed both by epithelial cells of non-metaplastic and metaplastic glands in IBD mucosa. Detected RNA levels clearly reflected changes observed in prevailing non-metaplastic epithelium.
Conclusion: In short, expression of sealing claudins is down regulated in epithelium of metaplastic glands compared to healthy controls and non-metaplastic glands, whereas epithelial cells show claudin-2 positivity both in non-metaplastic and metaplastic glands in IBD. Observed pattern of claudin expression by epithelial cells of metaplastic glands in IBD differs from that reported in colorectal carcinoma.

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P1527 A NOVEL PPAR-GAMMA AGONIST, AS002, INDUCES PPAR-GAMMA-ACTIVITY IN ULCERATIVE COLITIS MUCOSA, AND PREVENTS AND REVERSES INFLAMMATION IN DSS COLITIS

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Introduction: Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) characterized by severe chronic intestinal inflammation with a high impact on the patient's quality of life. Studies suggest that peroxysome proliferator-activated receptor-gamma (PPARγ), highly expressed in colon, is a critical regulator of the inflammatory response and has anti-inflammatory effects. It is a promising new target for the treatment of IBD. AS002 is a novel PPARγ agonist developed for local action in the gut, and would thus be an important addition to the treatment strategy in IBD. In order to study the potential of this compound for IBD treatment, the effects of AS002 were evaluated in the well-established dextran sodium sulfate (DSS) animal model (that shows similarities with human UC), and *ex vivo* in colonic biopsies of patients with UC and controls.

Aims & Methods: Male Balb/c mice (8/group) received 5% DSS dissolved in drinking water for 8 days. Control mice received water. To evaluate preventive effect of AS002, mice received PPARγ agonists (5-ASA (75 mg/kg), rosiglitazone or AS002 (10 and 100 μM)) or vehicle by intrarectal administration 2 days before the induction of colitis (day 0), and each day until day 8. In the curative model, mice received the compounds from day 3-8. At day 8, mice were sacrificed and colon were measured and weighed. Macroscopic damages were evaluated using Wallace's table. Colon samples were taken to measure PPARγ expression by qPCR and to measure the myeloperoxidase level, a protein expressed during inflammation. *Ex vivo*, human colonic biopsies from patients with UC or from normal controls (polyp screening patients) (n = 6 per group) were incubated 1 hour with compounds followed by 3 hours with cell medium only, to better mimic the clinic situation, in order to measure PPARγ activity by assessing mRNA of the PPARγ-responsive gene adipophilin by qPCR. Moreover, metabolism of AS002 in UC biopsies was assessed.

Results: Both AS002 and rosiglitazone increased mRNA expression of adipophilin (mean ± SEM) compared to control wells ($p < 0.05$), in both controls (AS002; 1.02 ± 0.14, Ros; 0.93 ± 0.23, control; 0.33 ± 0.06) and in human UC biopsies (AS002; 0.91 ± 0.21, Ros; 1.0 ± 0.23, control; 0.33 ± 0.1). Lactate dehydrogenase analysis showed that human biopsies were intact and viable after incubation. In DSS colitis, both preventive and curative applications of AS002 showed a significant improvement on colon length, colonic macroscopic damage and myeloperoxidase levels ($p < 0.05$). Rosiglitazone had significant effects only when administrated before DSS treatment ($p < 0.01$), but had no curative effect when given after DSS

Conclusion: AS002, a novel PPARγ agonist with local action in the gut, prevents and reverses acute colitis induced by DSS in mice, a model for UC. The induction of PPARγ expression in colonic biopsies of UC, suggests that AS002 may be used for treatment of UC, and warrants further studies in UC patients.

Disclosure of Interest: None declared

P1528 POSSIBLE INVOLVEMENT OF 5-HT OVER-SECRETION FROM ENTEROENDOCRINE CELLS OF ILEUM MEDIATED BY INCREASED LYSOPHOSPHATIDYLCHOLINE ACYLTRANSFERASE 3 AND PUFA-PC IN CROHN'S DISEASE

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Introduction: Crohn's disease (CD) has the high incidence of recurrence, impairing quality of life of patients for long period. The precise molecular etiology and the factors underlying the clinical symptoms of CD still remain largely unknown. In this study, we sought out molecules histologically unique to CD to provide novel molecular insight into CD.

Aims & Methods: We compared the distribution of phosphatidylcholine (PC) in the ileum mucosa of CD patients to that of non-CD patients with imaging mass spectrometry (IMS). We further analyzed the expression and localization of lysophosphatidylcholine acyltransferase 3 (LPCAT3) with quantitative RT-PCR (qPCR), immunohistochemical staining, and immunoelectron microscopy. We finally examined whether the secretion of hormone was regulated by LPCAT3 in enteroendocrine cells.

Results: IMS showed the overt accumulation of polyunsaturated fatty acid (PUFA)-containing PC, PC(36:4), PC(38:4), and PC(38:5), in the crypt-rich deep region of ileum mucosa in CD patients ($p < 0.01$ for non-CD patients). qPCR revealed the significant increase of LPCAT3 expression in the ileal mucosa of CD patients ($p < 0.05$ for non-CD patients). Immunohistochemical staining showed that the number of LPCAT3-positive cells was significantly increased in crypt of CD ileum ($p < 0.05$ for non-CD patient), especially in chromogranin A-positive enteroendocrine cells ($p < 0.001$ for non-CD). Immunoelectron microscopy revealed that LPCAT3 was increased on secretory granules of enteroendocrine cells in CD patients. LPCAT3 overexpression significantly enhanced ionomycin-stimulated 5-HT secretion from RIN-14B cells ($p < 0.01$ for control).

Conclusion: LPCAT3, an enzyme synthesizing PUFA-containing PC, was increased in ileal enteroendocrine cells of CD patients, and enhanced Ca^{2+}-depedent 5-HT secretion in a culture model. These findings imply that the enhanced LPCAT3 expression induces 5-HT secretion and exacerbates bowel inflammation in CD ileum, and can propose LPCAT3 as a therapeutic target for symptoms of CD.

Disclosure of Interest: None declared

P1529 EPITHELIAL TNFR2 SIGNALING IN THE SETTING OF IBD MAY BE INVOLVED IN THE DEVELOPMENT OF COLITIS-ASSOCIATED CARCINOGENESIS

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Introduction: We have previously reported that NFκB activation in association with specific up-regulation of type 2 receptor for TNF (TNFR2) was observed in the inflamed colonic epithelia and further in colitis-associated cancer (CAC). It has been suggested that prolonged inflammatory bowel diseases (IBD) may promote carcinogenesis in the epithelia, but the role of TNFR2 expression in the setting of CAC has not been elucidated.

Aims & Methods: The aim of this study was to analyze TNFR2 signaling in the colonic epithelial cells in the setting of CAC. A murine colonic epithelial cell line, MOC1, was established by the isolation of 'non-tumor' colonic epithelial cells from wild type mouse (WT) and transformation with SV40 large T antigen to pursue physiological morphology in vitro. For in vivo studies, WT were pre-injected with azoxymethane (AOM) and then administered three times with dextran sodium sulfate (DSS) to induce a model of CAC.

Results: As previously observed in vivo, Western blotting (WB) showed up-regulation of TNFR2 expression in MOC1 cells when stimulated with recombinant (r) IFN-γ. Associated with this, the phosphorylated p65 and IκBα, as well as the protein expression of myosin light chain kinase (MLCK), in these cells were also up-regulated in a rTNF dose-dependent manner. Immunofluorescence and transmission electron microscopies (TEM) revealed that the epithelial NFkB-induced up-regulation of MLCK was associated with induction of the disrupted tight junction (TJ). Such MLCK up-regulation and TJ disruption in MOC1 cells were abrogated by either treatment with anti-TNF mAb (MP6-XT22), TNFR2-specific siRNA or even MLCK inhibitor (ML-7). These results indicate that the epithelial permeability in the context of inflamed colon may be specifically induced by TNFR2 signaling via NFκB activation and MLCK up-regulation in the epithelial cells. Using an animal model of CAC involving AOM and DSS, semi-quantitative PCR revealed that the colonic lamina propria was found to have pro-tumorigenic cytokine production such as IL-1β, IL-6 and MIP-2. Moreover, WB and TEM showed that such up-regulated pro-tumorigenic cytokines in the inflamed colonic tissues were associated with epithelial NFκB activation, TNFR2 and MLCK up-regulations and TJ disruption. Injection with either MP6-XT22 or ML-7 into AOM/DSS-treated mice failed to suppress the severity of colitis. However, these treatments resulted in restored TJ in the colonic epithelial tissues, decreased pro-tumorigenic cytokine production in the colonic lamina propria and reduced CAC development.

Conclusion: Our studies showed that epithelial TNFR2 signaling in the context of IBD may be involved in epithelial permeabilization and pro-tumorigenic cytokine production that result in CAC development. These results suggest that MLCK may be a potential target for the prevention of IBD-associated tumor development in humans.

Disclosure of Interest: None declared

P1530 OLEUROPEIN EXERTS ANTIOXIDANT ACTIVITY AND REDUCES THE EXPRESSION OF COX-2 AND PROINFLAMMATORY CYTOKINES IN CACO-2 CELLS AND COLONIC MUCOSA FROM ULCERATIVE COLITIS PATIENTS

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Introduction: Oleuropein (OLE) is the major secoiridoid of olive tree leaves and its antioxidant and anti-inflammatory activities have been demonstrated in vitro and in vivo animal models.

Aims & Methods: The aim of this study was to investigate the activity of OLE in the colonic mucosa from pts with ulcerative colitis (UC). First, the toxicity, proliferative and antioxidant effects of OLE were assessed in Caco-2 cells using the MTT assay and ELISA (xMark™ Microplate Absorbance Spectrophotometer, Bio-Rad). Cells were treated with different concentrations of OLE for 3 h and then with H2O2. Untreated cells and cells treated with only H2O2 for 1 h stand for negative and positive controls, respectively. Second, biopsies obtained during colonoscopy from 14 pts with active UC (8 M,39-80 yrs, median 59; Mayo score 4-9, median 6) were immediately placed in an organ culture chamber and challenged with or without lipopolysaccaride from *Escherichia coli* (EC-LPS) at 1 μg/mL in the presence or absence of 3mM OLE for 24 h. Levels of cyclooxygenase (COX)-2 and IL-6, IL-8, MCP-1, VEGF, TNFα, IL-1α, IL-1β cytokines were assessed in total protein extracts from treated colonic biopsies and culture supernatant by Western blotting and Biochip Array on Randox Evidence Investigator (Randox Laboratories), respectively.

Results: Treatment with OLE did not show toxicity on Caco-2 cells while significantly improving cell viability when compared with untreated cells (i.e.,

121 ± 16% at 50 mM) or cells treated with only H2O2 (i.e., 67 ± 3% vs 53 ± 6% at 100 mM). In colonic mucosal biopsies from UC pts, levels of COX-2 were significantly lower in samples treated with OLE when compared with untreated (0.67 ± 0.16 a.u. vs 0.84 ± 0.16 a.u., p = 0.03) as well as in samples treated with OLE + ECLPS when compared with those treated with EC-LPS alone (0.80 ± 0.15 a.u. vs 1.06 ± 0.19 a.u., p = 0.003). Accordingly, the level of each of the cytokines IL-6, IL-8, MCP-1, VEGF, TNFα, IL-1α, and IL-1β was significantly lower (p = 0.02 to 0.003) in culture supernatants of colonic samples treated with OLE or OLE + EC-LPS compared with untreated samples or samples treated with EC-LPS alone, respectively.

Conclusion: Non-toxic, proliferative and antioxidant activities of OLE have been demonstrated in epithelial colonic cells. Together with the anti-inflammatory effects exhibited in human ex-vivo experiments, this suggests the possible use of OLE for treatment of UC pts.

Disclosure of Interest: None declared

P1531 LOCAL ROCK INHIBITION ATTENUATES DEVELOPMENT OF INTESTINAL FIBROSIS IN MURINE COLITIS

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Introduction: Intestinal fibrosis is a common complication of Crohn's disease. Fibrotic strictures are an important indication for surgery and current therapies are unable to prevent their development. Rho kinase (ROCK) is a key mediator in TGFß-induced activation of myofibroblasts and a promising anti-fibrotic drug target. However, systemic ROCK inhibition is known to cause significant cardiovascular (CV) side effects. Thus, we investigated the effects of AMA0825, a ROCK inhibitor with Localized Activity on the development of intestinal fibrosis.

Aims & Methods: CV effects of AMA0825 were assessed in spontaneous hypertensive rats (SHR). Disease activity, intestinal fibrosis and inflammation were evaluated in chronic DSS-induced colitis and in adoptive T cell transfer in C57BL6 and SCID mice respectively. In vitro effects on the production of fibrotic and inflammatory mediators were measured in human intestinal fibroblasts (HIF), HT29 colonic epithelial cells and THP1 macrophages. mRNA and protein expression was analyzed by qPCR, Luminex bead assays and immunohisto/cytochemistry.

Results: In SHR, AMA0825 had no CV effects at 10 mg/kg *p.o.* In the chronic DSS model daily treatment of mice with AMA0825 (3 mg/kg *p.o.*) did not induce toxicity nor significant differences in weight loss. At sacrifice, the colonic weight/length ratio was significantly reduced (p = 0.03) as well as Trichrome-positive fibrotic tissue in the distal colon of treated mice (p = 0.003). Lower colonic protein levels of pro-fibrotic cytokines IL6, IL13 and TGFb1-2 were observed, and DSS-induced production of matrix metalloproteinase (MMP) 2, 3 and 9 was prevented in treated mice. Interestingly, transcription of COL1A1 and ACTA2 was profoundly reduced, suggesting decreased activation of colonic myofibroblasts, which was confirmed by αSMA immunohistochemical staining. Although local levels of several pro-inflammatory cytokines (CXCL2, KC, IFNG, TNFα and MCP1) were diminished, inflammatory cell infiltration and myeloperoxidase activity remained unaffected by AMA0825 treatment, suggesting a direct anti-fibrotic effect.

The effect of AMA0825 with respect to a known anti-inflammatory agent (mouse anti-TNF IgG1) was evaluated in the adoptive T cell transfer model. Weight loss was not significantly different. AMA0825 did not affect the anti-inflammatory effect of anti-TNF (both on cytokine and histology level). Differences were found with respect to intestinal fibrosis, confirming the direct effect of ROCK inhibition on fibrosis.

In HIFs, AMA0825 dose-dependently inhibited TGFß1-induced formation of actin stress fibers and expression of COL1A1 and ACTA2. TGFb1-induced production of IL6, TGFß1 and MMP 2, 3 and 12 was also abrogated. AMA0825 did not however affect IL8 secretion from TNF-stimulated HT29 cells or LPS-challenged THP1 cells, which is in line with the lack of a profound anti-inflammatory effect in vivo.

Conclusion: Inhibition of ROCK by oral administration of AMA0825 in mice is safe and profoundly diminishes the development of intestinal fibrosis by suppressing pro-fibrotic expression profiles. These effects are mainly due to direct inhibition of myofibroblast formation and activation and less by suppression of inflammation.

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P1532 TNF-A STABILIZES ATOH1 PROTEIN IN COLITIS-ASSOCIATED COLORECTAL CANCER RESULTING IN ENHANCED MALIGNANT POTENTIAL

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Introduction: The risk of colorectal cancer are increasing among the patients with ulcerative colitis.Colitis-associated colorectal cancer (CAC) has been reported to acquire the enhanced malignant potential, resulting in the poorer prognosis than that of sporadic colorectal cancer. However, how CAC have malignant potential remains unknown. We have previously showed that transcription factor Atonal homolog 1 (Atoh1) was phosphorylated by glycogen synthase kinase 3β (GSK-3β), resulting in the proteasomal degradation of Atoh1 in sporadic colon cancer. It was, however, unclear how Atoh1 is stably expressed in CAC.

Aims & Methods: We aimed to elucidate the effect of Atoh1 expression on malignant potential in CAC. We generated the mCherry-Atoh1 gene to visualize protein expression and introduced it in colon cancer cell line, DLD1. Malignant character was assessed by sphere formation, cell cycle, chemoresistance and cell migration. The phosphorylation of Akt and GSK-3β was assessed by Western blot. immunofluorescence was performed human CAC samples (n = 3) to assess the ecpression of Atoh1 and NF-kB p65.

Results: Treatment with TNF-α induced the expression of Atoh1 protein in DlD-1, resulting in the mucinous phenotype. Moreover, stable expression of Atoh1 protein showed cancer stemness such as sphere-forming ability, cell cycle arrest. Furthermore, Atoh1 also showed enhanced malignant potential such as chemoresistance and cell migration. Western blot analysis revealed that TNF-α stabilized Atoh1 protein by suppressing GSK-3β via Akt activation. Accumulation of NF-kB p65 in nuclei with the expression of Atoh1 was shown in human mucinous CAC specimens.

Conclusion: CAC might acquire enhanced malignant potential by which inflammatory signaling might cancel the degradation of Atoh1 protein.

Disclosure of Interest: None declared

P1533 BUTYRIC ACID ATTENUATES INTESTINAL INFLAMMATION IN MURINE EXPERIMENTAL COLITIS MODELS VIA MILK FAT GLOBULE-EGF FACTOR 8

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Introduction: Butyric acid, a short-chain fatty acid, is one of the main metabolites of intestinal microbial fermentation of dietary fiber. It has been shown to play an important role in maintaining the integrity of the intestinal mucosa, and exerts potent anti-inflammatory effects both *in vitro* and *in vivo*. However, the precise mechanisms underlying those effects have not been fully identified. We explored the therapeutic role of butyric acid via milk fat globule-epidermal growth factor 8 (MFG-E8) in a murine experimental colitis model.

Aims & Methods: We exposed colonic epithelial cells to butyric acid, then extracted total RNA and hybridized the samples on microarray chips. To confirm the effects of butyric acid via MFG-E8 on DSS-induced experimental colitis, we gave intrarectal administrations of butyric acid to C57BL/6N (MFG-E8$^{+/+}$) and MFG-E8$^{-/-}$ mice. We also utilized an enzyme linked immunosorbent assay (ELISA) method to evaluate proinflammatory cytokine production in murine colonic samples.

Results: Among the upregulated genes found in the microarray study, MFG-E8 was elevated approximately 5-fold. Furthermore, the acetyl-H3K9 level around the MFG-E8 promoter region was significantly increased by butyric acid exposure in a time-dependent manner. Intrarectal administration of butyric acid during an acute phase of colitis attenuated intestinal inflammatory parameters and inhibited body weight loss only in WT mice but not in MFG-E8$^{-/-}$ mice.

Conclusion: Our novel findings suggest that butyric acid has significant anti-inflammatory effects partly via MFG-E8 on DSS-induced murine experimental colitis.

Disclosure of Interest: None declared

P1535 INTERLEUKIN-19 IS CRITICAL FOR THE DEVELOPMENT OF ACUTE TNBS-INDUCED COLITIS IN MICE

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Introduction: Inflammatory bowel diseases (IBD) result from the chronic dysregulation of the mucosal immune system and the aberrant activation of both the innate and the adaptive immune responses. Interleukin-19 (IL-19) is a member of the IL-10 family of cytokines. The last 10 years from the finding of IL-19, investigations underline the role of IL-19 in the immunological diseases. However, little is known about the exact biological role of IL-19 in IBD.

Aims & Methods: We have used 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis models to examine the roles of IL-19 in colonic inflammation and thus its possible role in IBD. Using gene-targeting, we generated IL-19-deficient mice. To study the activation of the immune response during colonic inflammation, we used a TNBS-induced colitis model that is associated with the expansion and accumulation of activated T cells in the colon.

Results: We show that IL-19-deficient mice are more susceptible to experimental acute colitis induced by TNBS, evaluated by body weight changes, leukocyte infiltration and epithelial cell damage. Furthermore, TNBS administration to WT mice revealed that the expression of IL-19 mRNA was induced in distal colon on day 1. This increased susceptibility was correlated with increased production of IFN-gamma, IL-12, IL-22, and IL-33 by the distal colon of mice. We next examined the levels of several types of cytokines in lymph node cells. Cells isolated from lymph nodes of IL-19-deficient mice with TNBS-induced colitis produced elevated amounts of IL-1alpha, IL-6, IL-12, IL-17, and IFN-gamma upon stimulation with anti-CD3 and anti-CD28 antibodies in vitro. In contrast, IL-2 and IL-4 levels were markedly decreased in lymph node cells isolated from IL-19-deficient mice with TNBS-induced colitis.
Conclusion: Using this model, our results revealed a crucial role for IL-19 in the control of colonic inflammation. The finding that IL-19 drives pathogenic adaptive immune responses in the colon suggests that the selective targeting of IL-19 may be an effective therapeutic approach in the treatment of human IBD.
Disclosure of Interest: None declared

P1536 MIR-124 REPRESSES GROWTH OF INTESTINAL EPITHELIAL CELLS BY TARGETING SNIP1 IN CROHN'S DISEASE

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Introduction: Environmental factors are believed to contribute to the increased prevalence of Crohn's disease (CD). In response to environmental stimuli, intestinal epithelial cells (IECs) elicit rapid changes in gene expression patterns to maintain epithelial homeostasis. Therefore, the integrality of epithelium and epithelial homeostasis have pivotal roles in improving pathophysiology and clinical outcomes of CD. Recently, microRNAs (miRNAs) have emerged as master regulators of intestinal epithelial homeostasis. However, the biological functions of aberrant expressed miRNAs in CD remain largely elusive. The balance of proliferation and death of IECs is also widely considered as an important factor to maintain the gut epithelial homeostasis. Smad nuclear interacting protein 1 (SNIP1) regulates the stability of cyclin D1 (CCND1) mRNA, which indicates that SNIP1 may play a role in cell proliferation. We therefore examined miRNA level in colon tissues and studied the potential functions of miRNAs that regulate SNIP1 during pathogenesis of CD.
Aims & Methods: To investigate the roles of SNIP1 expression-associated miRNAs in disruption of IECs, miRNAs were assayed in the inflamed colon biopsies of CD patients by microarray. The expressions of miR-124 and SNIP1 mRNA were assessed by quantitative real-time polymerase chain reaction (qRT-PCR), SNIP1 protein level was identified by western blot analysis and immunohistochemistry. Bioinformatics analysis and luciferase reporter assay were used to predict and test the direct binding of miR-124 to the target gene SNIP1, respectively. The effects of upregulation or downregulation of miR-124 on colonic epithelial cell lines were confirmed by CCK-8 assay and cell-cycle analysis. The levels of SNIP1 and CCND1 were determined by qRT-PCR and western blot analysis subsequently. Then we investigated whether overexpression of SNIP1 is sufficient to reverse the inhibitory effect of miR-124 on SNIP1 and downstream CCND1 expressions. The role of miR-124 was further studied in the 2,4,6-trinitrobenzene sulfonic acid (TNBS)–induced colitis mice by intracolonic administration of miR-124 inhibitor.
Results: The expression of miR-124 was significantly upregulated in colon tissues of active CD patients. An inverse correlation between miR-124 and SNIP1 protein levels was observed predominantly. By overexpressing or knocking down miR-124 in HT-29 and Caco-2 colonic epithelial cells, we experimentally validated that miR-124 is a direct regulator of SNIP1 *in vitro*. Overexpression of miR-124 suppressed SNIP1 and CCND1 protein expressions, inhibited cell proliferation, and altered the cell cycle by decreasing S-phase and increasing G1 phase. Forced overexpression of SNIP1 strikingly upregulated SNIP1 and CCND1 protein expressions and partly rescued the inhibitory effect of miR-124 on HT-29 and Caco-2 cells proliferation. *In vivo*, downregulation of miR-124 in the TNBS-induced colitis colon alleviated experimental colitis. Mice treated with anti-miR-124 experienced dramatic decreases of DAI levels and histological scores. Simultaneously, an appreciable improvement of macroscopic inflammation was also observed.
Conclusion: Together, this study presents the first evidence that miR-124 plays a critical role in disturbing epithelial homeostasis through inhibiting SNIP1 expression and subsequently triggering CCND1 degradation in CD.
Disclosure of Interest: None declared

P1537 MELATONIN TREATMENT MODULATES INTESTINAL MICROBIOTA ON DSS-INDUCED COLITIS

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Introduction: Melatonin has strong anti-inflammatory potentials in the GI tract. On our previous study, melatonin reduces various inflammatory cytokines on colon tissues and accelerates recovery from injured mucosa. We aimed to know the effect of melatonin on intestinal microbiota.
Aims & Methods: We used 3 groups of C57BL/6 mice. Group I: control, Group II: chronic colitis group: 2% DSS for 7 days and followed 2 weeks for recovery and then readministered 2% DSS for 7 days, Group III: chronic colitis with melatonin group: add daily melatonin treatment. Melatonin (10mg/kg) or saline was injected daily by intraperitoneal route. The mice were sacrificed on 28th day. Stool were collected during last 2 days. Genomic DNA from feces was extracted. After amplification of genomic DNA using barcoded primers targeting the V1 to V3 regions of bacterial 16S rRNA genes, pyrosequencing was performed.
Results: Fecal microbial analysis demonstrated that Firmicutes to Bacteroidetes ratio (F/B ratio) is 0.19in Group I, 0.38 in Group II and 0.21 in Group III. Melatonin treatment significantly decreased F/B ratio comparing with DSS colitis group ($p = 0.015$). The increase in bacteroidetes is mainly due to increased bacteroidaceae and prevotellaceae. The decrease in Firmicutes is due to decreased lactobacillaceae and erysipelotrichaceae. On principal coordinates analysis, three groups showed clearly separated each other. A phylogenic tree analysis using MOTHUR showed melatonin treatment group was more close to control Group.
Conclusion: This study showed that DSS induced colitis changed structure of intestinal microbiota. Melatonin treatments on DSS colitis could modulate intestinal microbiota and change them close to control.
Disclosure of Interest: None declared

P1538 PATIENT REPORTED-OUTCOMES IN A NATIONWIDE SURVEY AMONG INFLAMMATORY BOWEL DISEASE PATIENTS: THE BURDEN OF INFLAMMATORY BOWEL DISEASE (B.I.R.D) STUDY

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Introduction: Patient reported-outcomes (PROs) have emerged as a major therapeutic goal in inflammatory bowel disease (IBD) in both clinical practice and clinical trials.
Aims & Methods: Between January to June 2014, the main PROs questionnaires were completed by patients issued from the French national association of IBD patients (association Francois Aupetit (AFA)): quality of life (QOL) (Short IBD questionnaire [SIBDQ] + the Short-Form-36 [SF-36]), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F]), work productivity (and Activity Impairment [WPAI]), disability [IBD disability index], and anxiety/depression (Hospital Anxiety and depression scale [HADS]). Simple and multiple regressions were performed to identify factors associated with PROs.
Results: 1211 patients with IBD (females: 61.2%, median age: 45 years. Crohn's disease: 61.2%) could be analyzed. Median disease duration was 13 years. About one third of IBD patients have moderate to severe disease (Harvey-Bradshaw Index ≥ 8 and Walmsley score ≥ 6) and/or history of surgery (29.6%, n = 359), with a stoma in 8.4% (n = 99) (definitive: 39.4%, n = 39) of patients. Ongoing medications were oral 5-aminosalicylates (33.4%), thiopurines (26.2%) and/or anti-Tumor necrosis factor therapy (32.2%). Half of the population reported a low QOL (SIBDQ < 45: 53.1%), a severe fatigue (FACIT-F < 30: 46.8%), and/or a depression (HAD-D > 7: 48.9%). One third of patients had anxiety (HAD-A > 7: 29.8%) and/or moderate (23.8%) or severe (9.9%) disability. Of the 39.7% patients having a job, absenteeism was rare whereas presenteeism, work impairment and overall work impairment were moderate to severe in about one third of patients. Factors associated with a low QOL, severe fatigue, severe disease disability and/or depression were women, unemployment, severe disease activity and tobacco. Altered QOL was also associated with history of surgery and current use of steroids and/or anti-TNF. Obesity and age at diagnosis greater than 30 years were associated with severe fatigue and severe disability, respectively.
Conclusion: Disease burden is very high in IBD patients, with impaired QOL, disability, fatigue, work impairment and anxiety/depression. This is the first nationwide study addressing this issue and investigating all dimensions of PROs in a large cohort of IBD patients.
Disclosure of Interest: None declared

P1539 PRESENCE OF ANAEMIA IS AN INDICATOR OF LONG-TERM DISEASE COURSE IN INFLAMMATORY BOWEL DISEASES. RESULTS FROM A POPULATION-BASED INCEPTION COHORT

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Introduction: Anaemia is an important extraintestinal manifestation in inflammatory bowel disease (IBD) and it is partly associated to disease activity. Limited data are available on the association between different forms of anaemia and disease outcomes.

Aims & Methods: The aim of this study was to analyze the association between the prevalence of different forms of anaemia and treatment strategy and long-term disease outcomes in the population-based IBD inception cohort from Veszprem province between 1977 and 2012. Data of 506 incident CD patients (male/female: 251/255, age at diagnosis: 31.5 years, SD 13.8 years) and 347 incident UC patients (m/f: 200/147, median age at diagnosis: 36, IQR: 26-50 years) diagnosed between January 1, 1977 and December 31, 2010 were analyzed. Both in- and outpatient records were collected and comprehensively reviewed.
Results: Anaemia (iron deficiency, anaemia of chronic diseases or macrocytic anaemia) was present in 57.5% and 30.2% of CD and UC patients. Anaemia was associated to age at onset ($p_{CD}=0.001$, $p_{UC}=0.026$), location/extent ($p_{CD}=0.016$, $p_{UC}<0.001$), perianal fistulas ($p<0.001$) and complicated behavior ($p=0.002$)/time to behavior change ($p_{LogRank}<0.001$). In contrast, there was no association with gender and smoking status in either CD or UC. Need for steroids and/or azathioprine was significantly associated to anaemia in both CD and UC ($p<0.001$ for all both univariate and logistic regression). In addition, anaemia was associated with the need for anti TNF ($p=0.002$), time to azathioprine ($p_{LogRank}<0.001$, $p_{Cox}<0.001$), need for ($p<0.001$) and time to surgery ($p_{LogRank}<0.001$, $p_{Cox}<0.001$) and time to IBD-related hospitalization ($p<0.001$) in CD. In UC, anaemia, was associated with the need for colectomy ($p=0.004$, OR: 5.57, 95%CI: 1.67-18.54) and time to IBD-related hospitalization ($p<0.001$, $p_{Cox}<0.001$).
Conclusion: Anaemia is an indicator of long-term disease course, including treatment steps, hospitalizations and surgery requirements in both CD and UC.
Disclosure of Interest: None declared

P1540 ARE EXTRAINTESTINAL MANIFESTATIONS ASSOCIATED WITH DISEASE OUTCOMES IN INFLAMMATORY BOWEL DISEASES? RESULTS FROM THE VESZPREM POPULATION BASED INCEPTION COHORT DATABASE

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Introduction: Association between extraintestinal manifestations (EIM) and disease activity suggest a common pathogenic link. Limited data are available on the effect of EIMs on the long-term disease course in inflammatory bowel diseases (IBD).
Aims & Methods: The aim of this study was to analyze the association between the presence of EIMs (joint, skin, eyes) and treatment steps and long-term disease outcomes in the population-based inception cohort in the Veszprem province database after 1977. A well-characterized Hungarian cohort of 506 incident cases with Crohn's disease (male/female: 251/255, age at diagnosis: 31.5 years, SD 13.8 years) diagnosed from January 1, 1977 were included and data of 347 incident UC patients diagnosed from January 1, 2002 were analyzed (m/f: 200/147, median age at diagnosis: 36, IQR: 26-50 years, duration: 7, IQR 4-10 years). Follow-up data were collected until December 31, 2012. Both in- and outpatient records were collected and comprehensively reviewed.
Results: EIMs (Joint, skin and eyes) were present in 32.2% of the CD and 17.3% of the UC patients. Presence of EIMs was associated in both CD and UC with female gender ($p_{CD}=0.01$, $p_{UC}=0.07$), with ileocolonic and extensive location ($p_{CD}=0.009$, $p_{UC}=0.003$). In CD, there was an association with smoking ($p<0.001$), but not in UC. No association was found in both CD and UC between the presence of EIMs and need for surgery/colectomy. Presence of EIMs was associated with the need for azathioprine ($p_{CD}<0.001$; $p_{UC}=0.004$) and need for steroids ($p_{CD}<0.001$, $p_{UC}<0.001$) in both diseases, and with need for anti-TNFs in CD ($p<0.001$). In Kaplan-Meier analysis there was an association between the presence of EIMs and time to first UC-related hospitalization ($p=0.002$).
Conclusion:: In IBD, the presence of EIM was associated higher maximum treatment steps during the disease course including need for steroids, azathioprine. In CD, there was an association with anti-TNF therapy while in UC with the need for hospitalization.
Disclosure of Interest: None declared

P1541 SUBJECTIVE PAIN IN CROHN'S DISEASE PATIENTS AFFECTS THEIR PSYCHOLOGICAL FUNCTIONING AND COPING STRATEGIES. A SURVEY OF A COMMUNITY-BASED COHORT

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Introduction: Crohn's disease patients report varying levels of bodily pain, but the relationship of pain with psychological functioning in response to stress and the coping mechanisms used to deal with their illness is poorly understood. We investigated this issue in a community cohort of Crohn's patients.
Aims & Methods: Consecutive adult Crohn's disease patients were recruited from IBD clinics in 5 tertiary hospitals and from our website call, and filled out their demographics, disease status, Harvey-Bradshaw Index (HBI), SF-36 and SIBDQ questionnaires. Patients also completed 5 social questionnaires: Brief Symptom Inventory (BSI, measures psychological symptoms), Carver's COPE (evaluates coping strategies in disease), Family Assessment Device (FAD, measures family functioning and support), Satisfaction with Life Scale (SWLS), and WPAI. Questions related to pain in HBI, SF-36 and SIBDQ were formulated into 3 sub-scores for analysis of correlations with the social questionnaires, using parametric and nonparametric statistics.
Results: Significant Associations of SF-36 Pain with COPE.

COPE SUBSCALE	no pain	mild pain	severe pain
Self-distraction	5 (1,8)	6 (1,8)	6 (1,8)
Denial	2 (1,8)	2 (1,8)	3 (1,8)
Substance use	2 (1,8)	2 (1,8)	2 (2,8)
Emotional support	4 (2,8)	4 (1,8)	5 (2,8)
Behavioural disengagement	2 (1,8)	2 (1,8)	2 (1,8)
Venting	3 (1,8)	4 (1,8)	4 (2,8)
Planning	5 (2,8)	6 (1,8)	6 (1,8)
Acceptance	ns	ns	ns
Religion	2 (2,8)	2 (1,8)	3 (1,8)
Self-blame	3 (2,8)	4 (1,8)	4 (1,8)

The cohort comprised 439 patients, aged mean (± SD) 39.5 ± 14.6 years; women 60.4%; economic status: low 19.6%, moderate 50.3%, high 26.0%. Mean HBI (± SD) was 4.81 ± 5.05, median (min; max) 4 (0; 27). Pain was reported as follows: HBI – none 41.1%, mild 33.2%, moderate/severe 25.7%; SF-36 - none 15.8%, mild 33.7%, moderate/severe 50.5%; SIBDQ – never 29.4%, not much 38.8%, a lot 31.8%. There was more pain reported by HBI (correlation, $p<.01$) and SF-36 ($p<.05$) in females, and by HBI, SF-36 and SIBDQ (all $p<.001$) in poorer patients. There was more pain revealed by HBI, SF-36 and SIBDQ (all $p<.001$) in patients with a higher BSI-GSI (Global Severity Index), and by HBI, SF-36 and SIBDQ (all $p<.003$) in those with poor family functioning. The amount of pain documented by HBI, SF-36 and SIBDQ (all $p<.001$) correlated with WPAI, for "time missed", "percent impairment", "work impairment", and "activity impairment". There was less pain reported by HBI, SF-36 and SIBDQ (all $p<.003$) in patients with higher SWLS. Pain by SF-36 had significant associations with most COPE subscales [Table, values are median (min,max)], likewise for pain measured by HBI and SIBDQ.
Conclusion: HBI, SF-36 and SIBDQ agreed strongly in their assessment of pain. More pain was associated with high psychological stress, poor family functioning and inability to work. More pain required greater use of coping mechanisms, some of which were negative. Less pain meant greater satisfaction with life. IBD specialists can improve patients' well-being by reducing bodily pain.
Disclosure of Interest: None declared

P1542 EARLY CLINICAL COURSE OF INFLAMMATORY BOWEL DISEASE IN THE FIRST POPULATION-BASED INCEPTION COHORT STUDY FROM EIGHT COUNTRIES IN ASIA AND AUSTRALIA

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Introduction: Inflammatory bowel disease (IBD) is increasing globally but data on natural history of IBD in population-based settings in Asia are limited.
Aims & Methods: IBD cases diagnosed between 2011 and 2013 were prospectively followed-up and changes in disease phenotype, probability of medical therapy and surgery were assessed using Kaplan-Meier analysis.
Results: 403 IBD patients [222 ulcerative colitis (UC); 181 Crohn's disease (CD); median age 37 years] followed-up for 608 person-years and median of 18 months (Interquartile range, IQR: 12-23) were included. Cumulative probability of CD behavior change from inflammatory to stricturing or penetrating disease was 19.8%. Isolated terminal ileal disease was associated with a three-fold increased risk of change in behavior (HR, 3.67; 95% CI, 1.04-13.03). Cumulative probability of immunosuppressants and biologics was 58.1% and 11.3% for CD, and

13.0% and 0.9% for UC, respectively. Perianal CD was associated with an increased risk of biologics in the first year (HR 2.62; 95% CI, 1.04-6.59). Cumulative probability of surgery at one year was 9.4% for CD and 0.9% for UC. Patients with penetrating CD have a greater than five-fold increased risk of surgery (HR 5.94; 95%, CI, 1.91-18.48). At one year, the cumulative probability of colectomy for UC was 1.1% in Asia and 0% in Australia. Cancer was reported in 1.5% of patients. Overall mortality rate was 0.7%.
Conclusion: This prospective population-based study showed that early disease course in IBD patients in Asia was comparable to that of Western patients. Progression to complicated disease behaviour and acceleratedn use of immunosuppressants is common in CD. Early surgical rate for UC is low in Asia. Understanding the natural history of IBD in our population can help optimise therapeutics interventions.
Disclosure of Interest: None declared

P1543 INCIDENCE OF INFLAMMATORY BOWEL DISEASE ACROSS 13 COUNTRIES IN ASIA-PACIFIC IN 2011-2013: RESULTS OF THE ASIA-PACIFIC CROHN'S AND COLITIS EPIDEMIOLOGIC STUDY

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Introduction: The Asia-Pacific Crohn's and Colitis Epidemiologic Study (ACCESS) study determined incidence of adult inflammatory bowel disease (IBD) in Asia-Pacific.
Aims & Methods: Incident cases diagnosed from 2011 to 2013 across 18 centres and 13 countries in Asia and Australia were prospectively enrolled. Endoscopy, pathology and pharmacy records were reviewed for complete case capture. We analysed incidence, demographics and disease phenotype.
Results: 1,106 new IBD patients (2011, n = 419; 2012, n = 687; 131 Australia) were identified [606 ulcerative colitis (UC), 463 Crohn's disease (CD), 37 indeterminate colitis (IC)]. Mean annual incidence for IBD per 100,000 was 1.79 (95% CI, 1.66-1.93) in Asia and 21.83 (95% CI, 18.25 – 25.91) in Australia. The three countries with the highest incidence in Asia was India (7.2; 95% CI, 6.39-8.09), Mainland China (3.64; 95% CI, 2.97-4.42) and Hong Kong (2.98; 95% CI, 2.58-3.44). In Asia, annual incidence for IBD was 0.94 in 2011 and 1.69 in 2012. Mean age of diagnosis was 40 (IQR 27-52) and median time from symptom to diagnosis was 5 months (IQR 1-15). UC:CD in Asia and Australia was 0.67 and 1.51, respectively. There were more male patients (58%). Disease behavior (B1: 85.1%, B2: 26.5%, B3: 6.2%, perianal: 19.8%), location for CD and UC did not differ from previous year. 11.3% of CD were current smokers. Complicated CD was more common in Asia than Australia (45.1% vs 23.3%; $P = .001$). A family history of IBD was less common in Asia (2.3% vs 19.2%; $P < .001$).
Conclusion: This large-scale population-based study shows the incidence of IBD to be lower than the West, but continues to increase in Asia. The ACCESS inception cohort reflects the true incidence of IBD in Asia. Global variation in disease incidence supports environmental influence in disease development.
Disclosure of Interest: None declared

P1544 THE RISK OF OSTEOPOROSIS IS NOT INCREASED IN MICROSCOPIC COLITIS

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Introduction: Patients with microscopic colitis (MC) are often elderly postmenopausal woman and hence have an increased risk of developing osteoporosis. Due to chronic inflammation and relapsing disease patients may be exposed to significant cumulated doses of Budesonide. This may result in systemic effects and compromise bone-quality and –mass, resulting in increased fracture risk. The prevalence of osteopenia and osteoporosis in MC is unknown. The primary purpose of this study was to evaluate bone mineral density (BMD) in patients with MC, and secondary to evaluate the influence of Budesonide on bone mineral status and its effect on adrenal gland function.
Aims & Methods: It was a cross-sectional study including patients with documented MC and disease activity within the last 2 years. Exclusion criteria were prednisolone treatment within the last 6 month, malignancy, other chronic diseases of the gastrointestinal tract, liver, pancreas or small bowel resection. Bone mineral density (BMD) was measured with Dual Energy X-ray Absorptiometry (DXA) in hip and spine. Cumulative budesonide dosage until 3 years before inclusion was extracted from online prescription data, medical charts and patient interview. Adrenalcorticotropic hormone (ACTH) measurements and short ACTH–test were performed. Results were compared with gastrointestinal healthy age and sex-matched controls. Non parametric tests were applied.
Results: Fifty patients, 44 women, with MC participated, (35 with collagenous colitis, 15 with lymphocytic colitis). Median age 67 (range 45-93); median disease duration 28 month (range 2-163); median cumulative budesonide dosage was 1008 mg (range 0-5400). Patients with MC were significantly more often smoker (36%) than the control group (10%) (p = 0,001). No difference in other known risks factors for osteoporosis was detected; sex, age, age of menopause, family history or BMI level. No difference in ACTH levels between patients with MC and controls existed. Short ACTH test was normal in all patients (n = 35).
BMD did not correlate with disease duration/time since MC diagnosis while cumulative budesonide dose was associated with lower BMD in hip (Spearman's rho; p = 0.007) and spine (p = 0.021).

	MC (n = 50)	Controls (n = 49)	P-value
Osteopenia*, n(%)	22 (44%)	15 (31%)	0,23
Osteoporosis§, n(%)	6 (12%)	4 (8%)	0,23
T-Score hip, (median & range)	–0,80(-3,12 – +2,02)	–0,60(-2,3 – +1,0)	0,16
T-Score spine, (median & range)	–0,65(-4,03 – +3,22)	–0,45(-3,0 – +1,8)	0,87
BMD hip (g/cm^2), (median & range)	0,848(0,571 – 1,197)	0,866(0,091 – 1,101)	0,48
BMD spine (g/cm^2), (median & range)	0,952(0,160 – 1,327)	1,021(0,718 – 1,242)	0,77

* Def: -1 < T-score > -2,5§ Def: T-score < -2,5

Conclusion: The risk of osteoporosis in patients with MC is not increased. However the cumulative amount of budesonide is associated with lower BMD - directly or confounded by indication. Supplementation of calcium and D-vitamin is recommended. Long-term budesonide treatment does not affect adrenal gland function and seems safe in patients with MC.
Disclosure of Interest: S. Wildt Financial support for research: Dr Falk Pharma, Conflict with: Advisory board member in Tillots, MSD, M. Hitz Conflict with: Lilly and Amgen, S. Becker: None declared, H. Brockstedt: None declared, O. Bonderup Conflict with: Dr Falk Pharma. Advisory board member in Tillots, L. Munck Conflict with: Dr Falk Pharma, AMGEN

P1545 VITAMIN D DEFICIENCY; PREVALENCE, SEASONAL VARIATION AND CLINICAL ACTIVITY IN INFLAMMATORY BOWEL DISEASE

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Introduction: Vitamin D deficiency is common in Inflammatory Bowel Diseases (IBD) especially in patients with Crohns disease. The reported prevalence differs between 16-95%. Moreover vitamin D deficiency has been associated with active disease and smoking. The incidence of IBD increases with higher latitude and is more frequently diagnosed in the winter when vitamin D levels are lower. These observations support the importance of vitamin D in IBD.
Aims & Methods: The aims of the study were to determine the prevalence of vitamin D deficiency, seasonal variation and association between vitamin D deficiency and disease activity. Outpatients with an established diagnosis of IBD were recruited as a part of a Norwegian multicenter study. Serum 25OH vitamin D3 was analyzed at the same laboratory. Clinical and epidemiological data were collected by interview or from medical records. Possible associations between vitamin D and relevant variables was investigated with t-test, Chi-square and Pearson correlation coefficient.
Results: A total of 411 patients, CD; n = 231 (56%), UC; n = 180 (44%), agreed to participate in the study. Overall, mean age was 40.8 years and 50.9% of the included were men. There were no significant differences between UC and CD with regard to age and gender. Mean disease duration was 8.8 years in UC and 13.6 years in CD. In UC 57% (102/180) had extensive colitis, while 65% (151/231) of CD patients had small bowel involvement (L1 +L3) and 21% (48/231) colonic disease (L2). 40% (166/411) were on current treatment with anti-TNF. Vitamin D status (25OH) was complete in 408/411 patients, and vitamin D

deficiency (25OH vitamin D < 50 nmol/L) was found in 49% (200/408). In CD 53% were deficient, while the comparable number in UC was 44% (p = 0.07). Very low values (<25 nmol/L) with a potential risk to bone health, were measured in 8% (32/408). Of the included patients, 51.8 vs 48.2% had their 25OH level measured during summer and winter, respectively. Vitamin D levels < 50 nmol/L were more common in the winter than in the summer, 56 vs 43%, respectively (p = 0.01). Mean vitamin D levels between summer and winter were: UC; 59.5 vs 49.3 nmol/L (p = <0.01), CD; 53.5 vs 48.4 nmol/L (p = 0.08). In CD vitamin D deficiency was associated with higher SCDAI score (p < 0.05), but no such association was seen with SCCAI scores in UC (p = 0.13). CRP, calprotectin, gender and smoking were not associated with vitamin D deficiency in either of the two patient groups.
Conclusion: Vitamin D deficiency in this IBD population was common, and most common in CD. UC patients had a greater seasonal variation than CD patients. Increased disease activity was associated with vitamin D deficiency in CD.
Disclosure of Interest: None declared

P1546 SURGERY AND HOSPITALIZATION RATES DURING THE FIRST YEAR AFTER DIAGNOSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES FROM THE 2011 ECCO-EPICOM INCEPTION COHORT

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Introduction: The ECCO-EpiCom study investigates the differences in the incidence, disease characteristics and therapeutical management of inflammatory bowel diseases (IBD) between Eastern and Western Europe.
Aims & Methods: The aim of this study was to analyze the differences in the surgery and hospitalization rates in the 2011 ECCO-EpiCom inception cohort within the first year after diagnosis. Fourteen European (9 Western and 5 Eastern European centers) and one Australian center with 258 Crohn's disease (CD), 380 ulcerative colitis (UC) and 71 IBD unclassified (IBDU) patients (65% from Western, 25% from Eastern Europe, 10% from Australia; female/male: 326/383; mean age at diagnosis: 40.9 years, SD: 17.3 years) participated in the one-year follow-up. Patients' data regarding disease characteristics, surgical procedures and hospitalizations were registered and entered in the web-based ECCO-EpiCom database every third month during the first 12 months after diagnosis.
Results: In Eastern Europe, significantly more CD patients were hospitalized compared to Western Europe/Australia within the first year after diagnosis (34% vs. 21%, p = 0.02, pLogRank = 0.01). Patients with L3 ± L4 (ileocolonic ± upper GI, $pLogRank_{L3} = 0.007$, $pLogRank_{L3+L4} < 0.00$) and complicated disease behavior ($pLogRank_{B1\ vs\ B2/B3} < 0.001$, $pLogRank_{B2\ vs\ B3} = 0.05$) were more frequently hospitalized. In UC, we did not find a geographic difference in the hospitalization rates during the first year (16% vs. 16%, p = 0.93). In CD, more Eastern European patients underwent a surgical procedure within the first year after diagnosis (pLogRank = 0.001). Of note, this was associated to ileal only location and stenotic behavior ($pLogRank_{B2} = 0.09$, $pLogRank_{L1} = 0.008$). Overall, the disease behavior was the major driver for both hospitalization and surgery ($pLogRank_{hosp} < 0.001$, $pLogRank_{surg} < 0.001$). The majority of the surgical procedures were performed within a short time period after diagnosis. In UC, only 1 patient underwent colectomy.
Conclusion: In Eastern Europe, a significantly higher percentage of CD patients had surgery and were hospitalized compared to Western Europe/Australia within the first year after diagnosis. Disease behavior was the major predictor for both surgery hospitalization. In contrast, both hospitalization rates and risk for colectomy was low in UC.
Disclosure of Interest: None declared

P1547 TREATMENT STRATEGY DURING THE FIRST YEAR AFTER DIAGNOSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES FROM THE 2011 ECCO-EPICOM INCEPTION COHORT

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Introduction: The ECCO-EpiCom study aims to investigate the differences in the incidence, disease characteristics and therapeutical management of inflammatory bowel diseases (IBD) between Eastern and Western Europe.
Aims & Methods: Our aim was to analyze the differences in the therapeutical strategy in the 2011 ECCO-EpiCom inception cohort within the first year after diagnosis. Fourteen European (9 Western and 5 Eastern European centers) and one Australian center with 258 Crohn's disease (CD), 380 ulcerative colitis (UC) and 71 IBD unclassified (IBDU) patients (65% from Western, 25% from Eastern Europe, 10% from Australia; female/male: 326/383; mean age at diagnosis: 40.9 years, SD: 17.3 years) participated in the one-year follow-up. Patients' data regarding disease characteristics and medical therapy were registered and entered in the web-based ECCO-EpiCom database every third month during the first 12 months after diagnosis.
Results: Both in CD and UC, a significant difference was found in the probability of highest treatment steps reached within one year after diagnosis between Eastern and Western Europe and Australia (in CD p = 0.001, and in UC p = 0.003 for the maximum treatment steps at one-year between Eastern Europe and Western Europe/Australia). Overall, the disease behavior (B2 and B3) was the driver for immunosuppressive (IS) therapy (pLogRank < 0.001). In Eastern Europe, the total 5-ASA use was higher in patients with L1 (ileal) localization and B1 (non stricturing-non-penetrating) disease behavior (pLogRank = 0.001), in L3 (ileocolonic) location received earlier and more IS (pLogRank = 0.037). In Western Europe/Australia significantly more CD patients were treated with biological therapy (p = 0.04) compared to Eastern Europe. Overall, penetrating disease behavior was the driver for biological therapy (pLogRank = 0.035). In UC, patients in Western Europe/Australia received more steroids (43% vs. 26%, p = 0.03, pLogRank = 0.01) compared to Eastern Europe, however disease extent was not different. In contrast, time to 5ASA, IS, biological therapy and colectomy was not different between Eastern and Western Europe/Australia. Time to 5-ASA and steroid treatment was dependent on the extent ($pLogRank_{5ASA} = 0.007$ and $pLogRank_{steroid} < 0.001$).
Conclusion: We found a significant difference in the maximum treatment step in both CD and UC during the first year after the diagnosis between Eastern and Western Europe/Australia, with higher exposure to biologicals and lower exposure to 5ASA in CD patients in Western Europe/Australia, while only steroid exposure was different in UC.
Disclosure of Interest: None declared

P1548 NATIONWIDE PREVALENCE OF INFLAMMATORY BOWEL DISEASES IN HUNGARY. A POPULATION-BASED STUDY BASED ON THE NATIONAL HEALTH INSURANCE FUND DATABASE

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Introduction: Regional studies on inflammatory bowel disease (IBD) suggest an increasing prevalence over time, but no nationwide estimate has been published so far.
Aims & Methods: To estimate the IBD prevalence in 2013 in Hungary overall, by disease, and in specific patient segments. Patients were identified according to international classification codes for ulcerative colitis (UC) and Crohn's disease (CD) in in-patient care, day surgery, non-primary out-patient care and drug prescription databases (2011–2013) of the National Health Insurance Fund (OEP), the only nationwide state-owned health insurance provider in Hungary.
Results: Requiring two or more diagnoses of IBD in non-primary care, a total of 55 039 individuals (men: 44.6%) with physician-diagnosed IBD were alive in Hungary in 2013, corresponding to a prevalence of 0.55% (95% CI, 0.55–0.56). The prevalence of CD 0.20% (95% CI, 0.19–0.20), and UC was 0.34% (95% CI, 0.33–0.34). The prevalence both in men and women was highest in the 20-39 year-olds in CD, while it increased with age in UC, and peaked at ages 60–69 years. Prevalence of actively treated disease (defined as two or more IBD-related visits, plus at least yearly one dispensed prescription of IBD-related drugs in 2011-2013) was 0.31% (95% CI, 0.31–0.32), 0.13% (95% CI, 0.27–0.28) in CD and 0.18% (95% CI, 0.17–0.18) in UC.
Conclusion: The Hungarian IBD prevalence based on nationwide database of the National Health Insurance Fund was higher compared with previous estimates based on the Veszprem IBD cohort. While prevalence estimates were robust across different case definitions, once two or more non-primary out-patient care visits were required, only about 60% of prevalent patients were receiving regular IBD-related medical therapy.
Disclosure of Interest: None declared

P1549 CHANGES OF THE COLONIC WALL STRUCTURE PRECEDE MUCOSAL HEALING IN PATIENTS WITH ACUTE INFLAMMATORY BOWEL DISEASE UNDERGOING ANTI-INTEGRIN THERAPY – PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

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Introduction: Mucosal healing has become an established endpoint to prove the efficacy of new drugs in the therapy of inflammatory bowel disease (IBD). Vedolizumab (Vedo) blocks the translocation of inflammatory cells from the blood stream to the mucosal compartment by binding to a4β7-integrin. Although mucosal healing has been demonstrated in phase III trials in ulcerative colitis (UC), the endoscopic benefit of anti-integrin therapies seems to be delayed. No data are available that demonstrate Vedo induced mucosal healing in Crohn's disease (CD).

Aims & Methods: Aim: In a subgroup of patients within a larger prospective open label trial we examined the effect of Vedo on endoscopic mucosal healing and mucosal histopathology in comparison to inflammatory changes of the colonic wall structure using high resolution endoscopic ultrasound (EUS) before and 2 weeks after initiation of therapy.

Methods: 10 patients (6m) with acute IBD (6UC; 4CD) and 10 healthy controls (HC) (6m) were examined prior and 2 weeks after initiation of open label Vedo therapy at approved standard dose using a forward-viewing radial echoendoscope (Pentax-Hitachi, Japan). Total wall-thickness (TWT) was measured by EUS in the mid sigmoid. Vascularity of the gut wall was evaluated by dynamic contrast enhanced EUS (dCEUS) (contrast agent SonoVue). Contrast kinetics were quantified as Time to peak intensity (TTP). EUS results were compared to macroscopic IBD scores (Mayo-score for UC; SES-CD-score for CD) and histological inflammation scores (HIS).

Results: In HC TWT was 1.7 ± 0.05mm in comparison to 4.2 ± 0.6mm ($p < 0.001$) in patients with acute IBD. Vedo therapy reduced TWT by 38.1% ($TWT_{14d} = 2.6 \pm 0.4$mm; $p = 0.001$) within 2 weeks in comparison to baseline levels.

TTP in HC was 13.8 ± 1.9s; in acute IBD TTP was accelerated to 6.2 ± 1.6s ($p = 0.0002$). After initiation of Vedo therapy TTP almost normalized within two weeks with $TTP_{14d} = 9.9 \pm 0.8$s ($p = 0.006$) compared to baseline. Prior to therapy there was a strong correlation of TWT and endoscopic activity scores. In contrast to TWT, endoscopic activity scores remained unchanged in all patients ($Mayo_{baseline} = 2.2 \pm 0.2$; $Mayo_{14d} = 2.0 \pm 1.5$; $SES\text{-}CD_{baseline} = 7.2 \pm 0.3$; $SES\text{-}CD_{14d} = 6.5 \pm 0.5$). Throughout the therapy, a positive correlation between TWT and HIS ($r = 0.62$; $p < 0.001$) was observed.

Conclusion: EUS of the colonic wall can precisely quantify the level of inflammation in patients with acute UC and acute CD before and after initiation of VED therapy. Only thickening of the different wall layers and changes in vascularity strongly correlate with HIS as gold standard, whereas endoscopic scores remain unchanged. Therefore, mucosal healing seems to be a late marker to evaluate response to VED therapy and is preceded by normalization of the bowel wall architecture. These results await confirmation in the much larger cohort of Vedo-treated patients that presently enter endoscopic and EUS analysis.

Disclosure of Interest: None declared

P1550 MULTIDISCIPLINARY APPROACH IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND ENTEROPATHIC SPONDILOARTHRITIS: USEFULNESS OF A COMBINED ASSESSMENT IN DIAGNOSTIC DELAY AND OUTCOMES

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Introduction: Prevalence of Enteropathic-related Spondyloarthritis (SpAe) in inflammatory bowel disease (IBD) shows marked variations (18-45%) and may be underestimated by gastroenterologists. Joint pain is a frequent (22-33%) and relevant clinical manifestation in IBD patients and its management require rheumatological expertise in conjunction with gastroenterologist.

Aims & Methods: In a prospective, longitudinal study, we aimed to assess, in the context of a combined GastroIntestinal and RHeumAtologic "GI-RHe" Unit, to: (1) evaluate the prevalence of undiagnosed ESpA and other rheumatologic diseases in a cohort of IBD patients; (2) describe the ESpA population and the diagnostic delay; (3) explore impact and outcomes of a combined assessment on therapeutic modifications. For this purpose, from November 2012 to December 2014, 269 IBD patients were referred to the dedicated gastroenterology-rheumatology out-patients clinic because of suspected rheumatologic disease. Clinical and laboratoristic assessment was performed by an experienced rheumatologist. Statistic analyses were made using McNemar's test. Relative risk was calculated to compare the probability of systemic medication intake after the combined visit. Data were expressed as mean ± SD.

Results: Ulcerative Colitis (UC) group included 46 patients (15 male, 31 females; age 47.6 ± 15.2 yrs, UC duration 12 ± 9.7 years,), all with clinically inactive disease (partial Mayo score < 3). Crohn's Disease (CD) group included 86 patients (29 males, 57 females, age 47 ± 13.5 years, CD duration 18 ± 8yrs), clinically inactive (CDAI < 150) in 49 (89%) patients, mildly active (CDAI 150-220) in 6 (11%) patients. Diagnosis of SpAe was performed in 64 (48.5%) IBD patients, including: 38 (59.4%) peripheral SpA (11.8% type I and 47.6% type II), 13 (20.3%) axial SpA and 13 (20.3%) diagnosis of both peripheral and axial SpA. Clinical and laboratory characteristics in these 64 IBD patients with peripheral SpA were: 23 males and 41 females (age 45.06 ± 12.9 yrs), symptoms duration of 95 ± 113.6 months, ESR 23.09 ± 20.35 (mm/h), CRP 5.36 ± 8.2 (mg/dl), HLAB27 positivity in 4 patients, mean ASDAS-CRP of 2.25 ± 0.96. Diagnosis of Osteoarthritis was made in 34.1% (45) IBD patients, Fibromyalgia in 6% (8), Psoriatic Arthritis in 5.3% (7), Rheumatoid Arthritis in 3.8% (5) and Gout in 2.3% (3) of patients. Among these 132 IBD patients with arthralgias, rheumatologic assessment diagnosed new rheumatologic diseases in 68 patients: 45.6% in UC and 44.2% in CD patients. After rheumatological assessment, a higher percentage of IBD patients were treated with disease-modifying anti-rheumatic drugs (after vs before combined visit: 44.7% vs 31.8%; $p = 0.04$, RR 1.3) and/or with anti-COX2 (28% vs 8,3%, $p < 0.0001$; RR 1.7). The use of anti-TNFs significantly increased after combined visit (29.5% vs 16.6%, $p = 0.001$; RR 1.4).

Conclusion: Multidisciplinary care facilitated the diagnosis and the management of rheumatic disorders in IBD patients with a more comprehensive treatment approach, thus leading to an earlier diagnosis and proper treatment of chronic and debilitating inflammatory arthritis.

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P1551 AGGREGABILITY OF THROMBOCYTES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Thrombocytes play an important role in haemostatic and inflammatory processes. Recently, an increasing number of reports have described the contribution of thrombocytes to the pathogenesis of inflammatory bowel disease (IBD). Studies confirmed that thrombocytes of IBD patients remain activated even in remission. The aetiology of this phenomenon, however still remains unclear.

Aims & Methods: Aim is to determine whether biological therapy with infliximab influences the aggregability of thrombocytes in patients with Crohn's disease (CD) and ulcerative colitis (UC) in clinical and laboratory remission and whether there is any significant difference between the aggregability of thrombocytes in IBD patients treated with infliximab in comparison with IBD patients treated with 5-amminosalicylates (5-ASA) and/or azathioprine.

Method: CD, UC and healthy control subjects were studied. 55 patients (average age 34 yrs, 31F and 24M) in total with IBD met the criteria of this study - 18 CD patients treated with infliximab (CD-BT group), 17 UC patients treated with infliximab (UC-BT group), 10 CD patients and 10 UC patients treated with 5-ASA and/or azathioprine (CD-CT group; UC-CT group). For control group 16 healthy volunteers matching criteria were examined. All patients were in laboratory and clinical remission based on clinical indexes of activity and laboratory results. Blood samples after processing were examined on optical light transmission aggregometer using high and low concentrations of agonist (11μM, 1,1μM, 0,55μM epinephrine; 0,2μg/ml, 0,5μg/ml, 2,0μg/ml collagen, 1,0μM a 3,0μM adenosine diphosphate). The results were compared with healthy control group.

Results: For statistical analysis, the Mann–Whitney test was used. Compared with controls, aggregation of thrombocytes was significantly higher by low concentrations of collagen - 0,5μg/ml and 0,2μg/ml; using 0,5μg/ml of collagen in groups UC–BT ($p = 0{,}024$), UC-CT ($p = 0{,}003$); by concentrations 0,2μg/ml in groups CD-BT ($p = 0{,}007$), CD-CT ($p = 0{,}032$), UC-BT ($p = 0{,}029$), UC-CT ($p = 0{,}002$). Significantly higher aggregation was measured when using low concentrations of ADP- 1,0μM, in comparison to controls; in groups CD-BT ($p = 0{,}006$), UC-BT ($p = 0{,}001$) and CD-CT ($p = 0{,}003$). Using low concentrations of epinephrine (1,1μM) lead to significantly higher aggregation in group UC-BT ($p = 0{,}018$) and UC-CT ($p = 0{,}006$) in comparison to controls. CD-BT compared with CD-CT did not show any significant difference in aggregation of thrombocytes by using any of our concentrations of agonists. Significantly higher aggregation when compared UC-BT with UC-CT using concentration 1,0μM ADP ($p = 0{,}014$) was observed.

Conclusion: Our study confirmed that IBD patients, even in clinical and laboratory remission, present with activated thrombocytes in circulation. Biological therapy with infliximab does not significantly affect the activation of thrombocytes in comparison to conventional therapy with 5-ASA and/or azathioprine.

Disclosure of Interest: None declared

P1552 VALIDATION OF A TURBIDIMETRIC IMMUNOASSAY FOR FECAL CALPROTECTIN

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Introduction: Calprotectin is a multifunctional protein that plays an important role in the diagnosis and follow-up of inflammatory bowel disease (IBD). High levels of calprotectin in stool samples are associated with inflammation of the intestinal tract. We evaluated the analytical performance of a new particle enhanced turbidimetric immunoassay (PETIA) on the clinical chemistry analyser BS-380 (MINDRAY) including linearity, security zone, precision and correlation to BÜHLMANN fCAL® ELISA.

Aims & Methods: The new latex based turbidimetric calprotectin assay BÜHLMANN fCAL® turbo from BÜHLMANN Laboratories AG, Switzerland applies particles coated with anti-human calprotectin (MRP8/14) antibodies: the agglutination is proportional to the calprotectin concentration.

Calprotectin levels are measured in extracts of human stool samples collected with the BÜHLMANN CALEX® Cap Device.
For linearity study serial dilutions were analysed and theoretical values were calculated from measured values of undiluted specimen. The intra-assay precision was performed with 5 different stool extracts containing different calprotectin concentrations in the range from 30 to 1300 µg/g. The inter-assay precision was evaluated by measuring the same samples over a period of 20 days (2 runs per day in 2 replicates). Extracts of 60 fecal patient samples were analysed on the BS-380 and compared with the results generated with the BÜHLMANN fCAL® ELISA.
Results: The assay has been tested to be linear in the range from 12.5 to 4500 µg/g calprotectin in stool. The obtained recovery values were between 96 and 105%. Security zone: Samples up to 8'000 µg/g results in concentrations above the upper assay limit of 2000 µg/g. The intra- and inter-assay precision (CV) were ≤ 10%. Passing and Bablok regression analysis revealed an intercept of -6.5 (-16 to 5) µg/g (95% CI), a slope of 0.91 (0.87 to 0.96) (95% CI), and a regression coefficient (r) of 0.97, suggesting that the new PETIA method showed a good correlation compared to matched ELISA assay.
Conclusion: The new latex turbidimetric procedure for determining calprotectin is an attractive alternative to ELISA allowing random access and full automation of fecal calprotectin quantitation. Moreover, it represents an accurate and precise method to determine calprotectin levels in fecal extracts.
Disclosure of Interest: M. Schneider Conflict with: Employee of BÜHLMANN, K. Sunde Conflict with: Employee of Gentian, T. Nilsen Conflict with: Employee of Gentian, C. Niederberger Conflict with: Employee of BÜHLMANN, J. Weber Conflict with: Employee of BÜHLMANN, T. Jermann Conflict with: Employee of BÜHLMANN, E. Sundrehagen Conflict with: Employee of Gentian

P1553 BODY COMPOSITION PROFILE IS ASSOCIATED WITH ANTI-TNF RESPONSE IN CROHN'S DISEASE PATIENTS

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Introduction: Despite the well-established benefits of the administration of biological therapy in Crohn's disease (CD) patients, primary non-response (PNR) and loss of response (LOR) rates remain a major issue [i]. Variation in body composition (BC) in CD patients is an emerging prognostic factor of poor response to treatment. Visceral obesity is characterized by excess of intra-abdominal adipose tissue accumulation while muscle depletion is characterized by a reduced muscle mass (myopenia) and increased infiltration by inter-and intramuscular fat (myosteatosis).
Aims & Methods: This study aims to evaluate the role of Computer Tomography (CT) defined BC parameters on PNR and LOR to anti-TNF therapy for Crohn's disease.
Patients who were commenced on anti-TNF therapy (adalimumab or infliximab) from Jan 2007 - June 2014 and had a pretreatment CT available for analysis were included. PNR was defined by global assessment (clinical and biochemical) of lack of improvement within 6 months of commencement of anti-TNF therapy. LOR was defined as cessation of their anti-TNF in view of clinical deterioration as assessed by their gastroenterologist. CT image analysis *Slice-O-Matic* V4.3 software (Tomovision, Montreal, Canada) was performed as described previously [ii] In brief, total skeletal muscle and visceral adipose tissue (VAT) surface area (cm^2) were evaluated on a single image at the third lumbar vertebrae (L3). The sum of skeletal cross-sectional muscle areas and VAT were normalised for stature (m^2). Mean Muscle Attenuation [MA] was reported for the whole muscle area at the third lumbar vertebra level. Reduced skeletal muscle index (myopenia) and low MA (myosteatosis) were defined using the sex-specific lower quartile as the cut-off value. Increased VAT index (visceral obesity) was also calculated by using the sex-specific upper quartile.
Results: 49 patients of whom 24 (49%) were male with 33 (67%) receiving infliximab and 16 (32%) having adalimumab were included in the analysis. The median age was 39 years (IQR 29-50). PNR was present in 11 (22%) patients. Patients with visceral obesity were more likely to have PNR [OR 7.42 95%(1.12-49.24) p = 0.038]. From the patients that had PNR, 28% had visceral obesity. LOR was present in 18 (37%) patients. Patients with myosteatosis were more likely to have LOR [OR 4.01 95%(1.05-15.22) p = 0.042]. From the patients that had LOR, 44% had myosteatosis. None of the other factors (myopenia, age, gender and type of anti-TNF) were associated with LOR or PNR.
Conclusion: For patients with CD, certain BC profiles may have prognostic effect on the response to medical treatment. Visceral obesity prior to anti-TNF therapy was associated with PNR while myosteatosis was associated with LOR. CT BC-based assessment may identify patients at high-risk of PNR or LOR, which will allow early optimisation of patients undergoing anti- TNF treatments. Muscle depletion is a common feature of all chronic pathologies and may represent a modifiable risk factor in Crohn's patients.

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Disclosure of Interest: None declared

P1554 CLINICAL HEALING IS INACCURATE WHEN ASSESSING RESPONSE TO ANTI-TNF THERAPY FOR CROHN'S ANAL FISTULAE

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Introduction: Magnetic Resonance Imaging (MRI) is the gold standard assessment tool, which is used in the assessment of fistulising perianal Crohn's disease as an adjunct to clinical assessment. The use of anti-TNF therapy for the treatment of these fistulae relies heavily on clinical and radiological assessments in order to assess response. It is difficult to predict response based on MRI images as they are difficult to interpret. Having a three-dimensional (3-D) fistula model and being able to quantify the changes in the fistula volume would be more beneficial than relying on complex and subjective MRI reports.
Aims & Methods: We aim to use computer software and MRI segmentation to design 3D models of Crohn's anal fistula tracts, measure baseline and 3 years post-biologics treatment fistula volumes and compare with clinical and MRI healing at 3 years.
An initial pilot was conducted where ten MRI images of high and low volume, simple or complex Crohn's perianal fistulae were selected. The surgeon identified baseline and 1-year post-biologics treatment scans. A radiologist was blinded to the selection process. Three-Dimensional fistula models were independently created by the surgeon and radiologist using the previously validated surgical computer software. Thirty-eight patients were selected and volumes were measured at baseline and 3-years post biological therapy.
Three-dimensional fistula volumes were compared. Kappa statistics were used to assess correlation between the healing categories for the three assessment techniques: volume measurements, clinical healing and MRI healing. Binary logistical regression analysis was used to assess predictors of healing as assessed by changes in 3-D anal fistula volumes.
Results: A change in baseline and post-treatment volumes was observed. The three assessment tools were clinical healing, radiological healing and change in 3-D anal fistula volumes. Healing categories were: healed, improved, no change and worse. The agreement between each pair of assessment techniques were measured using Kappa values. There was fair agreement between 3-D volumes and MRI healing (K = 0.34; 95% CI = 0.11,0.57). Poor agreement was noted between 3-D volumes and clinical healing (K = 0.05; 95% CI = -0.15,0.25) and the agreement was also poor for clinical and MRI healing (K = 0.10; 95% CI = -0.12,0.32).
On univariable and multivariable binary logistical regressional analysis, the single independent factor predictive of 3-D volume change was the duration of the disease (p = 0.045). An increased duration of disease was associated with a reduced likelihood of an improvement in volumes (OR = 0.57; 95% CI = 0.33, 0.9) and a five-year increase in the duration of the disease was associated with the odds of improvement being almost twice as low.
Conclusion: MRI volume measurements of 3D Crohn's fistula models provide an accurate assessment tool. The measurement of perianal fistulae volumes is more is useful than using MRI reports alone as it gives a quantitative measure that can be used to assess the efficacy of therapy. Patients with a long duration of disease are less likely to heal. Serial fistula volume measurements should be used for monitoring the response to biological therapy for perianal Crohn's fistula patients.
Disclosure of Interest: None declared

P1555 UTILITY OF THE SIMPLE ENDOSCOPIC SCORE IN CROHN'S DISEASE (SES-CD) IN UPPER ENDOSCOPY

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Introduction: While there is improving standardization of the macroscopic description of colonoscopic findings in Crohn's disease (CD), it is not the case in the Upper Gastrointestinal (UGI) tract. This limits the ability to implicate clinical significance of UGI findings in CD.
Aims & Methods: We empirically applied the Simple Endoscopic Score for CD (SES-CD) in the UGI tract for the first time, and aimed to assess its utility and significance in pediatric CD.
We used prospectively recorded data of pediatric CD patients collected for the ongoing ImageKids study. SES-CD items were scored in real time during upper endoscopy at each of the UGI segments, including esophagus, body, antrum and duodenum; thus the calculated total SES-CD UGI score ranged from 0 to 48. Demographics, clinical findings, biochemical results and physician global assessment (PGA) were also recorded.
Results: 94 children (52 male; mean age 11.4 years ±3.0; range 3.3-17.3 years). Mean wPCDAI 17.2 (±14.3; range 0-52.5). 44% had UGI SES-CD score ≥1 the majority of whom had endoscopic abnormality in the duodenum (32%) with the least frequent finding being esophageal involvement (9%). Median UGI SES-CD was 0 ± 3; range 0-17 (Graph 1). Distribution of scored features per region is demonstrated in Graph 2. Narrowing was not identified in any region. Patients with perianal CD had higher UGI SES-CD score [Median (IQR) 3 (±5) vs 0

(±3); p = 0.01]. There was a poor but significant correlation of UGI SES-CD with ESR and wPCDAI (r = 0.2, r = 0.2 P = < 0.05).
Conclusion: UGI findings were present in almost half of patients in this cohort. UGI SES-CD is an easily reported objective scoring system which may standardize reporting of endoscopic features of UGI CD.
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P1556 AN IMAGING METHOD FOR EVALUATION OF EARLY ATHEREOSCLEROSIS IN INFLAMMATORY BOWEL DISEASE; EPICARDIAL ADIPOSE TISSUE

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Introduction: Inflammatory Bowel Disease (IBD), which is characterized by chronic inflammation and relapse course, is associated with increasing cardiovascular risks. Although underlying exact mechanism of this relationship is not clearly understood, substantial studies upon chronic inflammatory disorders including rheumatoid arthritis and systemic lupus erythematosus suggested that chronic inflammation plays a crucial role on the development of cardiovascular disease induced by atherosclerosis.
Therefore, non-invasive imaging methods such as carotid intima media thickness (CIMT), flow mediated dilatation and carotid femoral pulse wave velocity, have been utilized to assess the subclinical atherosclerosis. In addition, epicardial adipose tissue (EAT), which is correlated with atherosclerotic coronary artery diseases, can be evaluated easily by a basic imaging method called transthoracic echocardiography. On the other hand, the lack of strict similarity between patients and controls according to cardiovascular disease risk factors revealed conflicting results in patients with IBD compared with healthy control that were evaluated by CIMT.
Aims & Methods: The aim of this study was to evaluate CIMT and EAT in highly selected patients with IBD and healthy controls with regard to cardiovascular risk factors and put forward whether measuring EAT can be used to detect atherosclerosis.
50 patients with IBD (10 Crohn Disease (CD) and 40 Ulcerative Colitis (UC)) and 34 healthy volunteers matched for age and gender were enrolled to the study, 18 to 50 years old. Diagnosis was established according to clinical, endoscopic and histopathological criteria. Exclusion criteria for both groups were history of coronary, peripheral artery, or cerebrovascular diseases, inflammatory disorders other than IBD, chronic renal failure, total colectomy for IBD and cardiovascular risk factors including diabetes mellitus, hypertension, hyperlipidemia, and smoking.
On the day of assessment, detailed medical history and physical examination were performed. In addition, blood samples for laboratory evaluation were also obtained. CIMT and EAT was performed by the same physician blinded to the study groups.
Results: No significant differences observed between IBD group and control with respect to demographic features (Table 1). CIMT and EAT were significantly higher in the IBD group compared to the control group (0.01 and 0.001, respectively). EAT was correlated with CIMT in the IBD group (r = 0.544, p = 0.001).
Table 1: Characteristics and Values of CIMT and EAT of Study Population

Parameters	IBD	Control	*p*-value
Age (yr)	32.5 ± 7.7	31.4 ± 6.4	> 0.05
Gender (M:F)	28:22	16:18	> 0.05
BMI (kg/m^2)	24.1 ± 3.8	24.6 ± 3.2	> 0.05
ESR (mm/h)	23.6 ± 21.5	6.4 ± 5.7	< 0.001
CRP (mg/dl)	21.2 ± 41	4.2 ± 2.6	< 0.05
EAT (mm)	0.452 ± 0.211	0.233 ± 0.110	< 0.001
CIMT (mm)	0.530 ± 0.153	0.416 ± 0.176	< 0.01

Conclusion: This study suggests that patients with IBD without cardiovascular risk factors have increased risk of early atherosclerosis. In addition, both CIMT and EAT are functional imaging methods to detect atherosclerosis in patients with IBD. EAT may be used as an additional diagnostic tool to detect early atherosclerosis in clinical practice.
Disclosure of Interest: None declared

P1557 MEASUREMENT OF FUNCTIONAL BLOCADE OF TNF-ALPHA BY ANTI-TNF AGENTS IS A STRONGER PREDICTOR THAN TROUGH LEVELS AND ANTI-DRUG ANTIBODIES: 3-YEAR PROSPECTIVE CLINICAL DATA

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Introduction: In case of loss of response (LOR) to anti-TNF agents in inflammatory bowel disease (IBD) patients, interventions, such as dose increase and shorten the interval, lead only to a transient improvement and a majority of patients will eventually loss response. Patients could also be successfully switched within class following antibodies development. However, the LOR in some patients is due to a non anti-TNF driven pathway of inflammation. A functional in vitro test (CD-62L shedding) measuring TNF functional blockade should help us identify those specific situations.
Aims & Methods: An in vitro test was used to predict the response to the drug: the shedding of the L-selectin (CD62L) quantified by flow cytometry on the surface of granulocytes before and after the anti-TNF-agent administration. In a subgroup of patients trough level of the drug (TL) and antibodies against the drug (ADA) have been performed in order to compare both tests. The treatment strategy during the 2 years of the study was blinded to the results of the CD62L shedding, TL and ADA and followed clinical symptoms-based interventions or switch by IBD specialists.
Results: From June 2012 to May 2015, 33 IBD treated with anti-TNF agents at Bern University Hospital were followed prospectively (clinicians blinded) to correlated clinical outcome with their response profile tested at baseline. The 22 responders (R) and 11 non responders (NR) had similar clinical characteristics. During a mean follow up of 25 months (range 7- 41; 77 patient-years follow up), 25 medico- surgical events occurred (3 adverse events (AE), 1 CMV colitis, 16 flares treated with medication, 3 intestinal resections and 2 operations of fistula) 9 in R and 16 in NR, which means 14% vs. 60% (p< .001) of the patient-year follow up. The mean calprotectin during follow up (about 1 measurement per patient year available) was 119 (+/-139 SD) for R and 310 (+/-226 SD) for NR. ADA and TL measurement could be performed in 15 patients (45%; 9 R and 6 NR). Only 2 patients developed ADA (one in each group). There was no significant difference in trough levels between R and NR (2.8 vs. 4.8; p = 0.4) and 62% had a therapeutic level (>1.5). Patients stable without need for intervention were 16/21 (84%; 1 AE) in R vs. 1/9 (2 AE) in NR (p < 0.001). In the NR group all the dose optimization failed, whereas in the responders group, interventions that would have been suggested on the basis of TL and ADA have not been performed (clinicians blinded), but were finally not required, based on the favorable clinical outcome.
Conclusion: Testing the in vitro functional blockade of TNF alpha (CD62L shedding) in anti-TNF treated IBD patients seem to be a better long-term predictor than trough levels and antibodies against the drug measurements. This could minimize interventions and therefore reduce costs and risk of adverse events.
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P1558 FECAL CALPROTECTIN AND LACTOFERRIN AS PREDICTORS OF POSTOPERATIVE ENDOSCOPIC RECURRENCE IN CROHN'S DISEASE

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Introduction: Endoscopic recurrence after surgery for Crohn's disease (CD) is high, with important prognostic value. Endoscopy, the current gold-standard method for assessing postoperative endoscopic recurrence, is an invasive procedure with a limited acceptance by patients. Furthermore, a significant percentage of patients remain asymptomatic despite endoscopic recurrence.
Aims & Methods: To assess the role of fecal calprotectin and lactoferrin in monitoring postoperative recurrence in CD.
CD patients who previously undergone ileocolectomy were proposed for endoscopic revaluation between 2010 and 2014. Endoscopic recurrence was defined as a modified Rutgeerts score ≥ i2b. Stool samples for quantification of fecal calprotectin and lactoferrin were collected the day before preparation for colonoscopy.
Results: We included 99 patients with a mean age of 45 ± 14 years. The mean time between surgery and ileocolonoscopy was 105 ± 97 months. Thirty-four patients had endoscopic recurrence. The Harvey-Bradshaw index did not correlate significantly with the endoscopic score (p = 0.575) or with calprotectin (p = 0.352) and lactoferrin (p = 0.16) levels. The mean value of fecal calprotectin (417.2 ± 484.2 vs. 100.5 ± 201.4 μg/g, p < 0.001) and lactoferrin (39.3 ± 38.9 vs. 15.4 ± 40.3 μg/g, p < 0.001) was significantly higher in patients with endoscopic recurrence. The cut-off of 50 μg/g for calprotectin allowed distinguishing between patients with and without endoscopic recurrence [sensitivity 94%, specificity 55%, positive predictive value (PPV) 52% and negative predictive value (NPV) 95%]. The cut-off 7.25 μg/g for lactoferrin allowed distinguishing between patients with and without endoscopic recurrence (sensitivity 85%, specificity 75%, PPV 64% and NPV 90%). Fecal calprotectin and lactoferrin

showed a significant correlation in patients with endoscopic recurrence ($K = 0.729$; $p < 0.001$).
Conclusion: Fecal calprotectin and lactoferrin have high diagnostic accuracy to detect postoperative endoscopic recurrence in CD, and significantly correlate with endoscopic scores, thus having an increasing impact as an alternative method to colonoscopy.
Disclosure of Interest: None declared

P1559 NITRIC OXIDE AS PREDICTOR OF STEROID-RESISTANCE IN ACUTE FULMINANT COLITIS

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Introduction: Nitric oxide (NO) is up-regulated by the induction of nitric oxide synthase (iNOS) in inflammatory bowel disease. NO gas can be used as a marker of inflammatory activity in the gastrointestinal tract. In parallel, the NO oxidation products plasma nitrite and nitrate (NOx) can reflect ongoing inflammatory activity. We analyzed rectal NO before and after three days, as well as plasma NOx in patients on glucocorticosteroid (GC) therapy in hospitalized patients. The aim of the study was to evaluate the relationship of rectal luminal NO and circulating plasma NOx in acute fulminant colitis to the outcome as therapeutic response or colectomy.
Aims & Methods: Fifty patients with median age 41 (range 20-78) years, hospitalized due to acute fulminant colitis and received treatment with high-dose GCs. Luminal nitric oxide was analyzed with chemiluminescence with the use of a Foley catheter balloon before onset of therapy and day 3 of treatment. NOx was measured by nitrite/nitrate colorimetric assay. NO levels and plasma NOx were compared to clinical disease activity index and C-reactive protein (CRP).
Results: Thirty-two responded to GC treatment whereas 18 did not, resulting in colectomy. The responders had higher luminal NO than non-responders (day 1: 12525 ± 2600, day 3: 15590 ± 4157 ppb) vs non-responders (day 1: 2874 ± 1283, day 3: 1137 ± 297 ppb) ($p < 0.0114$). Using an optimal cut-off NO level of 2250 ppb, sensitivity and specificity was 86% and 81% for colectomy ($p < 0.0001$). The area under the curve was 0.88 and likelihood ratio 4.8. Similarly, plasma NOx was higher in responders vs non-responders (day 1: 6.2 ± 0.3 vs 3.9 ± 0.4 umol/L) ($p < 0.0001$). Using plasma NOx, we found a corresponding cut-off at 5 umol/L with sensitivity 87% and specificity 87%. The area under the curve was 0.88 and likelihood ratio 6.7. Luminal NO was also correlated to plasma NOx ($r = 0.33$, $p = 0.0205$). In the responder group, CRP levels decreased (day 1: 22.31 ± 2.95, day 3: 15.69 ± 3.57 mg/L), whereas among non-responders CRP levels increased (day 1: 45.83 ± 11.10, day 3: 76.35 ± 16.96 mg/L) ($p < 0.0167$). Kaplan-Meier analysis showed that patients with baseline NO levels lower than 2250 ppb were at a significantly higher risk of colectomy within one month from onset of GCS treatment ($p < 0.0001$). Twelve out of 18 (67%) in patients with day 1 NO $<$2250 ppb were colectomized, the corresponding number of patients with NO $>$2250 ppb was 3 out of 32 (9%). In a similar manner, using plasma NOx $<$5 uml/L for analysis, we found 13 (72%) to be colectomized, and with $>$5 umol/L only two (6%).
Conclusion: NO and its oxidation product NOx are useful biomarkers of inflammatory activity in the gut. However, with more intense inflammation and mucosal damage, less NO is elaborated. Luminal NO and its downstream oxidation product NOx can be used as a sensitive biomarker to predict steroid-resistance in the acute fulminant colitis.
Disclosure of Interest: None declared

P1560 FAECAL CALPROTECTIN MEASURED AFTER THE THIRD DOSE OF ANTI-TNFA IS AN EARLY AND HIGHLY ACCURATE PREDICTOR OF RESPONSE IN CROHN'S DISEASE

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Introduction: A poor response to anti-TNFα treatment in patients with Crohn's disease (CD) is not infrequent. As new biologics targeting other immune pathways become available, early prognostic markers of anti-TNFα treatment failure are needed to inform treatment decisions. Faecal calprotectin (fcal) has been shown to be an excellent surrogate marker of intestinal inflammation [1] and a useful prognostic marker of relapse in CD [2], correlating well with endoscopic disease activity scores [3]. Furthermore, a recently published study of gene expression profiling to detect prognostic markers of early response to anti-TNFα therapy, identified the two genes coding for the calprotectin subunits (S100A8, S100A9) to be among the most highly expressed gene transcripts in non-responders [4].
Aims & Methods: We hypothesised that a faecal calprotectin measurement after anti-TNFα induction would predict the response to these treatments at 6 months. We analysed results from a prospectively-kept database for CD patients, who commenced infliximab (IFX) or adalimumab (ADA) therapy at standard induction regimens and doses for active, inflammatory disease. As part of routine clinical practice, serial fcal measurements were obtained at pre-defined interval (before and after induction: IFX 8-12 weeks; ADA 6-8 weeks – i.e. after the third dose of anti-TNF, but before the fourth). Remission was assessed at 6 months and defined by Harvey Bradshaw Index (HBI $<$ 5). Fcal was measured using a commercially available ELISA kit (Buhlmann). Continuous variables are presented as medians followed by interquartile range.
Results: 26 patients had serial fcal at the set time points (16 IFX; ADA 10; median age: 32yrs, disease duration: 5yrs (3, 8), location: 17 ileocolonic, 8 colonic and 1 ileal]. At 6 months, 16/26 (62%) patients were in remission. Those in remission at 6 months were found to have significantly lower fcal post-induction [72 (40, 135) vs. 259 (159, 550)]. A cut-off of fcal $>$175mcg/g returned a 70% sensitivity and 94% specificity for predicting non- responders (likehood ratio: 11.2, area under curve: 0.94, $p = 0.0002$). HBI and fcal levels before anti-TNFα induction did not differ between the two groups (responders, non responders HBI 11 vs. 12.5, $p = 0.73$, fcal 804 vs 868, $p = 0.47$, respectively).
Conclusion: Fcal measurement after the third dose of anti-TNFα is a highly-accurate predictor of non-response. This early measurement could be used to identify patients who would benefit from an alternative treatment strategy.

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Disclosure of Interest: None declared

P1561 RECTOGISMOID BIOPSIES ARE SUFFICIENT TO CONFIRM INTESTINAL INVOLVEMENT IN SYMPTOMATIC PATIENTS WITH ACUTE OR CHRONIC GRAFT VERSUS HOST DISEASE: A RETROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Intestinal graft versus host disease (iGvHD) is a common complication of haematopoetic stem cell transplantation (HSCT) associated with significant morbidity and mortality. Gastroenterologists are frequently consulted to assist with the diagnosis, which is based on histological findings. Endoscopic evaluation practice varies between units with some favouring symptom guided investigations and others advocating lower gi endoscopy with rectosigmoid biopsies as the approach with the highest sensitivity.
Aims & Methods: In this study we describe the diagnostic efficacy of upper versus lower gi endoscopy (and biopsy sampling) in supporting the diagnosis of iGvHD. Post HSCT patients with symptoms suggestive of iGvHD who underwent simultaneous upper and lower gi endoscopy in one centre over the last 3 years were identified through prospectively kept electronic patient records. All of them had biopsies taken during procedure from relevant areas (duodenum, terminal ileum, right colon, L colon/rectosigmoid). Continuous variables are presented as medians followed by interquartile range. Categorical comparisons were performed using chi-square test. Predictive values are followed by 95% confidence intervals.
Results: We identified 32 eligible patients [median age: 50 (33, 60), female: male ratio 1:1). Presenting gi symptoms included diarrhoea: 29/32 (88%), anorexia/weight loss: 14/32 (44%), nausea/vomiting: 11/32 (34%), abdominal pain/bloating: 4/32 (13%), rectal bleeding: 3/32 (10%). The median time post HSCT was 107 (55, 178) with 15 patients presenting in $<$100 and 17 in $>$100 days post liver transplantation. There were 8/15 (53%) patients diagnosed with acute GvHD and 10/17 (59%) with chronic GvHD affecting the gut. There was no difference in the gi segments involved in acute and chronic forms of iGvHD, with 18/18 patients having left colon/rectosigmoid, 14/18 (77%) right colon, 8/18 (44%) terminal ileal and 3/18 (16%) duodenal involvement. Duodenal biopsies were positive in only 3/8 (38%) patients with small bowel involvement based on a positive terminal ileal biopsy. The negative predictive value of duodenal biopsies for the diagnosis of iGvHD was 68% (53, 81).
Conclusion: iGvHD in either acute or chronic form appears to always affect the rectosigmoid/left colon. A flexible sigmoidoscopy with biopsies should suffice to rule in or out the diagnosis. Duodenal biopsies do not appear to provide any additional diagnostic benefit in the context of iGvHD investigation.
Disclosure of Interest: None declared

P1562 DID THE 2009 ECCO GUIDELINES INFLUENCE SCREENING FOR INFECTIONS IN PATIENTS STARTING BIOLOGIC THERAPY?

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Introduction: In response to concerns regarding the safety of immunomodulator therapy, the European Crohn's and Colitis Organisation (ECCO) published consensus guidelines in 2009 on screening for preventable infections. Investigations for hepatitis B virus (HBV), human immunodeficiency virus (HIV), tuberculosis (TB) +/- hepatitis C virus (HCV) are all recommended prior to initiating biologics.
Aims & Methods: We aimed to assess the proportion of patients being screened in routine clinical practice pre and post publication of the ECCO opportunistic infection (OI) guidelines. A retrospective review of inflammatory bowel disease patients treated with biologic therapy until February 2015 at Imperial College Healthcare NHS Trust was performed.
Results: 187 patients (42.2% male) were prescribed biologic therapy (124 infliximab, 58 adalimumab, 5 certolizumab) between 2001 and 2015. Median age at

initiation was 37 years (range 17 - 87 years). 60.4% were receiving concomitant immunosuppressive, 43.3% had prior surgery and 21.9% had fistula.
Testing for HepB sAg (33.9% vs. 69.4%), HepC Ab (32.2% vs. 76.4%), HIV Ab (23.5% vs. 72.2%) and TB Elispot (9.6% vs. 65.3%) all significantly increased after the publication of ECCO OI guidelines ($p < 0.001$). HepB sAb testing (9.6% vs. 26.4%, $p = 0.002$) also increased but there was no significant change in testing for HepB cAb (8.7% vs. 6.9%, $p = 0.67$). Chest radiographs (CXR) were performed in 87% and 86.1% of patients pre and post guidelines, respectively ($p = 0.87$).

Table 1: Influence of ECCO Guidelines (2009) on screening for infections in patients starting biologic therapy

	All, n (%)	Pre ECCO, n (%)	Post ECCO, n (%)	p value
Hep B sAg	89 (47.6)	39 (33.9)	50 (69.4)	<0.001
HepB cAb	15 (8)	10 (8.7)	5 (6.9)	0.67
HepB sAb	30 (16)	11 (9.6)	19 (26.4)	0.002
Hep C Ab	92 (49.2)	37 (32.2)	55 (76.4)	<0.001
HIV Ab	79 (42.2)	27 (23.5)	52 (72.2)	<0.001
TB Elispot	58 (31)	11 (9.6)	47 (65.3)	<0.001
CXR	162 (86.6)	100 (87)	62 (86.1)	0.87

Conclusion: Screening for infections prior to starting biologic therapy has got considerably better since the introduction of the first ECCO OI 2009 consensus guidelines, but remains substandard. Shortfalls in the assessment of hepatitis B virus infection and vaccination status with HepB cAb and sAb is concerning. The publication of the second ECCO OI evidence-based consensus in 2014 along with a practical checklist for the prevention of infections may trigger further improvements.

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Disclosure of Interest: None declared

P1563 CLINICAL ROLE, OPTIMAL TIMING AND FREQUENCY OF MEASUREMENT OF SERUM INFLIXIMAB LEVELS AND ANTI-INFLIXIMAB ANTIBODY TITERS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The introduction of biological treatment has made a major breakthrough in the management of inflammatory bowel disease (IBD). However, a substantial number of patients show only partial response, and in approximately 40% of initially responders loses its effect. The cessation of therapy or the switching to another biological drug currently depends mainly on the clinical judgement. Serum infliximab (IFX) and anti-infliximab antibody (ATI) levels are objective parameters, that may have a great role in the therapeutic decisions, but the optimal timing and frequency of their measurements are still not clearly defined.
Aims & Methods: Our aim was to assess the optimal timing and frequency of sampling for measurement of serum IFX and ATI levels during biological therapy. 34 IBD patients receiving maintenance IFX therapy were prospectively enrolled: 17 patients were in complete remission (responder group) and 17 patients showed inadequate response including partial and loss of response or the need for dose escalation. Blood samples were collected before and two and six weeks after the administration of IFX.
Results: Our results confirmed that the expression of ATI in the circulation is transient. Using the three points' measurements the ATI expression showed significant difference between the responder and inadequate responder group (5.9% vs 41.2%; $p = 0.039$), however, single sampling of the ATI was insufficient for predicting the therapeutic response. On the contrary, the mean value of week 0 serum IFX levels were significantly higher in the responder group (3.35 ± 1.65 vs.1.41 ± 1.20; $p < 0.001$) without further difference on the second and sixth week. 79.4% of patients could have been categorized correctly based on the cut-off value of serum IFX level 2.246 μg/ml at week 0. However, prediction of therapeutic response was substantially improved when IFX and ATI levels were measured three times simultaneously (91.2%)
Conclusion: Our results suggest that the simultaneous measurement of serum IFX levels and ATI titers not only at week 0, but also at week 2 and week 6 after the administration significantly increase the diagnostic accuracy for the therapeutic decision in uncertainly responded patients and can serve as a highly precise tool for the evaluation of therapeutic response in the questionable situations.
Disclosure of Interest: None declared

P1564 ULTRASONOGRAPHY PROVIDES A VALID ALTERNATIVE TO MAGNETIC RESONANCE ENTEROGRAPHY IN CROHN'S DISEASE

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Introduction: Objective measures of disease activity in Crohn's Disease (CD) are necessary[1], but no gold standard exists for evaluation of inflammation in the small intestine.[2] Magnetic Resonance Enterography (MRE) is usually recommended over ultrasonography (US).[3] However, US is inexpensive, easily repeatable, and patient friendly. Prior studies comparing MRE and US have mainly focused on whether inflammation was present or not rather than on grading disease severity.[4]
Aims & Methods: Our aim is to compare objective measures of severity of small intestinal inflammation in Crohn's Disease (CD) assessed with bowel ultrasonography (US) and magnetic resonance imaging (MRE) and to correlate these to established clinical and biochemical biomarkers.
We included 20 patients with moderate to severe CD. MRE and US were performed less than one week apart applying standard protocols estimating maximum bowel wall thickness, length of disease involvement, and vascular pattern. Clinical scores, blood samples, and fecal markers were obtained at scan time.
Results: For the most affected segments the two methods showed good agreement for bowel wall thickness (US: median 7.0 mm (range: 4-11) and MRE: median 6.5 mm (range 3-14) mm, Spearman's $rho = .81$, $p < 0.001$) and length of involvement (US: median 10 cm (range: 3-57) and MRE: median 12 cm (range 1-70), $rho = 0.62$, $p < 0.05$). 95% limits of agreement were 0.5 mm (range -3 to 4) for thickness and 1.3 cm (range -11 to 14) for length. Inter rater variability between US and MRE ranged from $kappa = 0.54$ to 0.64 for thickness and $kappa = 0.46$ to 0.64 for length of inflamed segments. Data from both methods showed only weak correlation with CRP, f-calprotectin and clinical indices.
Conclusion: US is a valid and inexpensive alternative to MRE for assessing maximum length of inflammation and bowel wall thickness in CD. Objective structural findings may improve classification of disease severity in addition to existing clinical markers.

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P1565 ENDOSCOPIC APPEARANCE OF PEYER'S PATCHES PREDICTS SUSTAINED CLINICAL REMISSION IN ULCERATIVE COLITIS PATIENTS

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Introduction: Peyer's patches (PPs) are aggregates of lymphoid follicles mainly located in distal ileum and play a major role in mucosal immunity as an inductive site. Because gut flora or food antigens interact with PPs and are involved in the pathogenesis of ulcerative colitis (UC), it is speculated that immune responses in PPs play an important role in determination of the clinical course of UC patients. Using narrow-band imaging with magnifying endoscopy (NBI-ME), we recently reported that patients with UC have altered PPs. However, clinical significance of alterations in PPs is unapparent. In this study, we aimed to evaluate the relationship between clinical course and NBI-ME images of PPs in UC patients.
Aims & Methods: Fifty UC patients with clinical remission (partial Mayo score ≤ 2) who underwent total colonoscopy were enrolled from April 2009 to March 2013. NBI-ME images of PPs were collected, and changes in the villi were evaluated by "villi index" as the sum of three categories: irregular formation, hyperemia, and altered vascular network pattern (Hiyama S. et al,

Digestion 2013). Patients were divided into two groups based on "villi index": low (L) type = 0 or 1, and high (H) type = 2 or 3, and sustained clinical remission rate within 2 years after colonoscopy was evaluated. Temporal alteration of PPs images was also analyzed among 14 patients who underwent second PPs observation within 2 years after the first colonoscopy.
Results: UC patients included 24 men and 26 women, and mean age was 45.4 (17-75) years. Fifty-eight percent (29/50) of the patients had L type-PPs, while 42% (21/50) had H type. Age, gender, disease duration, endoscopic score and extent of disease involvement were not associated with the alteration in PPs. The sustained clinical remission rate of patients with L type-PPs was significantly higher than that of patients with H type-PPs [76% (22/29) v.s. 38% (8/21); $p < 0.01$]. There was no relation between sustained clinical remission rate and other clinical factors except older age (≥40). Multivariate analysis revealed that L type-PPs was an independent factor for sustained clinical remission (odds ratio: 7.7, 95% confidence interval 1.92 to 40.7; $p < 0.01$). Among 14 patients with repeated observation of PPs [mean interval: 19 (8-24) months], the type of PPs (L or H type) were unchanged at the time of first and second colonoscopy in 12 patients (86%).
Conclusion: UC patients with severe endoscopic alterations in PPs are at high risk of relapse, and the feature of PPs rarely altered in short interval. Observation of PPs using NBI-ME may be a useful method to predict clinical course of UC.
Disclosure of Interest: None declared

P1566 THE PREDICTIVE FACTOR REGARDING RELAPSE IN PATIENTS WITH ULCERATIVE COLITIS AFTER ACHIEVING ENDOSCOPIC MUCOSAL HEALING

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Introduction: Endoscopic mucosal healing (MH) has been proposed as the therapeutic goal in the treatment of patients with ulcerative colitis (UC). Despite achieving endoscopic MH, however, relapse of UC was found.
Aims & Methods: To validate risk factors of UC-relapse is useful for establishing therapeutic strategy in maintenance of remission and MH. The aim of this study is to evaluate the predictive factor for relapse in patients with UC after achieving endoscopic MH. From April 2010 to February 2015, 298 patients with UC who had been treated at Kitano hospital were analyzed, retrospectively. Clinical and endoscopic activities were evaluated with Lichtiger index and Mayo score, respectively. Endoscopic MH was defined as Mayo score of less than one. The relapse of UC was defined as any recurrence of UC-related symptoms. Cumulative relapse rate after achieving MH was evaluated and we analyzed the predictive factors for relapse in UC patients after achieving endoscopic MH by Cox regression analysis.
Results: Of 298 UC patients, total 88 patients (29.5%) could achieve endoscopic MH. In 21 of 88 patients with endoscopic MH (23.9%), the relapse of UC was found. The median time at relapse of UC was 1.2 years after achieving MH. Based on Kaplan-Meier analysis, the cumulative relapse rate at 1, 3 and 5 years after achieving MH were 12.1%, 29.8% and 36.2%, respectively. The cumulative relapse rate of Mayo-1 group tends to be high compared to that of Mayo-0 group (23.1% (Mayo-0) and 45.9% (Mayo-1) at 5 years, respectively), although there was no significant difference of cumulative relapse rate between Mayo-0 and Mayo-1 group ($p = 0.312$). Moreover, Cox regression analysis demonstrated that the use of immunomodulator was predictive factor for relapse in UC patients after achieving endoscopic MH ($p = 0.035$).
Conclusion: Our data suggest that, even if achieving endoscopic MH, we should keep the maintenance treatment deliberately in UC patients required the treatment with immunomodulator.
Disclosure of Interest: None declared

P1567 LACK OF CORRELATION BETWEEN ADALIMUMAB ANTIBODY AND TROUGH LEVELS AND NEITHER ARE PREDICTIVE OF CLINICAL ACTIVITY

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Introduction: Adalimumab (ADA) has been widely used in patients with moderate to severe Inflammatory Bowel Disease (IBD) to induce and maintain remission.However, a proportion of patients experience primary treatment failure and some lose response over time.
Aims & Methods: We wished to examine the correlation between ADA drug trough, antibody(Ab) levels and clinical activity defined by clinical and biochemical parameters. Patients receiving ADA, between 18 and 80 years were recruited from the IBD service. Clinical and physical parameters including weight and height, Harvey-Bradshaw Index (HBI), Partial Mayo Score (PMS), CRP and additional medication use were recorded. Two serum samples were collected from each patient ≤48 hours prior to their next scheduled ADA dose. ADA trough and Ab levels were measured by ELISA using commercially available Abs (MP Biomedical). ADA and Ab concentration were normalized to a standard curve using exogenous ADA and HRP-conjugated goat anti-human λ chain Ab (Serotec) respectively.A low trough level of < 0.63μg/ml and -ve Ab level of < 0.43μg/ml were determined using the mean concentration +- 3SD in patients and controls.A HBI of > 5 and PMS of > 3 were defined as clinically active disease.
Results: In total, 42 patients were included; mean age 44 (ranges 27-70), 52% (n = 22were male. In all, 36% (n = 15) had Ulcerative Colitis (UC) and 64% (n = 27) had Crohn's Disease (CD). The mean height and weight were 169 cm and 75kg, 38% (n = 17) were overweight BMI > 25 and 12% (n = 5) were obese BMI > 30. The mean duration of therapy was 3 years and 2.4% (n = 1) were on concomitant immunosuppressants. All patients were receiving 40mg subcutaneously with the majority on fortnightly dosing, 71% (n = 30). The mean HBI score and PMS were 2.5 and 0.4 respectively. In total, 17% (n = 7) had clinically active disease and the mean CRP was 5.5mg/dl(0-51). In all, 4.8% (n = 2) had low trough levels while 64% (n = 27) had a high ADA Ab level. Neither of the 2 patients with a low trough level had clinically active disease and only 1 had a significant Ab level. Neither Ab status nor mean Ab level correlated with disease activity, biochemical activity, dosing schedule or obesity. Similarly, low trough level or mean drug level did not vary according to these parameters (Table 1). One explanation for this finding could be that this study includes patients who are responders and are well maintained on ADA. In addition, very few had a low trough level (n = 2) presumably because 12 of our patients had already been escalated to a shorter dosing interval. Future observation of this cohort as well as a prospective study for patients commencing ADA may show correlation between trough level, Ab status and long-term outcome.
Conclusion: In our cohort, there seems to be a lack of correlation between ADA Ab and trough levels, with neither being predictive of clinical activity.
Disclosure of Interest: None declared

P1569 ASSOCIATION BETWEEN ELEVEN THIOPURINE METABOLITES AND MUCOSAL HEALING IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Thiopurine-related drug response in treatment of patients with Crohn's disease (CD) is still incompletely understood. Thus, therapeutic monitoring of thioguanine nucleotides (TGN) and methylthioinosine derivatives (MMPR) has been suggested to improve thiopurine therapy, however with limited success. The comprehensive assessment of thiopurine metabolite pattern instead of determination of total TGN and MMPR levels has been suggested to be beneficial for prediction of thiopurine response.
Aims & Methods: To evaluate the association between eleven thiopurine metabolites and mucosal healing in patients with CD.
Patients with CD on maintenance treatment with azathioprine (AZA) and a stable dose for at least 4 weeks were eligible. We established a novel highly sensitive liquid chromatography-tandem mass spectrometry method for simultaneous quantitation of eleven thiopurine metabolites including mono-, di-, and triphosphates of thioguanosine (TGMP, TGDP, TGTP), methylthioinosine (meTIMP, meTIDP, meTITP), methylthioguanosine (meTGMP, meTGDP, meTGTP), and thioinosine (TIMP, TIDP, TITP). Furthermore, thiopurine S-methyltransferase (TPMT) activity in red blood cell concentrations (RBC) was determined. Blood collection was performed on day of the ileocolonoscopy. Mucosal healing was defined as the absence of any ulcerated lesions on colonic and (neo-) terminal ileal mucosa.
Results: In total 101 patients (f/m = 54/47, median age: 25 years) were included. The median AZA dosage was 2.12 mg/kg/d (range: 0.28-3.13 mg/kg/d) which was stable for median 26 months (range: 1-111 months) before blood collection. Patients without achievement of mucosal healing (non-responder, n = 60) showed significantly lower concentrations of meTIDP (p = 0.04) and meTITP (p = 0.02) in RBC. After stratification of patients in normal and intermediate metabolizers for TPMT the association between non-response and lower RBC concentrations of meTIDP (p = 0.008) and meTITP (p = 0.004) held true in patients with normal TPMT activities (n = 91). No significant differences between

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	Activen = 7	Inactiven = 35	←CRP (n = 7)	↓CRP (n = 35)	BMI > 30 (n = 5)	BMI < 30 (37)	Fortnightly (n = 30)	Weekly (n = 12)
TroughMean μg/ml	3840	3407	3567	3649	2782	3589	3540	3228
Low Trough < 0.63 μg/ml	0	2(6%)	0	2(6%)	1(20%)	1(3%)	1(3%)	1(8%)
AntibodyMean μg/ml	534	583	459	440	441	593	582	557
(+) Antibody > 0.43 μg/ml	4(57%)	23(66%)	5(71%)	22(63%)	2(40%)	25(68%)	20(66%)	7(58%)

responders and non-responders were found for the isolated thioguanosine phosphate levels (TGMP, TGDP, TGTP).
Conclusion: There was no significant correlation of isolated thioguanosine phosphate levels (e.g. TGDP, TGTP) and mucosal healing. Lower concentrations of methylthioinosine levels in non-responders support the impact of the TPMT metabolizer phenotype regarding thiopurine response.
Disclosure of Interest: None declared

P1570 HAEMATOLOGICAL AND INFLAMMATORY MARKERS FOR NON-INVASIVE DIAGNOSIS OF CROHN'S COLITIS

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Introduction: Red Cell Distribution Width (RDW) is associated with active inflammatory bowel disease, as shown in recent studies. [1] RDW is cost-effective, readily available and may be used as a rapid, non-invasive tool in diagnosing disease activity. In our study, results show that C-Reactive Protein (CRP) and Erythrocyte Sedimentation rate (ESR) have low sensitivities (54% and 55%) and specificities (71% and 90%) in detecting Crohn's disease (CD) activity. [2] We then used RDW, platelet count, ESR and CRP to create a risk score which may be used to predict disease activity in CD.
Aims & Methods: Serum samples of CRP, ESR, platelet count and RDW in CD patients were collected on the day of colonoscopy and compared with CD activity according to endoscopic findings and histology results. A total of 308 endoscopic procedures on 161 CD patients were performed over a 48 month period. 89 of these patients were male with a median age of 40.2 years (9-85 years). Disease activity was determined according to endoscopic and histologic findings at colonoscopy. A risk score for disease activity was then created by awarding 1 point to each elevated marker (CRP > 10mg/L, ESR > 14mm1stHr, platelet count > 400,000 and RDW > 14.9%) and the sensitivity and specificity for each marker was calculated. Independent sample t-test was calculated in order to determine the statistical significance of elevated biomarkers in active colitis.
Results: Confirmation of active colitis was present in 191 colonoscopies (62%) at endoscopy and as reported by histology results. RDW, platelet counts, ESR and CRP were significantly elevated in patients with active CD (independent samples t test $p < 0.005$) when compared with patients with quiescent disease.
Table 1: shows the sensitivities and specificities for each biomarker as calculated in the risk score for active disease

Serum Biomarker	Sensitivity (%)	Specificity (%)
RDW	43%	73%
Platelet count	21%	93%
ESR	68%	40%
CRP	44%	64%

90% of patients with a score of 4 ($n = 10$) and 89% of patients with a score of 3 ($n = 37$) had histologically active disease at endoscopy. Meanwhile, 66.6% of patients with a score of 2 ($n = 72$), 53% of patients with a score of 1 ($n = 91$) and 54% of patients with a score of 0 had active disease at endoscopy. There was a statistically significant difference ($p < 0.0001$) between the mean risk score in histologically quiescent disease (mean 0.9145, $n = 117$) and the mean risk score in histologically active disease (mean 1.461, $n = 191$).
Conclusion: RDW when used as a single biomarker has a low sensitivity in detecting active CD. However, the presence of three or more elevated biomarkers should arouse suspicion of ongoing inflammation.

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P1571 GENERATION AND CHARACTERIZATION OF A UNIQUE PANEL OF ADALIMUMAB SPECIFIC ANTIBODIES AND THEIR USE IN THERAPEUTIC DRUG MONITORING ASSAY

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Introduction: Adalimumab (ADM; Humira®) is a human monoclonal antibody targeting tumour necrosis factor alpha (TNFα) used in the treatment of inflammatory bowel disease (IBD). It has been shown that ADM serum concentrations are associated with clinical outcome and that some patients develop antibodies towards ADM. Therapeutic Drug Monitoring (TDM) as well as determination of the anti-drug antibody response is therefore recommended. A number of TDM assays are currently available, but often lack specificity due to the use of non-specific, polyclonal antibodies (pAb) to detect TNFα-bound ADM.
Aims & Methods: Aim 1) To generate and characterize a panel of ADM specific monoclonal antibodies (MA-ADM); 2) to select MA-ADM suitable to be used in ADM assay; 3) to study the effect of neutralizing and non-neutralizing antibodies in the ADM assay; 4) to apply the ADM assay on serum samples derived from a cohort of ADM treated patients.
Methods Using hybridoma technology, two panels of MA-ADM were generated and characterized. MA-ADM were screened for reactivity towards infliximab, golimumab and human IgG using ELISA. The neutralizing capacity of the ADM-specific MA was determined by incubation of ADM with a two-fold excess of MA-ADM followed by measuring the residual binding (capacity) of ADM to TNFα using a goat anti-human IgG conjugate. A competition experiment in which an excess of cold MA over conjugated MA was used to perform epitope binning. MA were subsequently evaluated for their ability to detect ADM in the assay using ADM spiked buffer and serum samples. After selection of one MA, the impact of (non-)neutralizing antibodies on the determination of ADM in this MA-based assay was investigated. ADM concentrations in 96 serum samples of ADM treated patients were determined using the assay.
Results: Thirty-two MA-ADM were generated of which 11 were adalimumab specific. Four MA revealed a neutralizing capacity between 78-95% and five less than 11%. Epitope binning revealed at least 9 non-identical epitopes. MA-ADM40D8 was selected as a conjugate to determine adalimumab in a TNFα coated solid-phase ELISA (MA-based ELISA). The four neutralizing antibodies could completely hamper the determination of ADM in the MA-based ELISA while the non-neutralizing antibodies had no effect on ADM determination. The MA-based ELISA demonstrated good linearity of ADM dose-response curve and good intra-/inter-assay precision with a mean coefficient of variation of 5% and 9%, respectively. ADM concentrations ranging from 0.2 to 23.8µg/ml were measured in the cohort.
Conclusion: In this study, 11 highly specific monoclonal antibodies towards ADM were generated of which four revealed neutralizing properties. A MA-based ADM ELISA was established with good accuracy and precision. This assay, together with the previously described anti-drug antibody assay using MA-ADM6A10 as calibrator are valuable tools that can be used in routine monitoring of adalimumab-treated patients.
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P1572 POINT-OF-CARE ASSAYS FOR RAPID QUANTIFICATION OF INFLIXIMAB

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Introduction: The monoclonal antibody infliximab (IFX; Remicade®), which targets the pro-inflammatory cytokine tumour necrosis factor-alpha (TNFα), has revolutionized the treatment of patients with inflammatory bowel disease by inducing remission and mucosal healing. Therapeutic drug monitoring has been widely accepted as a tool to enhance the efficiency of IFX therapy. Recently, two biosimilars of infliximab received market authorization under trade names Remsima and Inflectra. Several assays are available to perform infliximab monitoring, but lack the speed to implement treatment algorithms immediately. In addition, available commercial infliximab assays require sample analysis in batch to reduce cost/sample.
Aims & Methods: To develop rapid assays for the quantification of infliximab concentrations using IFX-specific monoclonal antibodies (MA). Besides a sensitive, specific and quantitative read-out, an ideal point-of-care assay has a benchtop size, low cost, fast turn-around time and is easy-to-handle. In addition, data should be easily transferrable to electronic patient files.
1) A fiber-optic surface plasmon resonance assay was developed using a MA/MA sandwich approach. Surface plasmon waves are generated at the interface of an optical fiber/gold layer, which allow real time sensing of interactions between biomolecules at the surface. MA-IFX20G2 was covalently immobilized to a gold-sputtered fiber surface to capture IFX. MA-IFX3D5 was conjugated to gold nanoparticles and was used to detect bound IFX. 2) A lateral flow-based immunoassay was developed using TNFα as capture antigen and MA-IFX6B7 for the detection of IFX bound to TNFα. Conjugated gold nanoparticles were used for signal enhancement. A colorimetric signal was generated and read with a portable lateral flow test reader.
Results: 1) The fiber-optic surface plasmon resonance platform demonstrated a dose-response relationship with good reproducibility in the 0.7 to 75 ng/mL range (n = 6). 2) The lateral flow-based immunoassay revealed dose-response curves with good reproducibility in the 2.5 to 80 ng/mL range (n = 3). Both systems allowed at least a 1:200 serum dilution, a turn-around time less than 20 min and an easy transmission of data.
Conclusion: This work demonstrates the potential of two rapid assays for the determination of infliximab concentrations, a fiber-optic surface plasmon resonance MA/MA sandwich immunoassay and a lateral-flow based immunoassay. Both assays showed to sensitively detect infliximab, are currently applied on clinical samples and benchmarked to the clinically validated infliximab ELISA. The availability of these assays will allow a fast implementation of quantitative infliximab monitoring in a hospital/infusion center setting.
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P1573 THERAPEUTIC DEPLETION OF MYELOID LINEAGE LEUCOCYTES IN PATIENTS WITH ULCERATIVE COLITIS: DEMOGRAPHIC FEATURES OF NON-RESPONDERS AND RESPONDERS TO THIS NON-PHARMACOLOGICAL TREATMENT OPTION

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Introduction: Patients with active inflammatory bowel disease (IBD) have elevated myeloid lineage leucocytes, notably elevated CD14(+)CD16(+) monocyte phenotype, which is a major source of tumour necrosis factor-α (Belge, et al. *J Immunol* 2002). Hence selective depletion of elevated and activated leucocytes by adsorptive granulocyte/monocyte apheresis (GMA) with an Adacolumn is expected to alleviate inflammation and promote remission or at least enhance drug efficacy. However, studies in ulcerative colitis (UC) have reported contrasting efficacy, from an 85% (Suzuki, et al. *Gastroenterology* 2005) to a statistically insignificant level (Sands, et al. *Gastroenterology* 2008). Patients' demographic variables in the aforementioned studies were different.

Aims & Methods: In 143 UC patients we looked for clinical and endoscopic features, which could indentify a patient as a potential responder or otherwise as a non-responder to GMA. Seventy-three patients were steroid naive, and 70 were steroid dependent. Patients received up to 11 GMA sessions over 10 weeks. At entry and week 12, patients were clinically and endoscopically evaluated, allowing each patient to serve as her or his own control. Clinical activity index (CAI) $\leq$4 at week 12 was defined as response to GMA. Biopsies from colonoscopically detectable inflamed mucosa were processed to see the impact of GMA on leucocytes within the mucosa.

Results: At entry, the average CAI was 12.8, range 10-17. Ninety-two patients (64.3%) responded to GMA, 52 of 73 steroid naïve (71.2%) and 40 of 70 steroid dependent patients (57.1%). On average remission was sustained for 8.6 months in steroid naïve patients and for 10.4 months in steroid dependent cohort. Upon relapse, the majority of patients responded well to a second course of GMA. Over 1200 biopsies were processed. Infiltrating leucocytes were mostly neutrophils and monocytes. There was a marked reduction of infiltrating leucocytes in responders. Patients who had extensive deep UC lesions together with loss of the mucosal tissue at the lesion sites were identified as non-responders. Patients with the first UC episode were identified as the best responders (100%) followed by steroid naive patients. Additionally, a short duration of active UC marked a patient as a likely responder.

Conclusion: Depleting elevated myeloid lineage leucocytes was associated with efficacy in UC patients, most notably first episode and steroid naïve cases who attained a favourable future clinical course. GMA was more effective if applied immediately after a relapse than after a lag time. In general, GMA is very much favoured by patients for its safety profile and for being a non-drug therapeutic intervention. Patients with extensive deep ulcers, with long duration of UC and exposure to multiple pharmacologicals are unlikely to benefit from GMA.

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P1574 ENTEROSCOPIC AND MR FINDINGS OF SMALL INTESTINE IN CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is a lifelong inflammatory bowel disease. Evaluating the extent and severity of the disease is critical to determine appropriate therapeutic strategies in patients with CD. MR enterography can examine not only intra-luminal changes, but also extra-luminal abnormalities without ionizing radiation and anesthesia, which makes it appropriate for frequent examinations in CD. We developed novel MR enterocolonography (MREC) to simultaneously evaluate both small and large bowel lesions in patients with CD and recently reported its excellent correlation with endoscopy. Balloon-assisted enteroscopy (BAE) and MR procedure can assess the deep small intestine[1)] but clinical significance of small intestinal lesions is uncertain.

Aims & Methods: The aim of this study is to evaluate the correlation between endoscopic and MR findings in deep small intestine and to identify findings of the two modalities to predict patients' prognosis. This is a retrospective cohort study. We performed MREC and BAE in 90 patients for assessing the small intestinal lesions. Modified SES-CD and MaRIA scores were used to evaluate the correlation between BAE and MREC. We also assessed the correlation between small intestinal CD lesions and patients' prognosis (Recurrence: Aggravation of symptoms that need to change treatment. Surgery: Operation related with CD except for anal fistula).

Results: In BAE, the CD lesions were detected in the terminal ileum (57.0%) and proximal ileum (60.2%) at a similar rate. The sensitivity and specificity of MREC for ulcerative lesions in the small intestine (MaRIA $\geq$ 11) were 82% and 89%, respectively, and those for stenotic lesions were 50% and 90%, respectively, using BAE as the reference. Multivariable analysis showed that the presence of active lesions in small intestine with MREC (MaRIA $\geq$ 11) was an independent risk factor for recurrence (P = 0.005, Relative Risk 2.98 (95%CI 1.398-6.350)). Ulceration detected on BAE or stenosis detected with MREC were not a significant risk factor for recurrence. The Kaplan-Meier method showed that the patients with active lesions detected with MREC had a significantly higher cumulative rate of recurrence (more than 50% within 1 year) than those without active small intestinal lesions. Multivariable analysis showed that the detection of stenosis in small intestine with MREC was an independent risk factor for surgery (P = 0.005, Relative Risk 5.83 (95%CI 1.706-19.937)). The detection of ulceration on BAE or the presence of active lesions with MREC were not a significant risk factor for surgery. The patients with stenosis detected with MREC had a significantly higher cumulative rate of surgery (over 40% within one year) than those without stenosis.

Conclusion: Although BAE assesses small intestinal lesions more accurately than MREC, it can be an alternative examination to predict recurrence and surgery. Futhermore, prognosis was different depending on if the patient has an inflammatory lesion or stenotic lesion. Thus, it is important to separately consider inflammatory lesions and intestinal damage to assess prognosis of CD patients.

Reference

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P1575 DIFFUSION-WEIGHTED MAGNETIC RESONANCE ENTEROGRAPHY AND CAPSULE ENDOSCOPY ACTIVITY INDICES FOR QUANTIFICATION OF SMALL BOWEL INFLAMMATION IN PATIENTS WITH ESTABLISHED CROHN'S DISEASE

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Introduction: Background: Capsule endoscopy (VCE) and magnetic resonance enterography (MRE) are the prime modalities for the evaluation of the small bowel Crohn's disease (CD). Bowel inflammation on contrast-enhanced MRE can be quantified using the Magnetic Resonance Index of Activity (MaRIA). Clermont score is a novel diagnostic index based on diffusion-weighted (DW)-MRI that does not require administration of intravenous contrast material. The accuracy of both MRE indices was validated against ileocolonoscopic activity indices. Mucosal inflammation on VCE is quantified using the Lewis score (LS). In our previous study, MaRIA score was significantly correlated with LS in the distal small bowel. The Clermont score was never previously correlated with a VCE-based activity index.

Aims & Methods: The aim of this study was to correlate the quantitative assessment of the inflammatory activity by the Clermont score and the Lewis score in the distal small bowel.

Methods: Patients with known SBCD in steroid free clinical remission or with mild symptoms (CDAI < 220) for at least 3 months were prospectively recruited and underwent MRE, followed by Agile patency capsule. If patency was proven, VCE was performed. LS, MaRIA and Clermont scores were calculated for the distal SB. C-reactive protein (CRP) and fecal calprotectin (FC) levels were obtained and evaluated for their association with the clinical scores.

Results: All indices were calculated for 44 patients. Active disease was demonstrated in the distal SB in 62% of the patients by VCE and 72% by MRE (p = 0.4). Both MR-based indices significantly correlated with LS, however the correlation was somewhat stronger for the Clermont index (r = 0.56, p = 0.001 and r = 0.517, p = 0.001, respectively). A very strong correlation between the Clermont and MARIA score was demonstrated (r = 0.99, p = 0.0001). Fecal calprotectin levels equally correlated with Clermont and MaRIA score (r = 0.49, p = 0.001 and r = 0.50, p = 0.001, respectively), while CRP levels did not demonstrate a significant correlation with MR-derived indices.

Conclusion: There was a significant correlation between the capsule endoscopy and both MRE-derived activity indices. A strong correlation between contrast-enhanced and diffusion-weighted MRE indices was demonstrated. Diffusion-weighted MRI allows for an accurate assessment of the small bowel inflammation in CD patients while avoiding intravenous gadolinium injection.

*UK and EK equally contributed to the study
**RE and MM equally contributed to the study

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P1576 RELATIONSHIP BETWEEN PSYCHOLOGICAL FACTORS AND INFLAMMATORY BOWEL DISEASE-RELATED DISABILITY IN SINGAPORE

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Introduction: Inflammatory bowel diseases (IBDs) including Crohn's disease (CD) and ulcerative colitis (UC) are chronic, immune-mediated diseases which are known to adversely affect quality of life and cause disability. Recently, the inflammatory bowel disease-disability index (IBD-DI) has been validated as a useful tool to measure disability[1]. Previous studies have shown that high level of anxiety and depression was associated with reduction of health-related quality of life (HRQOL) in IBD. However, the relationship between psychological factors (anxiety and depression) and IBD-related disability has yet to be explored.

Aims & Methods: We hypothesize that psychological factors (anxiety and depression) are associated with disability in patients with IBD from Singapore.

Aims:

1. Determine the association between anxiety and depression, and IBD-related disability

2. Determine the other predictors associated with IBD-related disability
3. Determine the correlation between IBD-DI and health-related quality of life
We conducted a cross-sectional, prospective study of patients presenting to our IBD center. A total of 165 IBD patients were recruited into the study. Anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (HADS), with scores ranging from 0 (no anxiety) to 21 (severe anxiety) for the HADS-Anxiety (HADS-A), and from 0 (no depression) to 21 (severe depression) for the HADS-Depression (HADS-D). IBD-related disability was measured by the IBD-DI, with scores ranging from −80 (maximum degree of disability) to 22 (no disability). Health-related QOL was measured using the Inflammatory Bowel Disease Questionnaire (IBDQ). Clinical and demographic data were obtained from our electronic medical records. Univariate analysis and multiple linear regression analysis were performed to identify predictors associated with IBD-related disability.
Results: From November 2014 to April 2015, one hundred and sixty four patients completed the questionnaire. Eighty seven patients had UC and seventy seven had CD. The prevalence of anxiety and depression in our study population were 24.4%(40/164) and 13.4%(22/164) respectively. Patients with lower scores on IBD-DI (i.e. more disabled) had higher scores on HADS-A (Spearman's correlation coefficient, r_s -0.631, $p < 0.01$) and HADS-D (r_s -0.645, $p < 0.01$) (i.e. more anxious and depressed). Univariate analysis showed that older age, ethnicity, smoking status, older age at diagnosis of IBD, use of steroids within 3 months, use of azathioprine, prior hospitalization, anxiety and depression symptoms correlated with IBD-DI. Multivariate regression analysis revealed that being a non-smoker, and older age at diagnosis of IBD predicted lesser disability, whereas use of steroids within 3 months, anxiety and depression symptoms predicted greater IBD-related disability. IBD-DI positively correlated with IBDQ (r_s 0.835, $p < 0.01$).
Conclusion: Our study demonstrated that psychological factors (anxiety and depression) are associated with IBD-related disability. Patients with IBD should be screened for anxiety and depression and appropriate management instituted for better outcome.

Reference

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Disclosure of Interest: None declared

P1577 ROLE OF CONTRAST-ENHANCED ULTRASOUND (CEUS) IN ASSESSMENT OF INFLAMMATORY ACTIVITY IN PATIENTS WITH SMALL BOWEL CROHN'S DISEASE

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Introduction: Patients suffering from Crohn's disease (CD) often undergo several imaging studies, subjecting the mostly young patients to ionizing. Contrast enhanced ultrasound for capillary microvascular assessment might be a new diagnostic tool for identifying the activity of inflammation by ultrasound techniques.
Aims & Methods: Aims: To evaluate the clinical value of several quantitative parameters of CEUS, including peak intensity (PI), rise time (RT), time to peak (TTP) in assessing CD inflammatory activity, compared with the power Doppler image and enhancement pattern of CEUS.
Methods: We prospectively evaluated 55 consecutive patients with histologically proven CD. Ultrasound (US) was performed by an experienced radiologist applying baseline US, power Doppler imaging (PDI) and CEUS. After the injection of 2ml ultrasound contrast agent (SonoVue), the dynamic cine sequences were recorded as digital raw data for 120 seconds. Then we perform a quantitative analysis using TIC retrospectively. Quantitative analysis was firstly performed by the software within the ultrasound device, quantitative parameter, PI was obtained. Then the same clips were analysed by Sonoliver, which provided RT and TTP values. The concentration of hs-CRP was set as the gold standard. Quantitative results in patients with active and inactive inflammatory were compared using t-test and receiver operating characteristic curve (ROC) analysis. Cutoff values were determined using ROC analysis, and sensitivity, specificity, accuracy and Youden indices were calculated. Limberg classification of PDI and the enhancement patterns of CEUS were also compared and analyzed.
Results: The population with active inflammatory was 39, while the one with inactive inflammatory was 16. Determined by Limberg classification, 35 of the patients were with inflammatory activity, showed a sensitivity of 0.74, specificity of 0.75, accuracy of 0.75, Youden index of 0.49; Determined by the enhancement patterns of CEUS, 44 of the patients were with inflammatory activity, showed a sensitivity of 0.87, specificity of 0.38, accuracy of 0.73, Youden index of 0.25. Quantitative analysis showed a higher peak intensity (>19dB), a shorter rise time (≤6.2s), and a shorter time to peak (≤8.7s) in patients with active inflamation than in those with inactive inflammation ($P<0.05$). Peak intensity showed a higher efficiency in assessing inflammatory activity of CD according to the comparison of ROC with enhancement patterns of CEUS ($P<0.05$).
Conclusion: Power Doppler imaging, qualitative and quantitative analysis of CEUS can be used to identify the activity in CD, while the lateral was more objective.
Disclosure of Interest: None declared

P1578 EVALUATION OF PATIENT-REPORTED OUTCOMES FROM THE CROHN'S DISEASE ACTIVITY INDEX TO DEFINE REMISSION IN THE GEMINI 2 STUDY

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Introduction: Clinical trials in Crohn's disease (CD) are evolving towards including patient-reported outcomes (PROs) to evaluate drug efficacy; however, no validated PROs are available.
Aims & Methods: In post hoc analyses of data from the placebo (PBO)-controlled GEMINI 2 study,[1] we evaluated the use of the PRO components of the CD Activity Index (CDAI) to define vedolizumab (VDZ)-induced remission. Patients (pts) with moderately to severely active CD (CDAI 220-450) who responded to 6 weeks (wks) of VDZ induction therapy were re-randomised to maintenance therapy with PBO or VDZ for 46 wks. PRO components of the CDAI (stool frequency [SF], abdominal pain [AP], and general wellbeing [GWB]) were evaluated alone and in combination (PRO-2 [SF and AP] and PRO-3 [SF, AP, and GWB]) at wks 0, 6, and 52. Contributions of PROs to baseline and mean change from baseline CDAI total scores were analysed. The sensitivity of PRO-based definitions of remission (PRO-2 [SF ≤3 and AP ≤1]; PRO-2 ≤75; and PRO-3 ≤80) to detect clinical remission (CDAI ≤150), their agreement with CDAI ≤150, and the percentage of GEMINI 2 pts who met PRO-based entry criteria (SF ≥4 and/or AP ≥2) were evaluated.
Results: The SF, AP, and GWB subscores contributed 25%, 21%, and 31%, respectively, to the mean baseline CDAI score. PRO-2 and PRO-3 accounted for, respectively, 53% and 91% of the mean change from baseline CDAI score at wk 6, and 47% and 82% at wk 52. PRO-2 (SF ≤3 and AP ≤1), PRO-2 ≤75, and PRO-3 ≤80 detected clinical remission with a sensitivity of, respectively, 67%, 76%, and 57% at wk 6, and 74%, 95%, and 77% at wk 52. PRO-3 ≤80 had the best agreement with CDAI remission at wk 6 and PRO-2 ≤75 had the best agreement at wk 52 (**Table**). PRO-based entry criteria of SF ≥4 and/or AP ≥2 were met by 86% of GEMINI 2 pts.
Table: Definitions of Remission

Definition of remission	Wk 6			Wk 52		
	PBO (n = 148) Pts (%)	VDZ (n = 220)	Agreement with CDAI ≤150[a]	VDZ/PBO[b] (n = 153) Pts (%)	VDZ/VDZ[c] (n = 154)	Agreement with CDAI ≤150[a]
CDAI ≤150	7	15	1.00	22	39	1.00
PRO-2 (SF ≤3 & AP ≤1)	15	20	0.45	18	33	0.74
PRO-2 ≤75	21	29	0.37	23	38	0.84
PRO-3 ≤80	6	13	0.55	19	32	0.80

[a] Determined by kappa statistics; kappa agreement: <0, less than chance; 0.01-0.20, slight; 0.21-0.40, fair; 0.41-0.60, moderate; 0.61-0.80, substantial; 0.81-0.99, almost perfect.[b] Received VDZ during induction and PBO during maintenance.[c] Received VDZ during induction and VDZ every 8 wks during maintenance.

Conclusion: The PRO components of the CDAI contributed most to baseline and treatment-induced changes in CDAI score. Different PRO-based definitions of remission (PRO-2 ≤75 or PRO-3 ≤80) had the best agreement with clinical remission at wks 6 and 52. Interpretations of these post hoc analyses are limited, but applying the cut-offs used here to other datasets could clarify the reliability and clinical meaningfulness of PROs as outcome measures.

Reference

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P1579 INFLIXIMAB TROUGH LEVEL THRESHOLDS VARY DEPENDING ON THE EFFICACY CRITERION CHOSEN IN IBD PATIENTS

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Introduction: Several studies and meta-analyses have shown a correlation between infliximab trough levels (TLI) and clinical remission. Isolated cut-off points vary according to the techniques used. No study has been carried out to determine whether the variations in this therapeutic cut-off depend on the analysis criterion (remission, mucosal healing, etc.). The aim of our study was to compare whether there were similarities in this threshold for clinical remission or biomarkers assessment in IBD.

Aims & Methods: we included in a monocentric observational study including all consecutive BD patients treated with IFX between 2010 and 2013 and followed up in the gastroenterology service. The TLI measurements (ELISA technique, Theradiag) were performed immediately prior to an infusion of IFX (5mg/kg) simultaneously with the CRP (mg/L) and faecal calprotectin (µg/g of stools). The CDAI or partial Mayo scores were reported for all the patients. Exclusion criteria were primary non-responders to IFX, patients previously treated with another anti-TNF agent, and patients optimised at a dose other than 5 mg/kg/8W as well as those suffering exclusively from anoperineal CD. Clinical remission was defined for CD by a CDAI score of < 150 and for UC by a partial Mayo score of < 3. Normal CRP was defined as CRP < 5 mg/L in patients having a high CRP level at the start of treatment. Faecal calprotectin was defined as normal for a level below 250 µg/g of stools. The TLI cut-off was investigated using a ROC curve analysis to isolate a threshold associated with clinical remission, and normal CRP and calprotectin levels.

Results: 213 patients (131 with CD; mean age: 38+/- 16.2 years; M:F sex ratio: 0.8; mean duration of IFX treatment: 14.9+/-6.3 months) were included. 145 patients were in clinical remission. Mean TLI were significantly higher during remission (2.6 *vs.* 1.2 µg/ml; $p < 0.01$). The optimal cut-off associated with clinical remission was 2.1µg/ml (sensitivity: 78%; specificity: 76%). Of the 140 patients who had high CRP levels at the start of treatment, 85 showed normal CRP and clinical remission. The mean TLI were significantly higher when normal CPR levels associated with clinical remission observed (3.5 *vs.* 1.6 µg/ml; $p < 0.01$). The optimal cut-off associated with normal CRP associated with clinical remission was 2.9 µg/ml (sensitivity: 69%; specificity: 66%). 121 patients showed normal faecal calprotectin associated with clinical remission. The mean TLI were significantly higher in presence of normal faecal calprotectin levels associated with clinical remission (4.9 *vs.* 1.7 µg/ml; $p < 0.001$). The optimal cut-off associated with normal faecal calprotectin was 3.9 µg/ml (sensitivity: 74%; specificity: 80%).

Conclusion: The TLI to target varies depending on the treatment objective chosen in IBD patients. The therapeutic level required for obtaining deep remission defined by clinical and biomarker remission, is higher than the level required to achieve clinical remission only.

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P1580 FEASIBILITY AND VALUE OF STOOL ANTI-TNF MEASUREMENT IN IBD PATIENT IN LOOSE OF RESPONSE: A PRELIMINARY STUDY

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Introduction: In a preliminary study including 11 patients with severe UC on IFX induction treatment, the authors found an association between faecal IFX levels, a drop in circulating IFX trough levels (TLI) and treatment non-response. To our knowledge, no studies have been carried out on faecal anti-TNF levels (IFX and ADA) in cases of loss of therapeutic response in UC and CD patients. The aim of this preliminary study was to assess the feasibility of this test in determining faecal anti-TNF levels (IFX and ADA) in the two types of IBD and to investigate whether this correlates with clinical or endoscopic activity.

Aims & Methods: Retrospective study were including from a clinical database and from biological collection data, the first 36 IBD patients with faecal calprotectin levels above of 1800µg/g stools. Faecal anti-TNF assays were conducted on all of these patients and compared with the results of 6 IBD patients with a faecal calprotectin level below 500µg/g (below 500µg/g in 3 cases and below 100µg/g in the other 3 cases). At the same time, we analysed trough levels of anti –TNF and antibodies. All measurements were obtained just before infusion or injection of anti TNF drugs. Exclusion criteria were severe acute colitis and patients under anti TNF therapy under induction regimen.

Results: 42 samples were analysed (20 CD, 22 cases on IFX treatment). The 36 patients with faecal calprotectin levels > 1800 µg/g exhibited clinical activity. An anti-TNF (> 0.2µg/ml of stools) was reported in 7 cases. In 5 cases, the patient was treated with IFX (22.7%) and in two cases with ADA (10%) (p: NS). Anti-TNF was found to be present in stools in 5 cases of UC (22.7%) and in two cases of colonic Crohn's disease (10%) (p: NS). A positive anti-TNF threshold of stools was only isolated in cases where calprotectin was over 1800µg/g (19.4%). No correlation to clinical activity or response to optimisation was reported among patients with or without faecal anti-TNF. Circulating anti-TNF levels at the time of the measurement were higher for IFX and ADA in the presence of feacal anti-TNF. In the 7 cases showing faecal anti-TNF, an endoscopy detected ulcers in the colonic mucosa (100%) as compared with 5/29 colonic diseases showing ulcers in the absence of faecal anti-TNF (14%, $p < 0.05$).

Conclusion: Excluding severe colitis and induction regimen, feacal anti-TNF can be detected in cases of CD as well as UC, irrespective of the anti-TNF used. The presence of colonic ulcers appears to be a pre-condition of intestinal leaks which inversely have no effect in these cases on circulating anti-TNF levels. Large-scale prospective studies would better determine the potential value of this new parameter in IBD patients.

Reference

1. Brandse JF, *Presented at DDW* 2013.

Disclosure of Interest: X. Roblin Lecture fee(s): MSD, Theradiag, J. M. Phelip: None declared, S. Paul: None declared

P1581 THE USE OF FECAL CALPROTECTIN IN MONITORING OF INFLAMMATORY BOWEL DISEASE ACTIVITY IN PREGNANCY

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Introduction: Pregnant patients with inflammatory bowel disease (IBD) constitute a high-risk group for an unsuccessful pregnancy outcome when experiencing a period of high disease activity (recurrent miscarriage, premature delivery, underweight fetus). In this connection, it has been recognized that it necessary to manage the disease over the course of the pregnancy in order to ensure a successful gestation period. At the same time, the fact that the patient is pregnant significantly limits the number of options for objective and safe diagnostic methods. Measuring fecal calprotectin is a non-invasive way of determining IBD activity. However, its diagnostic utility for pregnant patients has not yet been determined.

Aims & Methods: The aim was to determine the diagnostic utility of fecal calprotectin in determining IBD activity during pregnancy.

To the prospective cohort study were included 14 pregnant women with IBD (12 – ulcerative colitis (UC), 2 – Crohn's disease (CD)). All patients underwent clinical laboratory testing over the course of the pregnancy during which non-specific inflammatory markers and fecal calprotectin were measured, and a clinical activity index (CAI) was determined.

Results: 7 patients from the study group experienced a flare-up of the disease over the course of the pregnancy. In cases of active IBD, the average value of calprotectin was at 292.57 ± 145.2 µg/g, and in cases of non-active UC and CD - $22{,}94 \pm 12{,}94$ µg/g. The calprotectin value during high IBD activity correlated with levels of C-reactive protein. In 3 observed cases, a higher level of calprotectin preceded the appearance of clinical symptoms of UC. Lower calprotectin levels correlated with less active IBD as the UC flare-up subsided. However, values of calprotectin measurements stayed elevated longer relative to the clinical signs and normalization of IBD (5 ± 2.2 weeks), indicating that it was necessary to continue treatment. At the same time, calprotectin levels were not linked with IBD activity after birth and thus cannot be used to predict the course of the disease during the postnatal period.

Conclusion: The initial findings suggest that fecal calprotectin is useful in determining IBD activity and in selecting a treatment method during pregnancy.

Disclosure of Interest: None declared

P1582 UPPER GASTROINTESTINAL INVOLVEMENT IN ASYMPTOMATIC CROHN'S DISEASE PATIENTS IN TWO COUNTRIES OF EMERGING DISEASE: ASIA AND EASTERN EUROPE

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Introduction: The incidence of inflammatory bowel disease (IBD) is still increasing in Asia and Eastern Europe. Disease phenotype may differ when compared the East and the West. However, limited studies have reported on the frequency of upper gastrointestinal (GI) involvement in patients with Crohn's disease (CD)

in non-Western countries. In this prospective, international, multicenter study we compared the prevalence of macroscopic and microscopic upper GI manifestations and *Helicobacter pylori* positivity in asymptomatic CD patients in Asia and Eastern Europe in comparison with sex- and age-matched non-IBD controls.
Aims & Methods: Consecutive asymptomatic CD patients were prospectively recruited for upper GI endoscopy between 2013 and 2015 in Hong Kong and in Hungary. Endoscopy and biopsy findings were recorded and histology was performed to assess for *Helicobacter pylori* and microscopic signs characteristic for CD.
Results: One hundred and seventy-one CD patients (91 Hong Kong; 80 Hungary; 71.3% male; median age, 38.5 years) and 122 controls (39 Hong Kong; 83 Hungary) were included. Significant differences were revealed between Chinese and Hungarian CD patients regarding to smoking status and history of appendectomy. Upper GI involvement of CD patients was significantly higher in Szeged (15 vs. 4.4%, $p = 0.018$). No difference was revealed between the two populations in locations and behaviour of CD, and the rate of surgery. There was no difference in the presence of macroscopic inflammation (30.8% vs. 38.7%), microscopic inflammation (84% vs. 80%). Gastroduodenal erosions (17.6% vs. 10%) and *Helicobacter pylori* positivity (13% vs. 3%; $p = 0.001$) was significantly higher in Hungarian CD patients. Granulomas were detected in 1% in Hong Kong and 7.5% in Hungary ($p = 0.001$). Two CD cases (2.5%) in Hungary were diagnosed with celiac disease. Overall CD subjects had a significantly lower *Helicobacter pylori* positivity as compared to controls (8.2% vs 15.5%; $p = 0.010$).
Conclusion: The rate of upper GI lesions in CD patients in Asia was lower to that of Hungary. CD patients had a significantly lower *Helicobacter pylori* positivity rate as compared to controls. The convincingly high frequency of macroscopic and especially microscopic inflammation observed in our study justifies the need of upper GI endoscopy in asymptomatic CD patients independently of ethnicity.
Disclosure of Interest: None declared

P1583 ADHERENCE TO TOPICAL THERAPY IN ULCERATIVE COLITIS

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Introduction: 5-aminosalicylic acid (5-ASA) is the mainstay of treatment for mild-to-moderate ulcerative colitis (UC) for both induction and maintenance of remission. Topical/rectal therapies (both 5-ASA and steroid) are included in national and society treatment guidelines due to their rapid onset of action and local effects. It is known that patient adherence to oral 5-ASA therapy is poor (around 50%) but there are no published studies examining adherence to topical therapies in UC. The aims of this questionnaire-based study were to establish the rate of non-adherence to topical therapy in UC and to ascertain patient reported reasons for and demographic factors associated with non-adherence.
Aims & Methods: A structured interview was conducted with patients with known UC and themes related to causes of non-adherence to rectal therapy were identified. A pilot questionnaire was developed based on the themes identified from the structured interview. 10 consecutive patients with UC completed the pilot questionnaire and gave their feedback on the questionnaire via a structured feedback form. The final study questionnaire, developed to incorporate patient feedback from the pilot study, was then given to consecutive patients with a confirmed diagnosis of UC in a teaching hospital gastroenterology outpatient clinic. The study questionnaire collected data on patient demographics (including: gender, age, ethnicity, co-habitation, marital status, occupation) and disease and medication history. Common reasons for non-adherence were also recorded (identified in the structured interview and pilot study, and included: difficulty remembering to take it every day, competing priorities and awkward route of administration).
Results: 122 patients, 59 male and 63 female, were recruited with a median age of 47 years. 82% of UC patients had been offered rectal therapy at some point. 7% of respondents had been offered rectal therapy but did not commence treatment. 93 patients had used rectal therapy of which 53% discontinued early. 35% of these patients stopped the medication because it was too difficult to remember to take it every night; however, 94% of these patients would have continued to take the medication if there was an option to take it every second or third night. There was a trend towards significance for male gender in non-adherence to rectal therapy ($p = 0.07$) but other examined factors were not found to be statistically significant.
Conclusion: 53% of patients did not take rectal therapy for the recommended duration, of which 35% cited difficulties remembering daily application of therapy as a major factor for stopping. Perhaps when prescribing topical therapy the clinician should emphasise that it is not an 'all or nothing' treatment and that pragmatism in frequency of application is reasonable, and indeed important to improve adherence.
Although the majority of patients with UC have been offered topical therapy at some point, 18% of patients have not. Clinicians should bear this in mind when considering escalation of therapy in UC, as globally increased use of topical therapy could doubtless reduce the need for escalation to immunosuppressant medications.
Disclosure of Interest: None declared

P1584 A RANDOMIZED, SINGLE-BLIND, SINGLE-DOSE, THREE-ARM, PARALLEL GROUP STUDY IN HEALTHY SUBJECTS DEMONSTRATING PHARMACOKINETIC EQUIVALENCE OF PROPOSED BIOSIMILAR ABP 501 WITH ADALIMUMAB

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Introduction: Adalimumab is a recombinant IgG1 monoclonal antibody that binds to TNFα blocking its interaction with p55 and p75 cell surface receptors. ABP 501 is a proposed biosimilar candidate to adalimumab; it contains a fully human recombinant monoclonal antibody with the same amino acid sequence. Evidence from analytical comparisons indicates that ABP 501 is highly similar to adalimumab. This report describes the results of a phase 1 pharmacokinetic (PK) equivalence study comparing ABP 501 with adalimumab.
Aims Methods: This was a single-blind, single-dose, parallel-group study in healthy men and women, 18 to 45 years of age with a body mass index of 18 to 30 kg/m^2. Subjects were randomized to receive 40-mg subcutaneous (SC) injection of ABP 501 or adalimumab reference products sourced from the EU and the US. The primary objective was demonstration of PK equivalence of ABP 501 relative to adalimumab EU and adalimumab US based on area under the serum concentration-time curve from time 0 extrapolated to infinity (AUC_{inf}) and the maximum observed serum concentration (C_{max}). Pre-specified equivalence criterion for the primary PK parameters was for the 90% confidence interval (CI) for geometric means (GM) ratio to fall within 0.80 to 1.25. Secondary endpoints included the safety, tolerability, and immunogenicity after a single dose.
Results: Pharmacokinetics: A total of 67 subjects received ABP 501, 67 received adalimumab EU, and 69 received adalimumab US. After a single dose, the adjusted least square (LS) GM of C_{max} and AUC_{inf} for ABP 501 were 3.22 μg/mL and 2140 μg.h/mL. The adjusted LS GM of C_{max} and AUC_{inf} for adalimumab EU were 3.37 μg/mL and 2050 μg.h/mL and that for adalimumab US were 3.11 μg/mL and 1920 μg.h/mL. The ratios of adjusted LS GM (90% CIs) between ABP 501 and adalimumab EU for C_{max} and AUC_{inf} were 0.96 (0.89, 1.03), and 1.04 (0.94, 1.17) and that for ABP 501 and adalimumab US were 1.04 (0.96, 1.12), and 1.11 (1.00, 1.24). The ratios of adjusted LS GM (90% CIs) for C_{max} and AUC_{inf} between adalimumab EU and adalimumab US were 0.92 (0.86, 0.99) and 0.94 (0.84, 1.04). The 90% CIs of these ratios were fully contained within 0.80 to 1.25, confirming PK equivalence between ABP 501 and adalimumab reference products, as well as between adalimumab EU and adalimumab US.
Safety: There were no deaths, treatment-related serious adverse events, or treatment-related adverse events leading to discontinuation from the study. The most frequently reported treatment-related AEs included headache, nausea, nasopharyngitis, and oropharyngeal pain.
Immunogenicity: No pre-existing anti-drug antibodies (ADA) were detected at baseline. Subjects developing binding antibodies in each group were – ABP 501: 36 (54%), adalimumab EU: 45 (67%) and adalimumab US: 38 (55%). Subjects developing neutralizing antibodies were – ABP 501: 12 (18%), adalimumab EU: 14 (21%) and adalimumab US: 15 (22%).
Conclusion: Results of this phase 1 study demonstrated PK equivalence of ABP 501 following a single 40-mg SC injection relative to that of adalimumab EU and adalimumab US, as well as PK equivalence between adalimumab EU and adalimumab US. Safety was comparable and ADA rates were similar in all three treatment groups.
Disclosure of Interest: P. Kaur Shareholder: Employee, Amgen, inc., V. Chow Shareholder: Employee, Amgen, inc., N. Zhang Shareholder: Employee, Amgen, inc., R. Markus Shareholder: Employee, Amgen, inc.

P1585 GRANULOCYTE, MONOCYTE/MACROPHAGE ADSORPTIVE APHERESIS IN STEROID-DEPENDENT ACTIVE UC WITH INSUFFICIENT RESPONSE OR INTOLERANCE TO IMMUNOSUPPRESSANTS AND/OR BIOLOGICAL THERAPIES (THE ART TRIAL): SAFETY RESULTS AT 48 WEEKS

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Introduction: Current medical treatment options for patients with steroid-dependent, active ulcerative colitis (UC) with insufficient response or intolerance to immunosuppressants (IS) and/or biologicals are limited.
Aims & Methods: This study was an uncontrolled, open-label, multicenter trial conducted in the UK, France and Germany (ART, NCT01481142). Consecutive eligible patients (18-75 years, steroid-dependent active UC with a Rachmilewitz (CAI) index $\geq$6 and an Endoscopic Activity Index (EAI) $\geq$4, and insufficient response or intolerance to IS and/or biologicals) were included. Patients received at least 5 weekly GMA apheresis. Evaluation visits were planned at Week 12, 24 and 48. The primary endpoint was the remission rate (CAI $\leq$4) at Week 12 in the Intention-to-treat (ITT) population. We report interim safety results observed at 48 weeks after baseline.
Results: The safety population comprised 85 subjects having received at least one apheresis treatment. 8 (11.1%) subjects withdrew from the study because of AEs; none of those were considered related to study treatment. 61/85 patients (71.8%) experienced at least 1 AE up to 2 weeks after the date of the last apheresis treatment. 30 (41.7%) experienced at least 1 AE through week 48. 6 (7.1%) of the 85 subjects experienced serious AEs (SAEs) up to 2 weeks after

the date of the last apheresis treatment. 15 (20.8%) of 72 subjects followed up through to week 48 experienced SAEs. None of the SAEs were considered to be related to study treatment. Headache was the most prominent adverse event (21.2% of patients).
Conclusion: We describe interim safety results from a cohort of steroid-dependent moderate to severe active UC patients with failure or intolerance to IS and/or biologicals treated with GMA apheresis induction therapy. While sustained clinical benefit was reported earlier in 46.4% of the patients at Week 24 and in 39.3% at Week 48, no new safety signals were found. GMA apheresis may be an effective and safe alternative treatment option in patients with UC even failing or intolerant to IS and TNF-inhibitors.
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P1586 THE FIRST JAK1-SELECTIVE INHIBITOR, FILGOTINIB, DISPLAYS SIMILAR MOLECULAR ACTIVITY IN THE GUT OF MICE WITH DSS-INDUCED COLITIS AND IN CULTURES OF COLON BIOPSIES FROM INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Filgotinib (known as GLPG0634) is a JAK inhibitor that has been shown to be selective for JAK1 over the 3 other family members (JAK2, JAK3 and TYK2) in biochemical and/or human whole blood assays. Filgotinib is currently being assessed as a treatment for Crohn's disease (CD) in a Phase 2 study. It has been shown to be particularly efficacious in arthritis as well as colitis mouse models. Here, we report that in mouse and human colon after treatment with filgotinib *in vivo* or *ex vivo*, respectively, the same signaling mechanisms are impacted, suggesting common JAK1 inhibition-related effects.
Aims & Methods: Chronic colitis was induced by adding 4% dextran sodium sulfate (DSS) to drinking water of Balb/c mice that were administered 30 mg/kg filgotinib QD during the 16 days of the study. Disease activity index (DAI) was evaluated daily by measuring weight loss, rectal bleeding, and stool consistency. Histological scoring of disease was based on an evaluation of severity and extent of inflammation and epithelial damage. Immune cell infiltration as well as STAT activation in mouse gut was analyzed by immunohistochemistry. Gene expression analysis in the colon mucosa was performed using qPCR. Inflamed colon biopsies from IBD patients were cultured for 18 or 24 hours in the presence of 5 μM GLPG0634 and gene expression as well as STAT phosphorylation were analyzed using qPCR and 5-Plex STAT kit Luminex, respectively.
Results: DAI revealed the strong protection against experimental colitis conferred by filgotinib. This was confirmed by histological assessment, which showed lower disease severity (54%), as well as reduced inflammatory cell infiltration in colon tissue from filgotinib-treated mice compared to controls. Colons from DSS-treated mice displayed higher STAT3 phosphorylation levels, which were prevented by treatment with filgotinib. Of interest, the expression of genes that activate (IL-6) or are induced by the JAK1 pathway (MX1, MX2) followed the same regulation as pSTAT3, suggesting a relationship between these readouts and a role of the pathway in the disease. Remarkably, the same repression of IL-6 and MX1 expression, as well as STAT3 phosphorylation by filgotinib were observed in cultured colon biopsies from IBD patients.
Conclusion: Taken together, these new data provide further mechanistic understanding for the pronounced efficacy of JAK1 inhibition in the pre-clinical mouse DSS-induced colitis model, with the efficacy observed at the macroscopic, histologic and molecular levels correlating with the inhibition of STAT3 phosphorylation in the colon. The striking concordance between molecular signatures related to JAK1 inhibition in experimental colitis and in a human colon biopsy model further stresses the importance of the JAK1 pathway in the etiology of IBD. These data suggest that filgotinib may be beneficial in treating CD patients and support its evaluation in a clinical study.
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P1587 MAINTENANCE OF CLINICAL REMISSION IN CROHN'S DISEASE PATIENTS AFTER DISCONTINUATION OF ANTITNF AGENTS: RESULTS FROM A SINGLE CENTRE COHORT

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Introduction: Introduction of antiTNF agents led to significative progresses in the treatment of Inflammatory Bowel Disease (IBD) and their complications, widening our possibilities of therapeutical approach. However we still don't know whether and when stopping the biological treatment in patients that are in clinical remission.
Aims & Methods: Aim of our study was to assess the rate of clinical remission in a cohort of Crohn's disease (CD) patients who discontinued antiTNF therapy because of clinical benefit and to evaluate if the mucosa healing is associated to a better outcome. A secondary objective was to assess response and tolerance to antiTNF re-treatment in relapsers.
Methods: Consecutive patients followed in a referral center for IBD, affected by CD and who received an antiTNF agent, infliximab(IFX) or adalimumab (ADA) for a period ≥12 months and discontinued the drug because in clinical remission were included. All patients had an endoscopy performed before and after the treatment with antiTNF. Demographic, clinical and endoscopic characteristics of patients were collected. Relapse was defined as need for rescue therapy (corticosteroids or new cycle of antiTNF) or surgery. Efficacy and tolerance of re-treatment with antiTNF for the relapse was evaluated.
Results: Between 516 patients treated with antiTNF agents from 1999 to 2011 in our Centre, 58 patients were included. 47 received IFX and 11 ADA. Median duration of treatment was 19 months. Median IFX infusions: 11. Median ADA administrations: 47. A concomitant treatment with immunosuppressant therapy (ISS) was seen in 66% of patients. When biological teatment was discontinued, 84% of patients were on ISS. Mucosal healing was achieved in 39 patients (67%). Kaplan-Meier curves showed a cumulative probability of a disease free course at 1 year of 69%. After 2 years from stopping antiTNF 48% of patients presented a flare of disease and probability of relapse after 5 years was 65%. In the univariate analysis no variables resulted related to the probability of mantenaince clinical remission. 30 patients received a new cycle of antiTNF: 63% obtained remission, 26% lost response after some months and 10% experience an acute reaction.
Conclusion: In our cohort of CD patients treated with antiTNF at least for 1 year, who discontinued the treatment because in clinical remission, the probability to maintain clinical benefit at 2 years was 52%. The rate of relapse was higher in the first 2 years from withdrawal. Mucosa healing did not predict sustained clinical remission. Re-treatment with antiTNF for relapsers was well tolerated and effective in the majority of patients. Discontinuation of antiTNF therapy does not seem a success strategy in the most of patients and future multicentric prospective studies on predictive factors are needed to identify patients with a higher risk of relapse.
Disclosure of Interest: None declared

P1588 LONG-TERM EFFICACY OF GRANULOCYTE-MONOCYTE-APHERESIS IN ULCERATIVE COLITIS ELDERLY PATIENTS. THE ITALIAN REGISTRY OF THERAPEUTIC APHERESIS

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Introduction: Granulocyte-monocyte-apheresis (GMA) is effective in the treatment of ulcerative colitis (UC). Thanks to its favorable safety profile, the use of this technique could be particularly suitable for elderly patients. However, information on the efficacy of GMA in this population is still scant.
Aims & Methods: This observational study investigates the efficacy of GMA in elderly patients included in the Italian Registry of Therapeutic Apheresis.
Data of elderly (>65 years) patients with mild/moderate UC treated with a standard protocol of GMA (5 sessions in 5 weeks) were evaluated. Clinical evaluations were performed at 3, 12 and 24 months since the end of GMA session. The following parameters were assessed: incidence of clinical remission (CAI [Colits Active Index] <4); erythrocyte sedimentation rate (ESR); c-reactive protein (CRP); white cells blood count (WBC). Endoscopical evaluations were performed at a 3-month follow-up: the incidence of endoscopical remission (EAI [endoscopical activity index] 0/1) was assessed.
Results: Data for 74 patients (51 males, median age 68 years; CAI 7.12) were available; 62 patients were either steroid-resistant or steroid-dependent. The proportion of patients with remission of disease was 64% at 3 months, 62% at 12 months and 60% at 24 months. At 24 months, all other efficacy parameters had improved from baseline: CAI (7.12 vs 3.2), ESR (34.82 vs 12.8 mm/h), CRP (4.45 vs 0.80 mg/dl) and WBC (8.11 vs 6.12) ($p < 0.001$ for all comparisons).
Endoscopic data were available for 32 patients. The incidence of mucosal healing was 44%; all patients with mucosal healing presented a clinical remission over the entire follow-up period.
No major adverse events were reported during GMA sessions.
Conclusion: Data collected on a sample of elderly patients included in the Italian Registry of therapeutic apheresis show that GMA is a safe and effective procedure over a long-term follow-up also in this population. Mucosal healing appears strongly associated with clinical remission.
Disclosure of Interest: None declared

P1589 COST-EFFECTIVENESS OF VEDOLIZUMAB COMPARED WITH INFLIXIMAB, ADALIMUMAB, AND GOLIMUMAB FOR TREATMENT OF MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS IN THE UNITED KINGDOM

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Introduction: The objective of this study is to examine the clinical and economic impact of vedolizumab (VDZ) compared with infliximab (IFX), adalimumab (ADA), and golimumab (GOL) in the treatment of moderately-to-severely active ulcerative colitis (UC) in the United Kingdom (UK).
Aims & Methods: A Markov decision analytic model in Microsoft Excel was used to compare VDZ with other biologic treatments (IFX, ADA, and GOL) for the treatment of UC patients in the UK. Due to a lack of data in comparable patient populations, this analysis was conducted in anti-tumor necrosis factor (TNF)-naïve patients only. Efficacy data were obtained from a network meta-analysis of Phase III clinical trials, using placebo as the common comparator. Other inputs (e.g., unit costs, adverse event disutilities, probability of surgery, mortality) were obtained from published literature. Costs are presented in 2014 British pounds. Outcomes included quality-adjusted life-years (QALY), time spent in clinical response, and time spent in clinical remission. Time horizons included 10-year (base case) and lifetime (scenario) horizons, with costs and outcomes discounted by 3.5% per year. Incremental cost-effectiveness ratios (ICER) were presented for VDZ compared with other biologics. Univariate and multivariate probabilistic sensitivity analyses were conducted to assess model robustness to parameter uncertainty.
Results: Over the base-case (10-year) time horizon, the model predicted that anti-TNF-naïve patients on VDZ accrued more QALY than patients on other biologics: 5.898 QALY vs 5.818, 5.760, and 5.790 QALY for IFX, ADA, and GOL, respectively. The incremental results over a 10-year horizon suggests that VDZ is a cost-effective treatment compared with ADA (ICER of £6,634/QALY), and VDZ is dominant compared with IFX and GOL. Patients on VDZ spent more time in clinical response (2.93 years vs 2.55 years for IFX, ADA, and GOL, respectively) and clinical remission (1.38 years vs 1.08, 0.99, and 1.04 years) than patients on any other biologic. VDZ was found to be dominant compared with all other biologics over a lifetime horizon. Sensitivity analyses suggest that results are most sensitive to treatment response and transition probabilities. However, VDZ remained cost-effective irrespective of variation in any of the input parameters.
Conclusion: Our model predicted that treatment with VDZ improves QALY, increases time in remission and response, and is a cost-effective treatment option for anti-TNF-naïve patients with moderately-to-severely active UC compared with all other biologics tested. VDZ may also be a cost-saving treatment strategy as well.
Disclosure of Interest: M. Wilson Financial support for research: Employee of RTI Health Solutions, a company hired by Takeda to conduct the study, M. Kerrigan Financial support for research: Employee of PHMR, a company hired by Takeda to conduct the study, M. Smyth Financial support for research: Employee of Takeda Pharmaceuticals, Inc., A. Bergman Financial support for research: Employee of Takeda Pharmaceuticals, Inc., H. Chevrou-Severac Financial support for research: Employee of Takeda Pharmaceuticals, Inc., R. Selby Financial support for research: Employee of Takeda Pharmaceuticals, Inc.

P1590 COST-EFFECTIVENESS OF VEDOLIZUMAB COMPARED WITH CONVENTIONAL THERAPY FOR TREATMENT OF MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS IN THE UNITED KINGDOM

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Introduction: The objective of this study is to examine the clinical and economic impact of vedolizumab (VDZ) compared with conventional therapy (CT) in the treatment of moderately-to-severely active ulcerative colitis (UC) in the United Kingdom (UK) based on results of the GEMINI 1 trial.
Aims & Methods: A Markov decision analytic model in Microsoft Excel was used to compare VDZ with CT (aminosalicylates, corticosteroids, immunomodulators) for the treatment of UC patients in the UK. We considered three populations: the overall intent-to-treat (ITT) population; anti-tumour necrosis factor (TNF)-naïve patients; and patients who previously failed anti-TNF therapy from the GEMINI 1 trial. Population characteristics, efficacy data, and UC health-state utility data were obtained from the GEMINI 1 trial. Other inputs (e.g., unit costs, adverse event disutilities, probability of surgery, mortality) were obtained from published literature. Costs are presented in 2014 British pounds. Outcomes included quality-adjusted life-years (QALY), time spent in clinical response, and time spent in clinical remission. Time horizons included 10-year (base-case) and lifetime (scenario) horizons, with costs and outcomes discounted by 3.5% per year. Incremental cost-effectiveness ratios (ICER) were presented for VDZ compared with CT. Univariate and multivariate probabilistic sensitivity analyses were conducted to assess model robustness to parameter uncertainty, and a scenario analysis was explored using efficacy data from a network meta-analysis.
Results: Over the base-case (10-year) time horizon, the model predicted that patients on VDZ accrued more QALY than patients on CT: 5.551 QALY vs 5.397 QALY in the ITT population (ICER = £33,297/QALY); 5.597 vs 5.403 QALY for anti-TNF- naïve patients (ICER = £24,657/QALY; network meta-analysis results: utilities 5.898 for VDZ vs 5.555 for CT and ICER = £4,862/QALY); and 5.463 vs 5.373 QALY for anti-TNF- failure patients (£64,999/QALY). Patients on VDZ spent more time in clinical response (e.g., 0.99 years vs 0.27 years for the ITT population) and clinical remission (0.64 years vs 0.13 years) than patients on CT. Scenario analyses with a lifetime horizon showed VDZ to be even more cost-effective (ITT population ICER = £20,599/QALY). Sensitivity analyses suggest that results are most sensitive to treatment response and transition probabilities.
Conclusion: Our model predicted that treatment with VDZ improves QALY, increases time in remission and response, and is a cost-effective treatment option for both anti-TNF naïve and anti-TNF failure patients with moderately-to-severely active UC compared with CT over both 10-year and lifetime horizons.
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P1591 REMICADE AT HOME: AN ALTERNATIVE SETTING OF INFLIXIMAB THERAPY FOR PATIENTS WITH CROHN'S DISEASE

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Introduction: Remicade (infliximab) is an anti-Tumor Necrosis Factor (TNF) agent that is frequently used as induction and maintenance treatment for patients with Crohn's disease (CD). Remicade is administered intravenously and is usually given at 6-8 weekly infusion intervals. As a consequence, patients have to come to the infusion clinic, which is a time consuming effort.
Aims & Methods: The aim was to evaluate if Remicade infusions at home could serve as a useful alternative, and whether this is safe. A pilot study was conducted in which CD patients received Remicade infusions at home for the duration of one year. Patients had to be in clinical remission (HBI $\leq$ 4 points) receiving Remicade maintenance treatment. Data collected from questionnaires were assessed to evaluate satisfaction and experience of the participants. Patients were asked to rate on a scale from 1 to 10 (1 = very unlikely, 10 = very likely) if they would recommend Remicade at home to other CD patients. Costs were analyzed and compared to Remicade treatment at the infusion clinic. All data were analyzed using IBM SPSS 21.0 software.
Results: In total, 36 patients were contacted of which 13 patients (36%) wanted to participate. Of the participants, 54% were female and 46% male, with a mean age of 39,8 years. Five patients discontinued home administration before the end of the year (2 because of stringent infusion planning during working hours, and in 3 patients Remicade treatment was stopped). In total, 59 Remicade infusions were administered at home with a median dose of 369 mg (dose range: 300 to 700 mg). No severe adverse events were reported. Differences in costs between Remicade infusions at home and in the hospital were based on costs of home care nurses and infusion unit costs. Drug costs of Remicade were equal in both settings. The mean costs of one Remicade infusion at home was €230 compared to €284 for one Remicade infusion at the infusion clinic (excluding drug costs), which means a cost saving of €54 per infusion when Remicade is administered at home. Ten out of 13 patients (77%) returned the completed questionnaires. Most of the patients would recommend Remicade at home to other patients: 20% scored 3 points, 20% 6 points, 20% 7 points, and the remaining 40% scored 8 points. Seven out of 13 patients (54%) would recommend the possibility of infusions in the evening hours or during weekends.
Conclusion: We here show that about one third of patients wanted to participate. Most patients were satisfied as indicated by a score of 6 or higher in 80% of participants who were asked if they would recommend Remicade at home to other CD patients. Five out of 13 patients stopped before the end of the 1 year follow-up period (2 patients because of logistic reasons, and in 3 patients Remicade treatment was stopped). Home administration was €54 cheaper per infusion as compared to Remicade infusions at the infusion clinic. Future studies should demonstrate the benefits for the patients and possible cost savings of Remicade infusions at home, in order to evaluate whether this alternative setting can be recommended for daily practice.
Disclosure of Interest: None declared

P1592 OUTCOME OF THIOPURINE INTOLERANCE IN INFLAMMATORY BOWEL DISEASE

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Introduction: Thiopurines are frequently used to maintain remission in patients with moderately to severe Ulcerative Colitis and Crohn's Disease. Up to 2/3 of patients will present side effects and about 15% will be intolerant to thiopurine therapy.
Aims & Methods: To evaluate the impact of thiopurine intolerance on various clinical outcomes in patients with inflammatory bowel disease (IBD). Single center, observational study, including patients with IBD under thiopurine therapy. Two cohorts were defined (patients intolerant and not intolerant to thiopurines). Outcomes included need of multiple steroid cycles (≥ 3), multiple surgeries (≥ 2), number of hospital admissions and need and response to anti-TNF therapy. Statistical analysis was performed using SPSS v21.0.
Results: From 523 patients under thiopurine therapy, 61 (11.7%) were intolerant. Multiple steroid cycles (39.3% versus 40.7%, $p = 0.844$), number of hospitalizations (4.22 versus 4.25 $p = 0.96$) and multiple surgeries (9.8% versus 5.9% $p = 0.24$) occurred equally in both groups. Although time until anti-TNF therapy did not differ between groups (109 versus 101 months, $p = 0.655$) the rate of utilization was superior in intolerant patients (68.9% versus 42.6%, $p \leq 0.001$). Need for intensification of anti-TNF was not statistically different between groups (23.3 versus 33.6 $p = 0.274$), but occurred sooner in intolerant patients (26.9 versus 37.0 months, $p = 0.019$). Despite not statistically significant, the percentage of patients not responding to therapy escalation was superior in intolerant patients (80.0% versus 39.0%, $p = 0.08$). These findings were independent of IBD subtype or anti-TNF used.
Conclusion: In our series, the percentage of patients intolerant to thiopurines was in accordance to the published literature. Although intolerance was not associated with a rise in steroid utilization, admissions or surgeries, this group required more anti-TNF therapy and demonstrated worse clinical response.
Disclosure of Interest: None declared

P1593 ANTI-TNF-ALPHA-INDUCED LUPUS-LIKE-SYNDROM AND ANTI-TNF-ALPHA-INDUCED LUPUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Drug-induced autoimmunity with elevated autoimmune antibodies, especially elevated ANA titres, is a common phenomenon in anti-TNF-alpha therapy of patients with inflammatory bowel disease (IBD). However, progression to anti-TNF-alpha-induced lupus-like syndrome (LLS) or even anti-TNF-alpha-induced lupus (ATIL) is uncommon. Yet, establishing this diagnosis is difficult since LLS or ATIL mostly manifests with arthralgia that is also frequent as extraintestinal IBD manifestation. Furthermore, there is no common definition for LLS and ATIL and the terms are often synonymously used in publications.
Aims & Methods: Our objective aims to describe precisely the characteristics of LLS and ATIL patients for proposing/discussing clear diagnostic criteria for anti-TNF-alpha-induced LLS and ATIL and to investigate the prognosis of patients with LLS or ATIL. For statistical analysis, a Mann-Withney test or a Spearman correlation was performed.
Results: So far, we have data from 18 patients with LLS or ATIL (10 female, 8 male; median age 41.5 (range 25-74); Crohńs disease (CD) $n = 13$, ulcerative colitis (UC) $n = 5$; Infliximab (IFX) $n = 10$; Adalimumab (ADA) $n = 8$. Median duration of IFX or ADA therapy until LLS or ATIL was 238 days (7-1825).
ANA titre was significantly lower before onset of LLS or ATIL (median ANA titre 1:320, $<$1:160-1:1280; $p = 0.0024$). When LLS or ATIL was present, the median ANA titre was 1:1280 ($<$1:160-1:20480), median anti-dsDNA level was 41.1 U/ml (10.8-104.3 U/ml) and median CLIFT (Crithidia luciliae immunofluorescence test) titre was $<$1:10 ($<$1:10-1:80). There was neither a correlation of ANA titres with dsDNA levels ($r = 0.341$) nor of dsDNA levels with CLIFT titres ($r = -0.065$). Almost all patients (16/18; except one patient with ANA titre of 1:320 and one patient with an ANA titre of $<$1:160) had ANA titres equal or above 1:640 with manifestation of LLS or ATIL.
Eleven patients had arthralgia as predominant symptom whereas 6 patients presented with arthritis (arthralgia + joint swelling). Other symptoms besides arthralgia or arthritis were rare (skin lesions $n = 3$; fever $n = 2$; myalgia $n = 2$; elevated liver function test $n = 2$). Mean total duration of anti-TNF-alpha therapy was 10 months (2-72 months). None of the patients fulfilled the ACR criteria for systemic lupus erythematosus.
Nine patients switched to another anti-TNF-alpha therapy (IFX to ADA $n = 4$; ADA to IFX $n = 4$; IFX to Golimumab $n = 1$) after cessation of symptoms and reduction of ANA titres below 1:1280. Four patients (IFX $n = 3$; ADA $n = 1$) experienced a recurrence of LLS or ATIL. The median ANA titre in these patients at the time point of recurrence was 1:1280 (1:640-1:2560).
Conclusion: In conclusion, in our cohort, almost all patients presented with arthralgia or arthritis and ANA titres equal or above 1:1280 at onset of LLS or ATIL.
Currently, we are investigating the prognosis of patients with LLS or ATIL with respect to failure of anti-TNF-alpha-therapy, worsening of disease, hospitalization and need for surgery in a case-control study.
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P1594 EARLY EFFECTIVENESS IN INFLAMMATORY BOWEL DISEASE PATIENTS WHO WERE TREATED WITH CT-P13

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Introduction: CT-P13 is a biosimilar to innovator infliximab (INX) that has been approved by the European Medicines Agency in 2013. In observational study of CT-P13 which is ongoing at 15 study centers in South Korea, the efficacy of CT-P13 was assessed in 92 naïve patients of Infliximab with moderate-to-severe IBD patients (39 active Crohn's disease (CD) and 53 active Ulcerative Colitis (UC)).
Aims & Methods: The objective is to compare response and remission rates of CT-P13 in observational study to historical data of INX.
Retrieved relevant references from public domains are SONIC (Colombel JF. 2010)[1] and ACT I/II (Rutgeerts P. 2005)[2]. Efficacy endpoints were assessed using Crohn's Disease Activity Index (CDAI) in patients with moderate to severe active CD and using the Mayo Scoring System (MSS) in patients with moderate to severe active UC disease. Non-inferiority (NI) margin was defined to preserve 50% of effectiveness of INX. NI test was performed at 5% one-sided significance level. NI of CT-P13 is concluded if the bound of the 95% one-sided confidence interval for the difference of response and remission between CT-P13 and INX is larger than the pre-specified NI margin.
Results: SONIC[1] and ACT I/II[2] were used to determine NI margin for the CD and UC, respectively. The response and remission rates in the observational study of CT-P13 were within the NI margin and showed the earlier effectiveness in CD and UC naïve patients of Infliximab.
Conclusion: The early response and remission rates up to week 14 in the observation study of CT-P13 are comparable with historical data of INX.

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P1595 HOW MUCH DOES OUR INFLAMMATORY BOWEL DISEASE PATIENTS ADHERE TO THE THERAPY?

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Introduction: Inflammatory Bowel Disease (IBD) often requires chronic therapy to reduce the risk of recurrence and possibly colorectal cancer. The adherence to therapy is therefore crucial to its success.
Aims & Methods: We aimed to assess adherence to therapy in IBD per os; determine potential predictors of ''non compliance''.
Results: We distributed 150 questionnaires regarding therapy adherence (Morisky medication adherence scale), beliefs in therapeutics (Questionnaire about the Beliefs in Therapy), therapeutic complexity (Questionnaire about the Therapeutics Complexity) and psychological factors (Hospital Anxiety and Depression Scale - HADS) to outpatients with IBD followed in a Gastroenterology department of a tertiary hospital. They were complemented in 139 cases (female sex-56%; mean age-40 years Crohn's disease-82, Ulcerative Colitis-57). We documented ''non-adherence'' to therapy per os (defined as Morisky questionnaire score <7) in 28.7% patients - 25% > 5ASA per os and 27% > azathioprine. The majority of ''non-compliance'' were intentional type - ''I decided to reduce the medication for IBD because I feel worse when I take it'' or ''I stop taking medication when I feel the disease controlled''. The complexity of the therapeutic regimen ($p = 0.003$), in particular the number of daily doses ($p = 0.012$), ''ambivalence'' (beliefs in the necessity of therapy score > 12/beliefs in concerns about the therapy score > 12) ($p = 0.038$) and depression (score HADS-D > 8) ($p = 0.046$) were associated with the ''non-adherence'' to therapy per os. Sex, age, disease time, disease type, bowel surgery or

previous hospitalizations, absenteeism and anxiety (score HADS-A > 7) had no impact on "non-compliance".
Conclusion: Non-adherence to therapy per os assumes a particular aspect in IBD. Optimizing the discussion about the concepts and concerns of patients to overcome perceptual barriers regarding medication, simplifying therapeutic schemes and timely manage behavioral changes may alleviate the negative aspects of the clinical course inherent to non- adherence.
Disclosure of Interest: None declared

P1596 INFLAMMATORY BOWEL DISEASE: ADHERENCE TO IMMUNOSUPRESSION IN THE ERA OF BIOLOGICAL THERAPY

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Introduction: Adherence to therapy is crucial for the impact in the disease prognosis and the implications in health costs. In Inflammatory Bowel Disease (IBD), infliximab is one of fundamental drug in the therapeutic approach, but its association with azathioprine provides greater efficacy. However, outside clinical trials, research on the adherence to the monotherapy with immunosuppression versus combined therapy with infliximab is scarce. Infliximab, with its administration features, determines particular conditions of adherence, but the same is not possible with azathioprine.
Aims & Methods: We aimed to assess adherence to azathioprine when combined with biological therapy; and determine potential predictors of "non-compliance".
Results: We distributed questionnaires regarding therapy adherence (Morisky medication adherence scale eight items) to 64 outpatients with IBD under azathioprine in a Gastroenterology department of a tertiary hospital, and 59 (93%) were completed. Female sex-58%; mean age-37 years; Crohn's disease-43, Ulcerative Colitis-16; 27 with combined therapeutic with infliximab. Adherence to immunosuppressive therapy (defined as the Morisky questionnaire score > 6) was similar in patients with and without infliximab (monotherapy with azathioprine-69% vs combined therapy-78%; p = 0.554). Overall, the "non-adherence" to immunosuppressants was greater in patients: male gender (p = 0.044); skeptics/indifferent about the need of therapy to control IBD (Questionnaire about Beliefs in Therapy) (p = 0.005), particularly about uncertainty about "life without drugs would be impossible". Age, disease type, previous bowel surgery, smoking, marital status, employment, academic, anxiety/depression (Hospital Anxiety and Depression Scale) and therapeutic complexity showed no increased risk for "non-compliance".
Conclusion: One in four patients with IBD do not adhere to immunosuppressants, but this rate does not seem to increase with the association with biological agents. Male and skepticism/indifference about the need for therapy for IBD, constituted risk factors for "non-compliance" with immunosuppression.
Disclosure of Interest: None declared

P1597 MANAGEMENT OF ABDOMINAL PHLEGMON IN ANTI-TNF NAÏVE CROHN'S DISEASE PATIENTS

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Introduction: An abdominal phlegmon is an inflammatory mass that can develop in Crohn's disease (CD), typically in the setting of stricturing and/or penetrating disease. The question of whether anti-TNF therapy is of benefit in treating CD patients presenting with phlegmon has not been well addressed.
Aims & Methods: In this retrospective study we aim to determine the efficacy of anti-TNF therapy in preventing surgery in the setting of an abdominal phlegmon complicating CD. Cases seen at single tertiary care IBD centre were identified using a radiology database searching for the words "Crohn's", "phlegmon" and "abscess". Exclusion criteria included a lack of follow up at the same institution, any underlying cause for phlegmon other than CD, postoperative complications resulting in a phlegmon, prior anti-TNF use or cases with > 2 prior resections.
Results: 59 cases were identified. All cases received antibiotic therapy and, of the 33 with an abscess, 22 underwent percutaneous drainage. The cohort was divided into 3 groups according to initial management: antibiotics with no additional therapy (n = 6), antibiotics followed by surgical resection (n = 45), antibiotics followed by anti-TNF therapy (n = 8). There were no major differences in clinical characteristics between the 3 groups at presentation.
45 cases underwent a surgical resection as a first line therapy following standard therapy with antibiotics +/- percutaneous drainage of an abscess. The median time from phlegmon diagnosis to surgery was 2 months (IQR 0-6 months). 8 cases received an anti-TNF as a first line therapy on top of standard therapy with antibiotics +/- percutaneous drainage of an abscess. The median time to commencement of an anti-TNF therapy was 7 months (IQR 0-38 months). There was just one abscess recurrence during follow up. This was in a case initially treated with surgical resection – this recurred at 11 months and after antibiotics and percutaneous drainage of an abscess an anti-TNF was commenced.
A second line intervention was more common in the anti-TNF treated group:12 of the 45 cases in the original surgical group later went on to receive an anti-TNF while 6 of the 8 originally treated with an anti-TNF went on to have surgery, (χ^2 p = 0.008). In a survival analysis, the time to an anti-TNF was significantly longer in the surgical group than the time to surgery in the group originally treated with an anti-TNF [126 months (95% CI 124-128) versus 32 (95% CI 20-44), p = 0.003]. In a cox regression analysis, receiving an anti-TNF prior to surgery was the only factor associated with a delay to surgery, see table.

	HR (95% CI)	P value
Anti-TNF therapy prior to surgery	0.15 (0.05-0.43)	< 0.0001
Phlegmon Resolution on Imaging	0.48 (0.22-1.04)	p = 0.063
Prior Surgery	1.47 (0.68-3.22)	p = 0.33

We did not see a difference in the rate of complications in those who received an anti-TNF prior to surgery nor was there a difference in the length of small bowel resected.
Conclusion: Anti-TNF can be safely used in the management of CD cases presenting with an abdominal phlegmon after antibiotic therapy and drainage of abscess where applicable. However, most cases will ultimately require surgery. Anti-TNF therapy may prolong the time to surgery but does not prevent surgery. Therefore we would propose an algorithm, where if possible, surgery is used first line to delay the need to use an anti-TNF.
Disclosure of Interest: None declared

P1598 MUCOSAL HEALING AND LONG-TERM FOLLOW-UP OF PATIENTS WITH CROHN'S DISEASE TREATED WITH ANTI-TNF AGENTS

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Introduction: The advent of anti-TNF agents has advanced therapeutic goals to encompass not only clinical response and remission but also to include mucosal healing (MH). From 2006, we have undergone balloon-assisted enteroscopy to evaluate mucosal lesion of Crohn's disease patients. We have reported the development of immunoassay for antibody to infliximab (ATI) and anti-adalimumab antibody (AAA). In this study, we assess the factors predicting mucosal healing among patients with Crohn's disease treated with anti-TNF agents.

Abstract number: P594 Table 1: Non-Inferiority test results using historical data of INX at early time point

Indication	Category	INX			CT-P13 at Week14[1]	
		Historical data	n/N (%)	NI margin[2]	n/N (%)[3]	The bound of one-sided 95% CI [4]
CD	Response	SONIC-Week10(5mg INX)	104/169(61.5)	-0.119	34/39(87.2)	0.133
		SONIC-Week10(5mg INX + AZA)	129/169(76.3)	-0.010		
CD	Remission	SONIC-Week10(5mg INX)	80/169(47.3)	-0.097	27/39(69.2)	0.066
		SONIC-Week10(5mg INX + AZA)	101/169(59.8)	-0.058		
UC	Response	ACT I-Week8(5mg INX)	84/121(69.4)	-0.168	40/53(75.5)	-0.072
		ACT II-Week8(5mg INX)	78/121(64.5)	-0.024		
UC	Remission	ACT I-Week8(5mg INX)	47/121(38.8)	-0.132	26/53(49.1)	-0.046
		ACT II-Week8(5mg INX)	41/121(33.9)	0.005		

[1] Including two CD patients with baseline CDAI < 220 identified through clinical data reviews.
[2] Margin is defined as the 50% of INX effect size obtained through meta-analysis conservatively.
[3] Last observation carried forward (LOCF) imputation was used.
[4] The bound of the 95% one-sided confidence interval for the difference of response and remission between CT-P13 and INX

Furthermore, the association with mucosal lesion and trough levels of anti-TNF agent and concentrations of anti-drug antibody were investigated.
Aims & Methods: We reviewed the medical charts of patients with Crohn's disease under anti-TNF maintenance therapy who underwent balloon-assiseted enteroscopy between January 2006 and August 2014. Mucosal lesion was scored using the modified Rutgeerts score (MRS) (Imaeda H *et al. J Gastroenterol* 2013). MH was defined as when MRS was 0 or 1. The levels of anti-TNF agents and antibody to anti-TNF agents were measured. Cut-off values of each parameters were set as previously reported (Imaeda H *et al. J Gastroenterol* 2013).
Results: 84 patients were enrolled. MH was obtained in 31 patients (37%), on the other hand 49 patients (58%) had active mucosal lesions (Non-MH). Four patients (5%) had re-appearance of mucosal lesion although once confirmed MH. Anti-drug antibody was positive for all of these patients. Multivariate analysis revealed shorter disease duration and lower C-reactive protein at 2 to 4 weeks after starting anti-TNF agents were the factors predicting mucosal healing. During maintenance therapy, C-reactive protein and serum albumin levels are important clinical markers for the prediction of MH. No patients obtained MH if trough levels of anti-TNF agents are below cut-off values.
Conclusion: Lower C-reactive protein at 2 to 4 weeks after starting anti-TNF agents were the factor predicting mucosal healing. If the concentration of anti-TNF agents were below cut-off levels, mucosal healing is not achieved. Re-exacerbation of mucosal lesions suggests the appearance of anti-drug antibody.
Disclosure of Interest: None declared

P1599 ANTI-TNF ANTIBODY INDUCED PSORIASIFORM SKIN LESIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE; AN IRISH COHORT STUDY

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Introduction: Introduction:TNF-α inhibitors have been widely used for the treatment of Inflammatory Bowel Disease (IBD). Studies have suggested an association between anti-TNFα and reactive psoriasis. This association appears paradoxical as TNF is a pivotal molecule in the pathophysiology of psoriatic skin lesions and anti-TNFα agents have been approved for treatment of psoriasis.
Aims & Methods: Aim: To determine the prevalence of psoriasis in an IBD cohort with reference to clinical characteristics and anti-TNFα use.
Methods:A retrospective cohort study design. Patients with a diagnosis of psoriasis and IBD were identified from a database at Tallaght Hospital from 2000 to 2015. Demographic and clinical data were recorded including diagnosis, age, gender, smoking status, anti-TNF α therapy. Prevalence rates of concomitant and reactive psoriasis were calculated and compared using a students T-test. A p value of <0.05 was considered significant.
Results: In total, 1384 IBD patients were identified; female 49% (n = 682), ever smoked 19% (n = 261), 30% (n = 403) anti-TNF α therapy, 59% (n = 237) and 41% (n = 166) on Infliximab and Adalimumab respectively, 35% (n = 483)had Ulcerative Colitis (UC) and 65% had (n = 901) with Crohn's disease(CD). A higher number, 21% (n = 189) of the CD group smoked compared to 15% (n = 72) in the UC cohort, p = 0.0001, 95% CI 0.15-0.21. The overall prevalence rate of IBD and psoriasis was 2.4% (n = 33). Of the 33 patients with psoriasis, mean age 46 years (range 18-66), 24% (n = 8) had reactive psoriasis, ie. psoriasiform lesions occurring after commencement anti-TNFα therapy. The prevalence rate of psoriasis in the non-biologic and biologic cohort were similar 2.5% (25 of 981) and 2% (8 of 403) respectively. Overall, psoriasis occurred more frequently in patients with UC (5.2%), Odds Ratio (OR) = 6, p < 0.001, 95% CI = 2.72-13.61. However, subjects with CD were more likely to develop reactive psoriasis, OR = 34.5, p = 0.0013, 95% CI 3.99-297.99. Of note, there was a trend towards higher rates of reactive psoriasis in Adalimumab users which was 3.6% (6 of 166) vs. 0.8% (2 of 237), OR = 4.4 (P = 0.07). However, overall relatively more CD patients, 44% vs. 31% with UC were prescribed Adalimumab, p = 0.02, 95% CI 0.02-0.25. In addition, in our cohort, smoking was not associated with any form of psoriasis in IBD, OR = 1.39, p = 0.06
Conclusion: In our large study, the prevalence rate of reactive psoriasis was similar to the background rate of psoriasis in the overall IBD cohort (2.0% vs 2.4%). However, our overall rate of reactive psoriasis was lower than previously reported (5%) [1] and could reflect the retrospective study design. Although it remains a possibility, especially as both are autoimmune TNFα mediated diseases, that our findings reflect the natural history of the two diseases. A 2% prevalence rate represents a common adverse event that clinicians should be aware of and our data suggests an increased rate of CD in particular which may reflect smoking status in this group. Psoriasis is common in IBD patients. There is an increasing awareness of the phenomenon of reactive psoriasis in patients with biologics. However, further work to better elucidate the pathophysiology is required.
Disclosure of Interest: None declared

P1600 GRANULOCYTE/MONOCYTE ADSORPTION IN PATIENT WITH INFLAMMATORY BOWEL DISEASE REFRACTORY OR INTOLERANT TO CONVENTIONAL TREATMENT. A SWEDISH LONG-TERM PROSPECTIVE REGISTRY STUDY

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Introduction: Inflammatory bowel diseases (IBD) are chronic with different character and intermittent or more rarely continuous inflammatory activity. The activity ranges from mild to severe. The response to treatment varies and the choice of treatment is still partly arbitrary. Some patients represent a particular problem due to lack of response or intolerance to conventional treatment.
Aims & Methods: 136 patients, 54 with ulcerative colitis (UC), 81 with Crohńs disease (CD) and 1 with indeterminate colitis (IC) were included in a registry covering the majority of patients treated with Granulocyte/Monocyte Adsorption (GMA) in Sweden. The disease activity was mainly mild or moderate. The inclusion criteria were intolerance to conventional treatment in 39 patients, refractory disease in 28, contraindications to conventional therapies in 16, other indication in 25 and unspecified in 45. In 17 patients there was more than one indication for inclusion. Included patients will be followed for 12 months after the last GMA session. Monitoring includes symptoms (short health scale), activity indices (HBI, UCDAI, SCCAI) and fecal calprotectin. The patients received 5-10 GMA sessions 1-2 times weekly and the clinical activity was assessed at baseline, after complete course, 3 month after complete course and 12 month after complete course. Here we present data from the first 3 months of follow-up, based on intention to treat.
Results: Overall, patients reported improved well being. In parallel activity indices and fecal calprotectin levels decreased. The treatment tolerance was high and no adverse events were documented.
Conclusion: GMA treatment improves patient status up to 3 months after completed course. GMA offers an alternative to patients refractory or intolerant to conventional treatment. The long-term benefits of GMA will be documented during the ongoing follow-up in the directory.
Disclosure of Interest: None declared

P1601 PROSPECTIVE, LONGITUDINAL OBSERVATIONAL STUDY OF THE THERAPEUTIC MANAGEMENT OF MILD TO MODERATE ULCERATIVE COLITIS- THE OPTIMUM STUDY: FOLLOW-UP AT TWO YEARS

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Introduction: The OPTIMUM observational study was set up in France in 2011. The purpose of this study is to describe the progression and methods of therapeutic management of mild to moderate ulcerative colitis (UC) and to assess remission rate and duration as well as the predictive factors for relapse.
Aims & Methods: This observational study included patients aged 18 years and above experiencing a mild to moderate UC flare-up. The patient's data were recorded in an electronic CRF during consultations conducted as part of regular monitoring. At each visit, a questionnaire regarding treatment compliance was completed by the patient (the Modified Morisky Adherence Scale: MMAS-8) and the activity was assessed by ulcerative colitis clinical score (UCCS). From June 2011 to June 2012, 812 patients (51% female, average age of 45 ± 15 years) were included in the observational study by 130 gastroenterologists.
A follow-up period of three years is planned. A descriptive analysis of the data at two years is presented here. It was agreed that an annual visit would be defined by an interval of ± 100 days.
Results: In August 2014, the one-year and the two-year visit data were available for 559 (69%) and 393 (48%) of the patients, respectively. Ninety patients (11%) stopped the study prematurely; this was primarily due to a colectomy for 10 patients, a change in diagnosis for 4 patients, 1 death related to malignant thymoma and 28 cases lost to follow-up. According to the UCCS, 437 patients (78%) were in remission (score of 0 to 2) during the first year and 317 (81%) at two years. UC treatment was on-going in 474 patients (85%) at 1 year and in 327 patients (83%) at 2 years (Table 1).
Table 1: UC treatment at each visit

Treatments	5-ASA	Corticosteroïd	Immunosuppressant	Anti-TNF α
1 year n(%)	359 (76)	86 (18)	81 (17)	21 (4)
2 year n(%)	253 (77)	46 (14)	59 (18)	20(6)

The MMAS-8 questionnaire was completed by 370 patients (78%) and 213 patients (65%) at one year and two years, respectively. Compliance was good (score = 8) in 104 patients (28%) at one year and 83 patients (39%) at two years. At least one relapse of UC over the year was reported in 183 patients (33%) at one year and in 119 patients (30%) at two years. Patients with poor compliance have an increased risk of recurrence OR 1.8 (95% IC [1.23–2.62]). Colorectal

cancer or dysplasia was reported in three patients. At least one adverse event was reported in 20 patients (3%) and 4 were recorded as serious AEs.
Conclusion: After two years' follow-up of the OPTIMUM cohort, oral 5-ASAs remain the most commonly prescribed treatment. The relapse rate was around 30% each year and about 80% of patients were in remission at 1 and 2 years. Poor compliance was associated with a higher risk of relapse.
Disclosure of Interest: None declared

P1602 DOSE ESCALATION AND HEALTHCARE RESOURCE USE AMONG ULCERATIVE COLITIS PATIENTS TREATED WITH ADALIMUMAB IN ENGLAND

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Introduction: Studies focusing on dose escalation of bioloigcs therapies are limited. Therefore, understanding treatment patterns (with a focus on dose increase) and any attendant increase in resource utilization becomes important from a societal perspective.
Aims & Methods: The objective of this study was to describe the real-world use of adalimumab (ADA) for maintenance treatment of ulcerative colitis (UC) and associated healthcare resource use and costs in hospitals in England. A longitudinal, retrospective cohort study was conducted using the Hospital Treatment Insights database, which links pseudonymised patient data with hospital pharmacy dispensing. Included patients were adults with UC who received ≥240mg of ADA in the induction phase and had ≥3 dispenses of ADA in the maintenance phase. Patients were grouped into cohorts according to whether they received ADA 40mg every other week or dose-escalated to ADA 40mg every week in the maintenance phase. Healthcare resource use considered prescriptions and inpatient, outpatient, and emergency department visits with associated costs evaluated via the 2013-14 Payment by Results tariff.
Results: One hundred and ninety-one patients (median age 40.0 years, 42.9% male) had sufficient dispensing data to determine a completed induction phase and to establish a pattern of maintenance dosing. Eight-three patients (43.5%) dose-escalated by ≥100% (median ADA dose after escalation was 107mg) and median time to dose escalation was 139 days. Further analysis revealed that 105 patients (55.0%) dose-escalated by ≥50% and 120 patients (62.8%) by ≥30%. Of the patients who dose-escalated by ≥100%, subsequent de-escalation of ≥50% occurred in 56 patients (67.5%) with a median time to de-escalation of 21.0 days. The median duration of adalimumab treatment in all patients was 1.1 years from the index dose, with a longer duration observed in patients who dose-escalated (1.4 years versus 0.9 years for patients who did not). The mean cost associated with all-cause healthcare resource use was £13,892 in the 12 months post-index ADA dose. All-cause costs were higher for patients who dose-escalated than for patients who did not (£14,596 and £13,351, respectively). Healthcare resource use specifically related to UC was associated with a mean cost of £11,494 in the 12 months post-index period; the dose-escalated cohort had higher costs than the cohort that did not dose-escalate (£11,751 and £11,296, respectively). Prescriptions accounted for the majority of costs (£11,090 in all patients, £11,423 and £10,834 in the dose-escalated cohort and the cohort that did not dose-escalate, respectively). Costs in females were found to be significantly lower than in males (mean difference £1709.65, $p = 0.0281$).
Conclusion: The proportion of UC patients who dose escalate from ADA 40mg every other week to ADA 40mg every week in maintenance is higher than previously reported in the UK Inflammatory Bowel Disease Audit[1]. This finding and the impact that dose escalation has on costs may have implications for healthcare professionals and budget holders in the English healthcare system.

Reference

1. Royal College of Physicians. *National clinical audit of biological therapies: adult report. UK IBD audit*. RCP2014.

Disclosure of Interest: C. Black Conflict with: Employee of Merck & Co., Inc., E. McCann Conflict with: Employee of Merck & Co., Inc., E. Yu Consultancy: Merck & Co., Inc., M. Nixon Consultancy: Merck & Co., Inc., S. Kachroo Conflict with: Employee of Merck & Co., Inc.

P1603 DISEASE CONTROL AND UNMET NEEDS AMONG MODERATE TO SEVERE ULCERATIVE COLITIS PATIENTS TREATED WITH THIOPURINES IN EUROPE: THE UC CARES (ULCERATIVE COLITIS CONDITION, ATTITUDE, RESOURCES AND EDUCATIONAL STUDY)

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Introduction: Thiopurine immunomodulators are recommended for moderate to severe ulcerative colitis (UC) patients. No prior study has comprehensively evaluated their effectiveness in disease control in real world clinical practice.
Aims & Methods: This analysis is to describe disease control among moderate to severe UC patients who were biologics naïve and treated with thiopurines. Patients with moderate to severe active UC (Mayo score >=6), aged >=18 years who were biologics naïve and received thiopurines during the 12 months prior to the enrollment date were recruited from 46 hospitals across the following 11 European countries. Patients who underwent colectomy procedure or ileo-anal Jpouch reconstruction were excluded. Medical charts for the 12 months prior to the enrollment date were reviewed to collect clinical data and patient-completed questionnaires were used to collect information on satisfaction with UC treatment, quality of life and level of disease control. The primary endpoint was disease control, defined as full Mayo score ≤2 with no individual sub-score > 1 (remission) and no corticosteroid use in the two months prior to enrollment or, if no endoscopy, partial Mayo score ≤2 with no individual sub-score > 1 and no corticosteroid use in the two months prior to enrollment. Descriptive and multivariate analyses were performed to summarize patients' disease control status and evaluate factors associated with this outcome. This post hoc analysis was limited to patients who received thiopurines for at least 4 months in the 12-months prior to enrollment.
Results: A total of 103 patients were included in this post hoc analysis. Patients' mean age was 44.3 years (SD = 15.4) and 66% were male. The median duration of UC was 7.6 years (IQR 3.6-12.2). Extent of UC included 12.7% proctitis, 29.4% left-sided, and 55.8% extensive colitis. At the enrollment date, the percentages of patients receiving thiopurines, aminosalicylates, corticosteroids and other types of immunosuppressants were 94.2%, 75.7%, 18.4% and 1.0%, respectively and the mean Mayo score was 5.08 (SD = 2.9). Eighty-nine percent of patients did not achieve disease control. Specifically, 84% of patients were not in remission at the enrollment date and 30% were treated with corticosteroids in the previous 2 months. Overall, 49.5% of patients were not satisfied with current UC therapies, and 74.4% still had uncontrolled UC according to endoscopy results, indicating active inflammation. The correlation coefficient between perceived severity and clinical measures of disease status by full or partial Mayo score was 0.5.
Conclusion: The majority of biologics naïve UC patients were not under control and half of patients were dissatisfied with their UC treatment. There was a significant gap between disease control perceived by patients and control measured objectively. Tighter disease control and step-up in therapy should be considered in UC patients who do not achieve full disease control while on standard medications.
Disclosure of Interest: G. Van Assche Consultancy: Merck & Co., Inc., L. Peyrin-Biroulet Consultancy: Merck & Co., Inc., Q. Ding Conflict with: Employee of Merck & Co., Inc., S. Kachroo Conflict with: Employee of Merck & Co., Inc., T. Fan Conflict with: Employee of Merck & Co., Inc., C. Black Conflict with: Employee of Merck & Co., Inc., M. Lynam Consultancy: Merck & Co., Inc., S. Rojas-Ferreras Consultancy: Merck & Co., Inc., N. Lara Consultancy: Merck & Co., Inc.

P1604 HEALTH-RELATED QUALITY OF LIFE AND PRODUCTIVITY LOSS AMONG MODERATE TO SEVERE ULCERATIVE COLITIS PATIENTS TREATED WITH CONVENTIONAL THERAPIES IN EUROPE: THE UC CARES (ULCERATIVE COLITIS CONDITION, ATTITUDE, RESOURCES AND EDUCATIONAL STUDY)

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Introduction: Ulcerative colitis (UC) is a chronic inflammatory disorder that can interfere with patient's ability to have full personal and professional lives. UC often requires long-term therapy with multiple medications resulting in a high burden of disease on patients.
Aims & Methods: This study is to describe the impact on Quality of Life (QoL) and work productivity among moderate to severe UC patients who were biologics naïve and treated with conventional therapies. Biologic naïve patients with moderate to severe UC (Mayo score ≥ 6), ≥ 18 years who received conventional therapies during the 12 months prior to enrollment were recruited from 11 European countries. Patients who underwent colectomy or ileo-anal J-pouch reconstruction were excluded. Patients were classified with controlled or uncontrolled disease; controlled disease being clinical Mayo score ≤2, no subscore > 1, and no corticosteroids in the two months prior to enrollment or, if no endoscopy, partial Mayo score ≤2 and no corticosteroids in the two months prior to enrollment. Medical charts for the 12 months prior to enrollment were reviewed to collect clinical data. Patients completed EQ-5D-5L plus a visual analogue scale (VAS, 0-100), Quality of Life in Inflammatory Bowel Disease (SIBDQ) and Work Productivity Activity Impairment: UC (WPAI:UC) questionnaires. QoL and work productivity loss between controlled and uncontrolled patients were compared using chi-square and t-test.
Results: A total of 250 patients were included and 218 (86%) had un-controlled UC. Patients' mean (SD) age was 46.6 years (16.3) and 59% were male. The median duration of UC was 6.9 years (IQR 2.3-14.4). Extent of UC included 21.6% proctitis, 28.4% left-sided, and 49.6% extensive colitis. At the enrollment date, the percentages of patients receiving thiopurines, aminosalicylates, corticosteroids and other types of immunosuppressants were 63.2%, 75.2%, 23.6% and 3.6%, respectively. The mean (SD) of EQ-5D-5L VAS score of 78.4 (14.9) among patients in controlled disease was significantly higher than for patients in uncontrolled disease 69.5 (19.4), ($p = 0.02$). Patients in controlled disease had numerically better scores in SIBDQ than the patients in uncontrolled disease, but not significantly different. The mean (SD) global score in SIBDQ for patients with controlled and uncontrolled UC was 5.1 (1.3) and 4.8 (1.3), respectively. WPAI: UC questionnaire indicated that 40.7% patients were not working. The mean percentages (SD) of patients reporting work time missed, impairment while working and overall work impairment were 12.3 (27.3), 20.5 (25.9), 26.5 (32.2), respectively. The mean percentage (SD) of impairment of non-work activity for patients with controlled and uncontrolled UC were 17.1 (25.5) and 27.4 (28.6) ($p = 0.02$) respectively.

Conclusion: Overall, uncontrolled UC patients experienced a significant lower QoL and a higher percentage productivity loss than controlled UC patients. Since only 32 (14%) patients were in the controlled UC group, more studies are needed to test the differences.
Disclosure of Interest: G. Van Assche Consultancy: Merck & Co., Inc., L. Peyrin-Biroulet Consultancy: Merck & Co., Inc., Q. Ding Conflict with: Employee of Merck & Co., Inc., S. Kachroo Conflict with: Employee of Merck & Co., Inc., C. Black Conflict with: Employee of Merck & Co., Inc., T. Fan Conflict with: Employee of Merck & Co., Inc., M. Lynam Consultancy: Merck & Co., Inc., S. Rojas-Ferreras Consultancy: Merck & Co., Inc., N. Lara Consultancy: Merck & Co., Inc.

P1605 EFFICACY OF THE NEW INFLIXIMAB BIOSIMILAR CT-P13 INDUCTION THERAPY ON MUCOSAL HEALING IN ULCERATIVE COLITIS PATIENTS

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Introduction: CT-P13 is the first biosimilar to infliximab that has been approved for the same indications than infliximab in June 2014 in Hungary. Studies examining whether CT-P13 is similar to that of reference infliximab will have a high importance.
Aims & Methods: The aim of this study was to examine the efficacy of CT-P13 induction therapy on mucosal healing in patients with ulcerative colitis (UC). Patients diagnosed with UC, who received CT-P13 induction therapy from June 2014 at three Hungarian IBD center, were prospectively enrolled. Medical records analyzed included patients' characteristics, previous history of infliximab administration, response to CT-P13, concomitant medications, and adverse drug reaction. Serum activity markers, trough levels and antibody titers have been measured. Sigmoideoscopy was performed at the end of the induction therapy within week 6 to 10. Mucosal healing was defined as Mayo endoscopic subscore of 0 or 1. Complete mucosal healing was defied as Mayo endoscopic subscore of 0.
Results: Thirty-eight UC patients who underwent CT-P13 induction therapy were enrolled in the study. Male-female ratio was 22:16. Mean age at diagnosis was 33.2 years (range 17-65). Indication of the therapy was acute, severe flare up and chronic, refractory activity in 16 and 22 patients. Mean value of Mayo endoscopic subscore was 2.7 points at the beginning of the study. Clinical response and remission at week 14 were achieved in 92% of the patients. Sigmoideoscopy revealed mucosal healing in 25 patients; complete mucosal healing in 12 patients at week 14. Endoscopic Mayo subscore decreased significantly at week 14 compared to week 0 ($p > 0.001$). None of the examined laboratory and clinical parameters predicted to the outcome of the therapy on mucosal healing at week 14. Trough levels of infliximab correlated with mucosal healing.
Conclusion: This was the first study examining the efficacy of CT-P13 induction therapy on mucosal healing in UC. CT-P13 induction therapy showed clinical response and remission in more than 90% of the UC patients. Mucosal healing was revealed in 65.8% of the patients after the induction therapy. Our results indicate that the induction with CT-P13 can result mucosal healing in a high proportion of the patients.
Disclosure of Interest: None declared

P1606 CLINICAL AND QUALITY ATTRIBUTE CONSISTENCY FOR A GLYCOSYLATED MONOCOLONAL ANTIBODY THERAPY (ADALIMUMAB)

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Introduction: To illustrate the structural consistency of adalimumab (D2E7), we present a series of quality attributes from >500 drug substance batches produced from 4 facilities and 5 production scales from 2001-2013. In parallel, the clinical performance of adalimumab in Crohn's Disease (CD) and Ulcerative Colitis (UC) trials displays consistency through time. Collectively, the data challenge the concept related to biologic therapy variability.
Aims & Methods: A series of structural quality attributes from over 500 adalimumab drug substance batches produced from 4 facilities and 5 production scales were assessed. Structural quality attributes analyzed include charge isoforms containing 0/1/2 C-terminal lysines and other acidic species, oligosaccharides on a conserved N-linked glycosylation site, and TNFa binding. An analysis of clinical response [clinical remission defined by Crohn's Disease Activity Index (CDAI) in CD, and partial Mayo score in UC] observed with adalimumab treatment in patients with Inflammatory Bowel Disease (IBD) facilitated comparison over time.
Results: Manufacturing changes for adalimumab primarily targeted scale increases, improvements in process robustness, and control across manufacturing sites. Charge microheterogeneity of adalimumab has been consistent as measured by proportion of lysines species over the product's history. Glycosylation patterns contribute to the unique structural signature of mAbs, influence function and are considered important product QAs when determining comparability. Identity and quantity of oligosaccharides on the conserved N-linked glycosylation site of adalimumab was evaluated on batches manufactured each year. Relative quantity of the agalactosyl fucosylated biantennary oligosaccharide forms of adalimumab has remained consistent through time, as have proportions of galactose-containing fucosylated biantennary oligosaccharides and detectable high mannose glycoforms. Concurrent to the molecule's structural consistency, potency of antibody for ligand binding was maintained through time. In parallel, the performance of adalimumab in IBD clinical trials that were performed to support regulatory approvals and commitments displayed consistency through time for patients having at least 3 years of adalimumab exposure in ADHERE (CD) or ULTRA3 (UC) (**Table**).
Table: Long-term Remission[a] in Crohn's Disease (CD) and Ulcerative Colitis (UC) for Patients Who Had at Least 3 Years of Adalimumab (D2E7) Exposure

	3 months	6 months	12 months	24 months	36 months
Crohn's Disease, N ± 256	64.8	65.1	65.0	70.4	68.7
Ulcerative Colitis, N ± 346	68.3	68.2	71.4	75.1	76.6

[a]Clinical remission for CD is defined by CDAI < 150; clinical remission for UC is defined by partial Mayo score as a decrease in partial Mayo score of ≥2 points from Baseline AND a decrease in partial Mayo score of ≥30% from Baseline AND a decrease in the rectal bleeding subscore ≥1 from Baseline.
Conclusion: Adalimumab has demonstrated a highly consistent quality attribute profile, exhibiting minimal variability through over 500 batches produced over 12 years, globally aligned and maintained across multiple sites and process scales. The consistency of the structural attributes of adalimumab provides the foundation for consistency in clinical performance. Collectively, these data contribute to the ongoing scientific debate on criteria necessary to establish and maintain biosimilarity.
Disclosure of Interest: T. Albuquerque Shareholder: AbbVie, Inc., Conflict with: AbbVie, Inc., A. Varga Shareholder: AbbVie, Inc., Conflict with: AbbVie, Inc., B. Huang Shareholder: AbbVie, Inc., Conflict with: AbbVie, Inc., M. Naill Shareholder: AbbVie, Inc., Conflict with: AbbVie, Inc., P. Tebbey Shareholder: AbbVie, Inc., Conflict with: AbbVie, Inc.

P1607 ETROLIZUMAB TREATMENT INCREASES BLOOD LEVELS OF CD3, TREG AND TH17 CELLS MEASURED THROUGH EPIGENETIC ACTIVATION OF THE CD3, FOXP3 AND IL-17 LOCI

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Introduction: Identification of blood biomarkers reflecting GI pathology and disease modification upon treatment is challenging. We assessed the effect of etrolizumab, an anti-$\beta7$ integrin mAB, on peripheral blood lymphocytes in ulcerative colitis patients (UC pts). We utilized a novel approach to quantify the number of CD3+ lymphocytes and those committed to Treg or Th17 lineage by measuring epigenetic activation of the CD3, FoxP3, and IL-17 loci. Epigenetic activation at all 3 loci has been previously shown to correlate with the respective immune cell content. Importantly, different epigenetic activation patterns have been shown within the FoxP3 gene exclusively in Treg cells and not in FoxP3+ effector T-cells.
Aims & Methods: Immune cell content in peripheral blood samples from healthy controls and UC pts was determined by measuring the presence of epigenetic activation at the respective loci in relation to epigenetic activation of the GAPDH locus, which determines the total cell number. Demethylation of a particular DNA CpG motif can be detected through a demethylation-specific qPCR analysis that quantifies the presence of epigenetically active loci.
Results: Biomarker data was analyzed in 42 anti-TNF-naïve (aTNF-naïve) and 62 anti-TNF-experienced (aTNF-experienced) pts from the placebo-controlled phase 2 study of etrolizumab in pts with moderate to severe UC (EUCALYPTUS). No differences in T cell (CD3+), Treg (FoxP3), and Th17 (IL-17) content were observed at baseline for the 3 treatment arms (placebo, etrolizumab 100 mg, etrolizumab 300 mg). However, compared with healthy controls (n = 60), UC pts showed generally reduced T cell and Treg values. Additionally, aTNF-experienced pts demonstrated lower median T cell and Treg values at baseline compared with aTNF-naïve pts (CD3+ T cells 21.3% vs 25.5%, $P = 0.008$; Treg 1.01% vs 1.35%, $P = 0.01$, respectively). Over the course of the study, peripheral levels of all 3 cell types were relatively stable in the placebo group, whereas etrolizumab-treated pts showed a trend towards an increase in all 3 cell types. The median increase of CD3+, Treg and Th17 cells in the 300 mg group was greater compared with placebo at day 29 ($P \leq 0.05$). After induction with etrolizumab, trends in increases of CD3+, Treg and Th17 cells were associated with clinical remission, however statistical significance was observed only at day 29 for the 300 mg group ($P \leq 0.05$ for CD3 and FoxP3). The median increase in CD3+ T cells appeared more profound in remitters who were aTNF-experienced than in those who were aTNF-naive (2.9-fold and 1.27-fold, respectively, at day 71). Interestingly, different levels of Treg cells at baseline appeared to be associated with an increased likelihood of remission: increased levels in the aTNF-naïve pts and decreased levels in aTNF-experienced pts.
Conclusion: UC pts have lower peripheral blood T cell and Treg levels compared with healthy donors, especially aTNF-experienced pts. Upon treatment with etrolizumab, all tested T cell types in peripheral blood increased with more pronounced increases seen in pts who achieved clinical remission. Finally, levels of Treg at baseline may be associated with clinical remission upon etrolizumab treatment.
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P1608 INTENSIVE VERSUS DAILY GRANULOCYTE AND MONOCYTE APHERESIS AS FIRST-LINE THERAPY IN PATIENTS WITH ULCERATIVE COLITIS WHO WISHED TO AVOID PHARMACOLOGICS

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Introduction: At our clinic, we receive patients with ulcerative colitis (UC) who wish to avoid hospitalization and therefore require treatment in an outpatient setting. Additionally, with the availability of granulocyte/monocyte apheresis (GMA, Adacolumn), most patients favour this non-pharmacologic intervention as the first-line treatment to avoid pharmacologicals. Therefore, we initiate GMA therapy for patients with UC before any drug-based medication.

Aims & Methods: GMA was applied as the first-line therapy for remission induction in consecutive patients with moderate to severe UC according to the Mayo score for ulcerative colitis. All patients had come to our clinic soon after a relapse, and none needed immediate hospitalisation. In under age cases consent from one of the patient's parents who had accompanied the patient to our clinic was sought. Patients received either daily GMA (dGMA) up to 11 sessions, or received 2 to 3 GMA sessions per week (ndGMA), up to 11 sessions. In all cases, safety including haematology and efficacy was determined prior to each GMA session and final evaluation was done one week following the last session.

Results: Twenty-one consecutive patients, average age 35 years, range 14-64 years were treated. Eleven patients had left-sided colitis, and 10 had pan colitis. Patients received either dGMA (n = 11) or ndGMA (n = 10). In the dGMA group, the average number of GMA sessions was 10.8 within 12.8 days. The corresponding values in the ndGMA group were 10.8 sessions and 23.9 days. The average Mayo score at entry was 8.4 in the dGMA group and 8.6 in the ndGMA group. At the final assessment, the Mayo score had decreased to 3.0 in the dGMA group and to 2.4 in the ndGMA group. A small number of patients with extensive deep ulcers did not respond to GMA. No statistically significant differences was found between the two groups in terms of the Mayo score. In these patients, in spite of daily GMA or up to 3 sessions per week, no significant abnormality was observed in the haematological data and no other serious adverse event related to GMA was observed.

Conclusion: Applying GMA immediately following a clinical relapse is a favourable factor for efficacy. Further, prior to GMA, colonoscopy is essential to avoid futile use of GMA in patients who may not respond. The findings in these 21 patients represent routine clinical practice during which GMA therapy was applied for the treatment of patients with an active flare of UC. The GMA treatment frequency we applied is very much more intensive than routine weekly GMA most hitherto studies have reported. The treatment was well tolerated by the patients without any safety concern. However, GMA is very much favoured by patients for its good safety profile, as well as for being a non-pharmacologic intervention.

Disclosure of Interest: None declared

P1609 SAFETY AND TOLERABILITY OF METHOTREXATE IN INFLAMMATORY BOWEL DISEASE- A MULTICENTER EUROPEAN COHORT STUDY

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Introduction: Methotrexate (MTX has been utilized for treatment of inflammatory bowel disease (IBD) or decades. However, its clinical utility is limited by safety and tolerability concerns. Long-term retrospective safety data from large cohorts is sparse. The aim of our study was to describe the safety and tolerability of MTX in a multicenter European retrospective referral center cohort.

Aims & Methods: Consecutive patients treated with MTX for IBD were included. The main outcomes included prevalence of adverse effects requiring dose modification or drug discontinuation.

Results: A total of 216 IBD (CD-182 (84.3%) patients were treated with MTX between July 1992 and January 2012. The clinical and demographic characteristics of the included patients were as follows: age at diagnosis –33 ± 14.6 years, males- 47.2%: duration of disease before onset of MTX therapy- 7 ± 8.1 years, current smokers-23.9%. The induction administration route was oral in 38%, and subcutaneous or intramuscular in 62% of patients. The maintenance administration route was oral in 46.3%, and subcutaneous or intramuscular in 53.7% of patients. The mean weekly dose was 21.1 ± 6.1 mg for induction, and 18.3± 6.4 mg for maintenance treatment. The mean duration of maintenance treatment was 22.4+ 26.7 months. Concomitant treatment was received by 114 (54.6%) of the patients; 66 (30.6%) received concomitant anti-TNFs, 21 (9.7%)- AZA. Corticosteroids were required at least once by 95 (44%) of the patients.

At least 1 adverse effect was experienced by 67 (31.13%) of the patients, leading to reduction in 30 (14%) and temporary discontinuation 6 (2.8%) of the patients. MTX discontinuation was required by 38 (17.8%) of the patients. The reason for modification was gastrointestinal intolerance in in 7.5% hepatotoxicity in 7%, and hematological abnormalities in 1% of the patients. Hospitalization for an adverse effect was required for 14 (6.5%) patients Infectious complications were documented in 34 (15.9%) of the patients during the course of the treatment. Nausea was reported by 20 (9.4%) patients and required medical treatment (metoclopramide or odansetron) in 6 of them. Malignancy was diagnosed in 3 patients. Two deaths occurred during MTX treatment from unrelated causes (1 from urothelial carcinoma and another patient from renal failure and arrhythmia)

Conclusion: MTX treatment in IBD patients is associated with a favorable long-term tolerability and safety profile.

*U. Kopylov and K. Katsanos have equally contributed to the study

Disclosure of Interest: None declared

P1610 METHOTREXATE FOR MAINTENANCE OF REMISSION IN CROHN'S DISEASE- A MULTICENTER EUROPEAN COHORT STUDY

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Introduction: Methotrexate (MTX) has been utilized for the treatment of Crohn's disease (CD) for decades. Nevertheless, clinical trials as well as retrospective series provide equivocal evidence regarding the efficacy of MTX in CD.

The aims of this study were to describe the efficacy of MTX for maintenance of remission in CD and to identify the factors associated with MTX failure in a multicenter European referral center cohort.

Aims & Methods: Consecutive patients treated with MTX for CD were included. Patients treated with a combination of TNF-alpha inhibitors and MTX were excluded from the analysis. The main outcome was steroid-free clinical remission, without a need for a concomitant biologic/thiopurine therapy or need for Crohn's related surgery.

Results: A total of 182 CD patients were treated with MTX between July 1992 and January 2012; 66 patients were excluded from the analysis due to a concomitant treatment with a TNF alpha inhibitor. The clinical and demographic characteristics of the included patients were as follows: age at diagnosis – 33 ± 14.6 years, males- 44.8%: duration of disease before onset of MTX therapy- 7 ± 8.7 years, current smokers-19.3%; 24.3% had a stenotic and 25.2% -a penetrating phenotype; 43.1% had a history of anti-TNF treatment. The induction administration route was oral in 34.6%, and subcutaneous or intramuscular in 63.4% of patients. The maintenance administration route was oral in 47.1%, and subcutaneous or intramuscular in 52.9% of patients. The mean weekly dose was 22.1 ± 5.6 mg for induction, and 18.8± 5.1 mg for maintenance treatment. Steroid-free remission was achieved in 39/118 (33.1%) patients and was maintained for 27 ± 28.8 months. The mean time to achieve remission was 2.9 ± 3.5 months. On multivariate analysis, oral induction route (OR: 0.23, p = 0.03) and previous anti-TNF therapy (OR: 0.16, p = 0.013) were associated with a risk of therapeutic failure, while non-smoking (OR: 4.7, p = 0.049) was protective. Neither weekly dose nor route of maintenance MTX administration were associated with a likelihood of achieving remission.

Conclusion: MTX treatment achieves durable clinical remission in a third of CD patients, and should be considered a viable treatment option. The likelihood of clinical remission is lower in smokers, patients with a history of anti-TNF treatment and when oral induction treatment is used.
*Kopylov U and Katzanos K equally contributed to the study
Disclosure of Interest: None declared

P1611 EVIDENCE BASED PRESCRIBING TRENDS IN CROHN'S DISEASE IN THE UK: NATIONAL POPULATION-BASED STUDY

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Introduction: Over the past twenty years the research base has improved sufficiently to enable evidence based guidelines to specify indications for optimal use for 5-aminosalicylic acids (5-ASAs), steroids and thiopurines (TPs).
Aims & Methods: Our aim was to determine trends in Crohn's disease (CD) related prescribing patterns of oral and topical 5-ASAs, steroids and TP over the past 20 years.
We constructed an incident cohort of patients with CD diagnosed between 1990 and 2009 using the Clinical Practice Research Datalink (CRPD). We divided our cohort to compare patterns between era: era 1 (1990–1993), era 2 (1994–1997), era 3 (1998–2001), era 4 (2002–2005) and era 5 (2006–2009). We evaluated trends in prescribing by calculating the proportion (number of patients receiving a prescription/number of patients diagnosed in the era) of patients, adjusted for age and sex, receiving at least one prescription for each oral or topical 5-ASAs, oral or topical steroids and TPs (azathioprine and mercaptopurine) within 1 year from the time of diagnosis. We evaluated trends based on the publication of key research during the study period. χ^2 test for trend was used to compare proportions between groups.
Results: There were 6997 patients who met our inclusion criteria. The proportion of patients with at least one prescription for oral 5-ASAs within a year of diagnosis increased from 32.7% to 47.3% ($p < 0.001$) between era 1 and era 5 but plateaued after era 3 (era 3 vs era 5, $p = 0.59$) which coincided with a publication by Hanauer *et al* [1]. The use topical 5-ASAs was stable at just below 5% ($p = 0.48$) between era 1 and era 5, respectively. Oral steroid prescriptions have been the mainstay of treatment in CD [2] and increased from 51.7% to 61.3% (era 1 vs era 5, $p < 0.001$), but plateaued after era 3 (era 3 vs era 4, $p = 0.98$) in keeping with a meta-analysis [3]. Topical steroid use within 1 years of diagnosis declined from 13.2% to 5.4% ($p < 0.001$). There was an increase in TP prescriptions between era 1 and era 5 from 14.0% to 47.1% ($p < 0.001$) which was supported by evidence published in 1995 [5].
Conclusion: 5-ASA use remains common despite the lack of evidence base in CD, although this stabilised after era 3. Topical therapies in CD are on the decline or at low levels, but steroid use remained high throughout the study period. TP use has increased in keeping with current evidence and guidance but it is conceivable that more patients should be maintained on these agents.

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P1612 EVIDENCE-BASED PRESCRIBING TRENDS IN ULCERATIVE COLITIS IN THE UK: NATIONAL POPULATION BASED STUDY

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Introduction: Over the past twenty years the research base has improved sufficiently to enable evidence based guidelines to specify indications for optimal use for 5-aminosalicylic acids (5-ASAs), steroids and thiopurines (TPs).
Aims & Methods: Our aim was to determine trends in ulcerative colitis (UC) related prescribing patterns of oral and topical 5-ASAs, steroids and TP over the past 20 years.
We constructed an incident cohort of patients with UC diagnosed between 1990 and 2009 using the Clinical Practice Research Datalink (CRPD), a validated research database representing an 8% sample of the UK population. We divided our cohort to compare patterns between era: era 1 (1990–1993), era 2 (1994–1997), era 3 (1998–2001), era 4 (2002–2005) and era 5 (2006–2009). We evaluated trends in prescribing by calculating the proportion (number of patients receiving a prescription/number of patients diagnosed in the era) of patients, adjusted for age and sex, receiving at least one prescription for each oral or topical 5-ASAs, oral or topical steroids and TPs (azathioprine and mercaptopurine) within 1 year from the time of diagnosis. We evaluated trends based on the publication of key research during the study period. χ^2 test for trend was used to compare proportions between groups.
Results: There were 16512 patients who met our inclusion criteria. The proportion of patients with at least one oral 5-ASA prescription within a year of diagnosis increased from 33.1% to 44.6% ($p < 0.001$) between era 1 and era 5 in keeping with a study published by Sutherland *et al* [1] although its use plateaued from era 3 onward (era 3 vs era 5, $p = 0.26$) (figure 1). Topical 5-ASAs use, increased from 23.1% to 49.9% ($p < 0.001$) between era 1 and era 5 in keeping with evidence published by Marshall *et al* [2]. Topical steroid use decreased from 49.2% to 36.8% between era 1 and era 5 ($p < 0.001$) which was in keeping with supporting evidence [2]. Oral steroid prescriptions rose steadily from 19.6% to 39.7% between era 1 and era 5 ($p < 0.001$). This was despite an increase in TP users from 4.6% to 20.8% ($p < 0.001$) between era 1 and era 5 in keeping with study performed by Hawthorne *et al* [3].
Conclusion: Oral 5-ASA use increased in UC but unexpectedly stabilised after era 3 which was not anticipated as we expected a larger number to receive these drugs. Topical 5-ASAs, considered first line for mild proctitis or left sided colitis, increased whilst topical steroid use decreased during the study period. Steroid use in UC has continued to increase despite improvements in medical therapy such as increasing TP use during the study period which was in keeping with current research and guidance.

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P1613 FECAL LACTOFERRIN AND CALPROTECTIN AS SURROGATE MARKERS OF MUCOSAL HEALING: POST-HOC ANALYSIS FROM THE PURSUIT SC INDUCTION STUDY

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Introduction: Previously we reported greater improvement in both fLac&fCal levels observed in UC pts who demonstrated clinical response & endoscopic healing in PURSUIT SC induction golimumab (GLM) study[1].
Aims & Methods: To assess the association of fecal inflammatory markers, lactoferrin (fLac) & calprotectin (fCal), with Mayo endoscopy subscores using data from this study. The Ph3 portion of PURSUIT-SC was a multicenter, rand, PBO-controlled dble-blind study conducted to evaluate safety & efficacy of induction therapy with SC GLM. Pts with Mayo scores of 6-12 inclusive, including endoscopic subscore ≥ 2 were rand to PBO/PBO, GLM 200 mg/100 mg, or GLM400 mg/200 mg at Wks 0 & 2. Mucosal healing was assessed at Wk6 using Mayo endoscopy subscore. Stool samples were collected for fLac & fCal Wk0 thru Wk6. Assays for fLac & fCal concentrations were performed using validated methods. The area under a ROC curve(AUC) was used to assess the association of baseline & Wk6 fLac & fCal with Mayo endoscopy subscores of 0 (defining normal or inactive disease) & subscores of 0 or 1(defining endoscopic healing in this study)at Wk6. Various cut offs of fLac & fCal concentrations were explored to determine the balance of sensitivity&specificity for endoscopy subscores of 0 or 0 or 1.
Results: Mayo endoscopy subscores of 0 or 1 were associated with the lowest concentrations of fLac & fCal (Table). Baseline fLac & fCal were poor predictors for endoscopic healing at Wk6 (AUCs < 0.63). Area under the ROC curve analysis showed that fLac & fCal at Wk6 are fair surrogate markers for normal/inactive endoscopic disease activity (endoscopy subscore of 0) at Wk6 with AUCs of 0.77 & 0.79, resp. Similar AUCs were observed for endoscopy subscores of 0 or 1. Cutoffs of fLac $< 50\mu g/ml$ & fCal $< 250mg/kg$ at Wk6 offered reasonable sensitivity & specificity(fLac 0.74,0.67 & fCal 0.79,0.70) for normal/inactive endoscopic disease activity at Wk6. In contrast, cutoffs of fLac $< 100\mu g/ml$ & fCal $< 500mg/kg$ at Wk6 offered similarly reasonable sensitivity & specificity (fLac 0.73,0.63 & fCal 0.74,0.64) for endoscopy subscores of 0 or 1.
Table: Fecal Inflammatory Marker Concentrations and Mayo Endoscopy Subscores at Wk 6

	PBON Median (IQ range)	Combined GLMN Median (IQ range)	PBON Median (IQ range)	Combined GLMN Median (IQ range)
	FLac (μg/mL)		**FCal(mg/kg)**	
Endoscopy scores				
0	1029.8 (7.7-72.9)	523.5 (0.6-53.2)	10127 (53-502)	5242 (14 -159)
1	6235.9 (5.4-156.9)	17135.4 (4.9-145.3)	62252 (47-706)	171182 (40-577)
2	119157.0 (50.4-442.2)	168146.6 (40.5-441.7)	119672 (268-1564)	168559 (258-1083)
3	59364.0 (70.4-794.1)	117304.4 (94.1-707.6)	59945 (527-2024)	1171159 (532-2544)

Conclusion: At Wk6, Mayo endoscopy subscores were positively associated with levels of fLac & fCal. Cut-offs of fLac $< 50\mu g/ml$ & fCal $< 250mg/kg$ at Wk6 demonstrated reasonable sensitivity & specificity for normal/endoscopic disease activity. Overall these data suggest that fecal inflammatory marker levels might be useful surrogates for endoscopic improvement.

Reference

1. Presented at ACG 2014.

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P1614 PATIENT-REPORTED OUTCOMES CAN BE USED TO MONITOR CONTINUOUS CLINICAL RESPONSE IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS TREATED WITH GOLIMUMAB: RESULTS FROM THE PURSUIT MAINTENANCE STUDY

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Introduction: In the PURSUIT maintenance (M) trial, continuous clinical response (CCR) was associated with achievement of conventional endpoints, including endoscopic healing in patients with active ulcerative colitis (UC).[1] We characterize the association of components of the Partial Mayo score, including stool frequency (PRO1), rectal bleeding (PRO2), and their combination (PRO1 + 2), with CCR in PURSUIT-M.
Aims & Methods: Patients who responded to golimumab induction at week 6 and were randomized to placebo or golimumab 50 or 100 mg every 4 weeks (Q4W) were included. UC disease activity was assessed using the Mayo score at weeks 30 and 54, PRO1 and PRO2 (averaged over 3 days before visit) Q4W, and Physician Global Assessment (PGA) Q4W. CCR was defined as response maintained through week 54; loss of response was confirmed by endoscopy.[2] Logistic regression of imputed data (last observation carried forward) was used to evaluate the association of subscores with CCR at weeks 30 and 54 in PURSUIT-M. Missing data were not imputed. Area under ROC curves (AUC) were calculated for each Mayo score component; comparisons were made using the DeLong method.[3]
Results: The AUCs for each Mayo score component at weeks 30 and 54 to predict CCR are summarized in the **Table**. Sensitivity analysis excluding patients with missing Mayo subscore data at >2 visits showed similar results.
Conclusion: Stool frequency and rectal bleeding combined (PRO1 + 2) and endoscopy subscore each showed comparable accuracy with Partial Mayo score in the ability to predict CCR. PRO1 + 2 can thus be used to monitor patients' UC symptoms remotely and may provide a useful tool to assess for maintenance of CCR in daily clinical practice.

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P1615 THE EFFECT OF C2, FACTOR B AND C3 DEFICIENCIES ON STEM CELL MOBILIZATION AND INFLAMMATION IN A MURINE MODEL OF CHRONIC COLITIS: IMPLICATIONS FOR FUTURE THERAPY

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Introduction: Ulcerative colitis (UC) is a chronic inflammatory disease of complex etiology. There is a great need for developing new effective methods to treat UC. The strategy based on the use of drugs modifying complement system (CS) cascade is a new promising therapeutic option allowing for control of stem cell mobilization (1) and inflammatory process in the intestine (2). In the current study we investigated the role of C2, factor B (fB) and C3 in mobilization of various stem cell populations, such as very small embryonic-like stem cells (VSEL-SCs), hematopoietic stem cells (HSCs), clonogenic progenitors and intestinal epithelial stem cells. We also evaluated the clinical response compared with the level of intestinal damage.

Aims & Methods: A well-established murine dextran sulfate sodium (DSS) model of chronic UC was used to study stem cell mobilization and intestinal inflammation in wild type (WT) C57BL/6, C2.fB deficient (C2.fB-/-) and C3 deficient (C3-/-) mice. Briefly, UC was induced by oral administration of 5% DSS in drinking water for 5 days, followed by the consumption of tap water for the next 11 days. The severity of DSS-induced colitis was evaluated daily based on calculation of the disease activity index (DAI). On day 16 the animals were sacrificed for detailed analysis. Flow cytometry, colony-forming unit (CFU) assay and real-time PCR were performed to study the mobilization of selected stem cell populations into peripheral blood. The level of intestinal damage was evaluated by standard histological and immunohistochemical methods.
Results: In the used model of chronic colitis we observed the mobilization into periheral blood of all examined populations of stem cells. The number of mobilized VSELs, HSCs, clonogenic progenitors and cells expressing markers of intestinal epithelial stem cells was higher in C3-/-mice and lower in C2.fB-/- than in WTmice. More severe inflammation was observed in C2.fB-/- mice than in WT mice. Although the stem cell mobilization in C3-/-mice was higher than in WT mice no significant reduction of inflammation in the large intestine was observed in these animals. As noticed, both C3-/- and C2.fB-/- mice exhibited a higher histological colonic damage than WT colitis mice.
Conclusion: We have determined for the first time the role of C2, fB and C3 deficiency in stem cell mobilization and inflammatory process in experimental model of chronic colitis. Pharmacological inhibition of C2 and fB should not be considered as a therapeutic approach for UC treatment. C3 inhibitors might be considered as a part of complex UC therapy due to beneficial effect on stem cell mobilization, but shall not be used alone because the lack of C3 has no effect on tissue repair.
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P1616 ULCERATIVE COLITIS: A TIGHT JUNCTION DISORDER CAUSING LOSS OF PHOSPHATIDYLCHOLINE SECRETION INTO MUCUS

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Introduction: The intestinal mucus forms a hydrophobic barrier against colonic microbiota[1]; a defective mucosal barrier has been suggested as an underlying cause of ulcerative colitis (UC)[2]. We propose that the key pathogenetic feature of UC is an intrinsically low mucus phosphatidylcholine (PC) content[3, 4]. What remains unclear is how PC accumulates in mucus under physiological conditions, and how this process fails in UC and induces an inflammatory phenotype.
Aims & Methods: We determined the transport of PC across polarized CaCo2 cells. Genetic animal models of UC were generated by intestinal specific knockout mice of kindlin 1 and 2. They were examined in regard to their microarchitecture, PC secretion capacity, the mucus PC content and the functional capacity of microbiota penetration and induction of inflammation as well as the mucosal protection by oral PC supplementation. Finally, mucosal microarchitecture, PC transport and its mucus concentration was evaluated with biopsy specimens of human UC.
Results: We identified a novel paracellular transport route specific to choline-containing phospholipids that are driven by an electrochemical gradient across tight junctions (TJs) to form a hydrophobic mucosal barrier via mucin binding. Interfering with this pathway blocked luminal PC secretion, and mice with lateral TJ disruption due to intestinal kindlin 1 and 2 deletion developed a UC phenotype. The same TJ disturbance was observed in human UC: lateral TJ disruption impaired mucosal PC secretion, and PC-deficient mucus had reduced hydrophobicity that allowed gut microbiota penetration, which consequently induced mucosal inflammation. This was mitigated when the hydrophobic barrier was reestablished by PC supplementation, which is an innovative treatment option for UC.
Conclusion: Disruption of PC paracellular translocation across the TJ barrier is an attractive hypothesis to explain the pathogenesis of UC.

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P1617 INFLIXIMAB DE-ESCALATION BASED ON TROUGH LEVELS IN INFLAMMATORY BOWEL DISEASE PATIENTS: A PROOF-OF CONCEPT STUDY

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Introduction: A significant number of patients with inflammatory bowel disease (IBD) treated with infliximab (IFX) require dose intensification due to secondary loss of response (LOR). Due to both economic and safety concerns, such IFX regimen cannot be maintained in the long-term. The aim of this study was to investigate the long-term efficacy of dose de-escalation in patients under optimized IFX regimen, who achieved deep remission, and with TRI > 8 μg/mL.
Aims & Methods: We have included in this prospective study, all adult patients with IBD and followed in the Gastroenterology department. All included patients were treated with IFX at 10mg/kg every 8 weeks for secondary loss of response. These patients were in deep remission for at least 4 months. Deep remission was defined as a CDAI < 150 with fecal calprotectin < 250 μg/g of stool for Crohn's disease (CD) and a total Mayo score <3 with an endoscopic Mayo score <2 for ulcerative colitis (UC). If TRI using an Lisatracker (Theradiag) were > 8 μg/mL following two consecutive IFX infusions, patients were included in this prospective, single-center, observational, longitudinal study after giving their signed consent. All patients with concomitant use of an immunomodulator agent were excluded. Patients had a minimum follow-up of one year. For dose de-escalation, IFX dose was decreased by 1 mg/kg at each infusion to a dose to 5 mg/kg or to get a TRI between 3 and 7 μg/mL. Thereafter, this dose was maintained during follow-up.
Results: We have included 20 patients with a median follow-up of 8 months (6-12) (CD 12, sex ratio M/F: 1, median age at inclusion 30 (21-40), median age at diagnosis 24 (16-35), duration of IFX 10 mg/kg = 12 months (8-14)). All the patients had at the inclusion a TRI > 8 μg/mL and 5% (one patient) of the patients a CRP > 5 mg/L. A decrease of IFX dose until having TRI between 3 and 7 μg/mL and with persistence of a deep remission was obtained in 18 patients. IFX dose used when stopping the de-escelation were 5 mg/kg for one patient, 6mg/kg for 4 patients, 7 mg/kg for 10 patients, and 8 mg/kg for 3 patients (Figure 1a). The average CDAI rates were comparable before and in the follow-

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	PRO1	PRO2	PRO1 + 2	PGA	Mayo Endoscopy Subscore	Partial Mayo (PRO1 + PRO2 + PGA)
Week 30 (n = 361)						
AUC (SE)	77.8 (1.39)	77.5 (1.81)	82.6 (0.84)	80.2 (1.17)	82.1 (1.58)	83.6 (2.20)
P-value*	< 0.0001	0.0007	0.2415	0.0032	0.3444	
CP/sensitivity/ specificity	1/89.9/57.6	0/91.5/60.5	1/84.1/70.9	1/95.2/61.0	1/89.4/70.3	3/94.7/63.4
Week 54 (n = 322)						
AUC (SE)	90.0 (2.93)	88.2 (2.87)	94.9 (3.07)	94.3 (2.99)	94.1 (2.92)	96.8 (2.02)
P-value*	0.0201	0.0028	0.5265	0.4055	0.3553	
CP/sensitivity/ specificity	1/92.6/79.7	0/94.2/79.7	1/88.4/91.7	1/95.8/87.2	1/91.0/93.2	3/96.8/90.2

CP=cutpoint; SE=standard error.*Comparison of subscore with the Partial Mayo score regarding the ability to predict CCR.

up after therapeutic de-escelation as the Mayo score, the endoscopic score and the fecal calprotectin levels. Only two patients had a clinical relapse during de-escalation at an IFX dose of 8 mg/kg with TRI > 8 μg/mL. In these two patients, at the moment of LOR, TRI were in our therapeutic definition range. The other 18 patients were followed with a median of 8 months (6-12) after stopping the de-escalation according to TRI (between 3 and 7 μg/mL) for all patients. All these patients remained in deep remission as previously defined. TRI remained stable between 3 and 7 μg/mL during follow-up for all patients. So de-escalation was associated with maintenance of deep remission for 90% of cases with a follow-up of 8 months.

Conclusion: Therapeutic de-escalation is possible in patients with deep remission and with high suboptimal TRI as defined previously [6]. De-escalation to obtain therapeutic TRI is feasible and has no impact on clinical or endoscopic scores and on biomarkers as CRP or fecal calprotectin in 90% of cases without increase of immunogenecity. Finally, therapeutic strategies based on de-escalation is highly interesting in term of health economics.

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P1618 RATES OF COLECTOMY IN ULCERATIVE COLITIS THROUGH TIME IN A LATIN-AMERICAN IBD UNIT

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Introduction: Ulcerative colitis (UC) is a chronic relapsing disease that carries the risk of potential severe complications and disability. Ileal pouch anal anastomosis (IPAA) was postulated as a suitable curative alternative for unresponsive UC, but a substantial proportion of patients present short-term and long-term complications. Thus, several factors could change the natural history of UC decreasing surgical rates (a rapid diagnosis, information to patients, tight control, treatment algorithms at right time). We designed an IBD specific electronic system functiong as a network for a reference IBD Unit working from 1990 in Buenos Aires.

Aims & Methods: We aimed: 1) to evaluate colectomy rates of UC with disease onset in this century compared with those patients with debut in that last decade of century XX (dated at time of our IBD unit creation). 2) to study the major demographic characteristics associated with surgery. Data were obtained from the software created 2 decades ago (in improvement process), where information were recorded and coded. Data revision and entry from diverse sources of medical reports was carried out. We included all UC patients assisted in our unit in such periods with available information to define colectomy prevalence (survival times) age at UC onset, disease extent, complications. We compared by survival analysis colectomy rates of UC with disease onset from 1990 to 1999 with the rates of patients that started the disease from the 2000 or later.

Results: We inform results of surgical rates (categorized in the two mentioned time periods) of a cohort of 1903 UC patients (Female 996, M 907), mean age (mean ± SD) at disease debut 33.45 ± 15.3, disease extent (Montreal classification) E1: 25,2%, E2: 30.5%, E3: 44.3%. **Group 1:** UC onset from January 1990 to end of December of 1999 (n 884) **Group 2:** UC debut from January 2000 to current time (n: 1019). Mean ages at onset and gender were similar in both periods. Main results about surgery requirement: colectomy rates in UC with disease onset in this century (group 2) were significant lower compared with the historical patients of **group 1**. Cumulative probabilities of surgery at 1, 2, 3, 4, 5, 7 and 10 years for **Group 1** were 4.4%, 8.8%, 13.0%, 14.0%, 16.0%, 18.3%, 22.0% and for **Group 2:** 3.6%, 6.2%, 7.8%, 9.1%,10.3%, 12.7%, 16.1% (Log rank test: $p < 0.006$). The colonic involvement (E3, E2, E1) was significant more extensive in patients who required colectomy (82.7%, 16.2%, 1.1%) compared with UC responsive to medical treatment (37.6%, 33.0%, 29.4%) $p < 0.0001$ (Chi square) for all disease groups of UC extent. The median age of UC onset was lower in patients requiring surgery: 27.5 (QR 20-42) vs. 30.0 (QR 22-43) $p < 0.012$ (Kruskal Wallis Anova test). The more frequent cause of surgery was a severe flare in hospitalized patients.

Conclusion: Colectomy rates in UC showed a significant decrease in the current century compared with last decade of past century. As we are a reference IBD unit, these data could reflect a regional trend in the management. Colectomized patients showed more extensive compromise and younger UC onset, confirming the relevance of opportune algorithms for control and treatment of the risk groups.

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P1619 PREOPERATIVE MAINTENANCE THERAPY WITH ANTI-TNF IN ULCERATIVE COLITIS PATIENTS WHO UNDERWENT ILEAL POUCH-ANAL ANASTOMOSIS (IPAA) IS NOT ASSOCIATED WITH HISTOLOGICAL FIBROSIS

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Introduction: While it is known that exposure to anti-TNF in Crohn's disease causes a unique histologic fibrosis, the effects of anti-TNF on the histology of colorectal resection specimens in patients with ulcerative colitis (UC) has not been documented. We sought to determine whether preoperative exposure to anti-TNF affects histological measures of fibrosis which may be also be a potential factor in adverse anastomosis complications following ileal pouch anal anastomosis (IPAA) surgery.

Aims & Methods: We performed a retrospective study of patients with UC who underwent IPAA at our institution between 2003 and 2013. Individuals who received anti-TNF as maintenance therapy (i.e. >3 doses of anti-TNF) and who received their last dose in <180 days from the first stage of IPAA were selected. The control group was comprised of UC patients not exposed to anti-TNF pre-operatively, matched 1:1 by age, sex, BMI, disease duration, albumin, and post-operative leak outcome. Hematoxylin-eosin and trichrome slides from the most distal, full-thickness section of colorectum from each total colectomy specimen were evaluated. Blinded assessment of the degree of fibrosis in large bowel layers was performed. Fibrosis was scored on a scale of 1 to 4 for each layer. The histology analysis was performed by a single observer using a semi-quantitative pictorial scale. McNemar's test and paired t-test for categorical and continuous variables, were performed.

Results: 765 UC IPAA patients were reviewed. 138 patients met the inclusion criteria. Histological fibrosis in 69 patients from the therapy group was compared to 69 patients from the matched control group. There were no statistically significant differences in the level of fibrosis in any of the bowel layers individually nor in the combined fibrosis does score in all layer together (Table 1).

Table 1

	Control (n = 69)	Anti TNF Treated Group* (n = 69)	p Value
Fibrosis in Lamina propria, n (%)			0.18
1	25 (37.9)	26 (40.0)	
2	21 (31.8)	21 (32.3)	
3	5 (7.6)	11 (16.9)	
4	15 (22.7)	7 (10.8)	
Fibrosis in submucosa, n (%)	9 (13.6)	6 (9.2)	0.29
1	14 (21.2)	16 (24.6)	
2	27 (40.9)	23 (35.4)	
3	16 (24.2)	20 (30.8)	
4			
Fibrosis above muscularis propria (%)			0.36
	5 (7.8)	0 (0)	
1	9 (14.1)	13 (20.0)	
2	27 (42.2)	22 (33.9)	
3	23 (35.9)	30 (46.2)	
4			
Fibrosis in subserosa, n (%)			0.71
1	26 (40.6)	22 (33.9)	
2	23 (35.9)	22 (33.9)	
3	9 (14.1)	14 (21.5)	
4	6 (9.4)	7 (10.8)	

*Anti TNF Treated Group- Maintenance therapy, >3 infusions/doses within 180 day before Stage 1.

Conclusion: Resection specimens from UC patients treated with maintenance anti-TNF therapy who underwent IPAA surgery showed no significant differences in the degree of histologic fibrosis compared to a matched control group.

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P1620 CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION OF LARGE NON-POLYPOID SUPERFICIAL NEOPLASMS IN ULCERATIVE COLITIS

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Introduction: Endoscopic resection of superficial neoplasms in inflammatory bowel diseases (IBD) is appropriate if a complete resection can be achieved. However, EMR is ineffective for large non-polypoid neoplasms, especially in IBD due to the submucosal fibrosis, and no data are available on the efficacy of endoscopic submucosal dissection (ESD).
Aims & Methods: To assess ESD feasibility and efficacy for large non-polypoid neoplasms in IBD patients. Study design was: prospective multicenter case series conducted in a Italian and Japanese center. Consecutive patients with long-standing ulcerative colitis and a superficial non-polypoid neoplasm, >20 mm within the colitic mucosa were included. Neoplasm was characterization and delineation by chromoscopy and narrow band imaging. ESD performed according to the standard technique. Main outcomes were: feasibility, safety, curative resection rates.
Results: Nine patients with 10 neoplasms were included (7 and 3 in the Italian and Japanese center, respectively). Neoplasms were LST-NG in 5 cases, in the left colon in 7, had median size of 33 mm, associated with scar in 5. Delineation of neoplasm margins was difficult in 5 cases due to subtle elevations extending beyond gross edges and pit and capillary patterns suggestive of non-neoplastic tissue. Margins were profiled by acetic acid in 3 cases. Submucosal fibrosis was present in 9 cases.
ESD was en bloc and R0 in 8 (80%) cases (Video). SM fibrosis was present in 9 lesions: in all 5 lesions which underwent previous resection or biopsies, and in 4 naïve cases. A curative resection was achieved in 7 (70%) cases.
No endoscopic invisible dysplasia or cancer was found during the follow-up (median 24 months, range 6-72) at the resection site and elsewhere within the colitic mucosa.
Conclusion: ESD achieves curative resections in IBD patients but the procedure is difficult due to the high prevalence of submucosal fibrosis. Patients need to be accurately evaluated before resection and adhere to strict long-term follow-ups.
Disclosure of Interest: None declared

P1621 STEROID USE BUT NOT BIOLOGICS INCREASE THE RATE OF COMPLICATIONS AFTER IPAA SURGERY

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Introduction: There is increasing use of biologic therapy in ulcerative colitis (UC). As a result there is concern regarding the impact of biologics on operative outcomes. This study examines the exposure and impact of biologics and corticosteroids on postoperative outcomes for patients undergoing an ileal pouch anal anastamosis (IPAA) over an 11 year period at a single institution.
Aims & Methods: A retrospective chart review was performed for subjects with UC who underwent IPAA between 2002 and 2013. Inpatient and outpatient charts were reviewed for demographic data, clinical data, anti-TNF therapy, steroid and immunosuppressant use, and surgical outcomes. Early complications were defined as occurring within 30 days of IPAA construction and late complications were defined as within 12 months following ileostomy closure. Pearson Chi-square and Student's t-test was used; multivariate logistic regression analysis was performed to identify significant factors associated with postoperative complication.
Results: 758 patients underwent IPAA. 57.5% (n=437) of patients were female. At the time of first surgery the median age was 36 with a median BMI of 25 (range 22-28.4). Mean preoperative disease duration was 5.3 years (range 2.4 – 10.6y). 16.2% (n=106) of IPAA were performed laparoscopically. The reconstructive IPAA procedure was performed in 2- (n=460) and 3- (n=285) stages and the remainders were performed in non-traditional staged operations. 88 patients had anti-TNF exposure within 180 days of surgery whereas 128 patients had immunosuppressant use within 90 days of surgery. 54.3% of patients (n=369) had systemic corticosteroids (>15mg/day) within 30 days prior to surgery. Of these, 286 patients had high dose (>30mg/day via intravenous) corticosteroids within 7 days of their first surgery. Early complications consisted of pelvic abscess (n=135.17.8%), small bowel obstruction (n=134.17.7%), wound infection (n=108.14.3%), and deep vein thrombosis (n=33, 4.4%). Late complications consisted of anal stricture (n=55, 7.3%), pouch fistula (n=26, 3.4%), and functional pouch failure (n=7, 0.9%). The overall pouch leak rate was 92 (12.1%). There was one death. The median length of stay was 9 days. Exposure to biologics was not significantly associated with post-operative complications (OR 0.81, CI 0.54-1.23) whereas a 3 stage procedure (OR1.61, CI 1.17–2.54), and use of high dose corticosteroids within 7 days of surgery (OR 1.59, CI 1.11–2.27) were significantly associated with increased complications.
Conclusion: The use of high-dose steroids preoperatively increases the risk for developing post-operative complication. However, the use of biologics was not shown to be associated with early or late complications following IPAA surgery for UC.
Disclosure of Interest: E. Zittan: None declared, G. Ma: None declared, N. Wong-Chong: None declared, R. Milgrom: None declared, R. McLeod: None declared, G. Greenberg: None declared, G. Nguyen Consultancy: Advisory Board for Janssen and Abbvie, K. Croitoru Financial support for research: Janssen, Abbvie and Takeda, Consultancy: Abbvie and Takeda, A. Steinhart Financial support for research: Abbvie, Amgen, Pfizer, Millenium, Lecture fee(s): Abbvie, Janssen, Takeda, Shire, Consultancy: Abbvie, Actives, Janssen, Takeda, Pharmascience, Shire, M. Silverberg Conflict with: Financial support for research and consultant for Janssen, Abbvie, Takeda, Prometheus, Z. Cohen Conflict with: Educational Grant from Janssen

P1622 LONG-TERM RESULTS OF POUCHOSCOPY AFTER ILEAL-POUCH ANAL ANASTOMOSIS IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Ileal-pouch anal anastomosis (IPAA) has been the standard treatment of choice for patients with ulcerative colitis (UC) who require surgery. Although patients' quality of life after IPAA is largely satisfactory, some suffer from pouchitis. Also, the development of carcinoma in the ileal pouch or the remnant rectal mucosa has been concerned.
Aims & Methods: The aim of this study was to investigate the frequency of pouchitis and to assess the results of surveillance pouchoscopy. One hundred three patients with UC who underwent IPAA in the University of Tokyo hospital were included. Out of 103, ninety-three patients who received pouchoscopy were retrospectively investigated. The background data were obtained by reviewing patients' charts. The diagnosis of pouchitis was made according to modified pouchitis disease activity index, which was determined by clinical and endoscopic scores. The cumulative pouchitis rate was calculated by Kaplan Meier curve, and risk factors for the development of pouchitis were investigated by the Cox regression test. Pathological reports were also reviewed for assessing the development of dysplasia and cancer after IPAA.
Results: A total of 572 pouchoscopies were performed in 93 patients. The cumulative pouchitis rate was 4.5%, 12.5%, and 27.6% at 1, 5, and 10 year after IPAA. The presence of immune-related extraintestinal manifestations was an independent risk factor for the development of pouchitis (Hazard ratio 3.82, 95% CI 1.33-10.45, p=0.014). Although low-grade dysplasia was detected in a biopsy specimen from the ileal pouch with pouchitis in a patient, subsequent pouchoscopies were negative for dysplasia. None developed high-grade dysplasia or invasive cancer.
Conclusion: Pouchitis developed in 4.5%, 12.5%, and 27.6% after 1, 5, and 10 years. The presence of immune-related extra-intestinal manifestation is an independent risk factor for the development of pouchitis. The development of carcinoma in the ileal pouch or the remnant rectum after IPAA is considered minimal.
Disclosure of Interest: None declared

P1623 DURABILITY OF THE ANTI-HBS TITERS AFTER VACCINATION AGAINST HEPATITIS B VIRUS (HBV) IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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Introduction: Among immunocompromised patients who respond to the HBV vaccine, clinically significant HBV infection has been documented in those who do not maintain anti-HBs concentrations > 10 IU/l.
Aims & Methods: 1) To understand the kinetics of the anti-HBs titers over time in IBD patients who have initially responded to the vaccination. 2) To identify predictive factors of negativization of anti-HBs titers over time.
This multicenter study included IBD patients vaccinated in the COMVI-B trial (EUDRA CT number: 2010-023947-14), where patients with negative HBV serology and without previous vaccination against HBV were randomized 1:1 to receive Fendrix® or double doses of Engerix® at months 0, 1, 2 and 6. Patients with anti-HBs > 10 IU/L 2 months after the 4th dose were followed-up. Anti-HBs titers were then measured at 6 and 12 months. When anti-HBs titers were < 10 IU/L during the follow-up, they were considered negatives. Long-term maintenance of positive anti-HBs titers was estimated using Kaplan-Meier curves. Cox-regression analysis was performed to identify potential predictive factors for losing anti-HBs protective titers during follow-up.
Results: 118 patients were included. Fifty percent of patients received each of the vaccines (Engerix® or Fendrix®). There were no differences in the main characteristics (age, anti-HBs concentration after complete vaccination or IBD treatment) between the study groups (Engerix® or Fendrix®). The cumulative incidence of negativization of the anti-HBs titers was 14% after 6 months and 22% after 12 months of follow-up. The incidence rate of negativization of the anti-HBs titers was 23.5% per patient-years of follow-up. In the multivariate

analysis (adjusted by the patient's age and the treatment with thiopurines or anti-TNF drugs), to have had anti-HBs ≥100 IU/L (vs. < 100 UI/L) after the vaccination was the only factor that was associated with a lower probability of negativization of anti-HBs titers during the follow-up (HR = 0.07, 95%CI = 0.02-0.2, p < 0.0001). The type of vaccine administered was not associated with the risk of negativization of anti-HBs titers.
Conclusion: A high proportion of IBD patients with protective anti-HBs titers after vaccination loose them over time (approximately, 25% of patients per year of follow-up). The risk of loosing protective anti-HBs titers is dramatically increased in patients achieving anti-HBs below 100 IU/L after the vaccination. Thus, anti-HBs > 100 IU/L should be the threshold to consider HBV vaccination success in IBD patients.
Disclosure of Interest: None declared

P1624 EFFICACY OF CONCOMITANT MESALAMINE SUPPOSITORY IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS WHO SHOWED INADEQUATE RESPONSE TO AN ORAL 5-AMINOSALICYLIC ACID PREPARATION: A PROSPECTIVE STUDY

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Introduction: Hitherto, oral 5-aminosalicylic acid (5-ASA) preparations have been widely administered as first-line mediation for inducing and maintaining remission in patients with mildly to moderately active ulcerative colitis (UC). Further, for distal UC, topical preparations as enema or suppository have been applied. However, patients who do not respond well to an oral 5-ASA preparation alone should benefit from concomitant mesalamine suppository.
Aims & Methods: We were interested to evaluate the efficacy of concomitant Pentasa suppository for inducing remission in patients who had active UC including the rectum while on an oral 5-ASA preparation. In a single-centre prospective setting, 192 consecutive patients with mildly to moderately active UC with rectal inflammation while on oral 5-ASA preparations for at least 4 weeks were included. All patients received concomitant Pentasa 1g suppository rectally once a day for 4 weeks together with the ongoing oral 5-ASA preparations. No patient received corticosteroid or immunosuppressant. At week 4, clinical efficacy for Pentasa suppository was evaluated by applying the UC-Disease Activity Index (UC-DAI), including the 3 sub-scores. Clinical remission was defined as the bleeding sub-score = 0, and a decrease of ≥ 3 in the UC-DAI, while clinical response meant a decrease of ≥ 1 in the UC-DAI.
Results: At week 4, the average UC-DAI fell from 3.2 ± 0.7 at entry to 1.4 ± 1.7 (n = 192, P < 0.001). Of the 192 patients, 90 (46.9%) achieved clinical remission, and 43 (22.4%) achieved response level. The bleeding sub-score fell from 1.0 ± 0.2 to 0.4 ± 0.5 (P < 0.001). Regarding the response rate vs extent of UC, the UC-DAI fell from 3.2 ± 0.7 to 1.4 ± 1.7 in patients with proctitis (n = 171, P < 0.001) and from 3.1 ± 0.5 to 1.3 ± 1.5 in patients with left-sided colitis (n = 20, P < 0.001). One patient with pancolitis worsened. Further, by concomitant Pentasa suppository, the bleeding sub-score in patients who did not respond well to oral 5-ASA preparations alone (n = 129) fell from 1.0 ± 0.1 to 0.3 ± 0.5 (P < 0.001); in sulphasalazine-treated subgroup (n = 49, mean dose 3.7 ± 1.0g/day, range 1.5-6.0/day) fell from 1.0 ± 0.1 to 0.3 ± 0.5 (P < 0.001); in Pentasa (n = 20), 2.3 ± 0.8g/day, range1.5-3.0/day fell from 1.0 ± 0.0 to 0.2 ± 0.4 (P < 0.001); in Asacol (n = 60), 3.4 ± 0.4g/day, range 2.4-3.6/day fell from 1.0 ± 0.1 to 0.4 ± 0.6 (P < 0.001), reflecting significant efficacy for concomitant Pentasa suppository in patients who did not respond well to high dose oral 5-ASA preparations alone. No serious adverse event was observed.
Conclusion: This is the first study in Japan that has investigated the efficacy of Pentasa suppository in patients who did not respond well to an oral 5-ASA preparation. Based on the outcomes of the present investigation, we believe that patients with distal UC who have active disease while on an oral 5-ASA preparation alone should benefit from concomitant Pentasa suppository.
Disclosure of Interest: None declared

P1625 MANAGEMENT OF UC-LIKE CROHN'S DISEASE AFTER IPAA

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are the two major types of idiopathic inflammatory bowel disease (IBD) with unknown pathogenesis. Approximately 20% of CD cases involve the colon causing difficulty in differential diagnosis between UC and Crohn's colitis, even in colectomy specimens. Standard surgical management of UC patients is total proctocolectomy (IPAA) but for the subgroup of patients referred to as ulcerative colitis-like Crohn's colitis or indeterminate colitis management remains obscure.
Aims & Methods: To identify features associated with "ulcerative colitis (UC)-like" subgroup of Crohn's colitis and to present treatment options.
Six patients diagnosed as having UC and underwent IPAA from 1983-2013 and subsequently developed CD of the small bowel (ileum or ileal pouch) were identified. Six other patients operated with IPAA for "true" UC were used as controls. UC diagnosis was based on clinical, endoscopic, and pathologic grounds pre-operatively. Demographics were recorded and pathology-endoscopy reports pre-surgically were reviewed and compared with histopathology results from resection specimens for both groups. All patients were followed-up and treated differently according to their symptoms and extent of the disease.
Results: Patients with "UC-like" CD were on average 7 years younger than those with "true" UC (P < 0.01). More active disease in the proximal colon and active inflammation of the ileum were noticed in 4 of 6 "UC-like" CD cases, but in none of the "true" UC cases (P < 0.05). In most "UC-like" CD cases there were many hospital admissions for early or late small bowel obstructions or pouch related fistulas. Crohn's granulomas and transmural inflammation in non-ulcerated areas were absent in both groups. In one patient with severe bowel obstruction stricture resection and anastomosis were performed. Three other patients were faced with seton placement and biologics and in two only a permanent ileostomy was performed with/or without pouch extraction.
Conclusion: UC-like Crohn colitis is highly suspected when pre-surgically it is found more active disease in the proximal colon or inflammatory involvement of the terminal ileum. Additionally, when there is small bowel obstruction or early development of pouch related fistulas post surgery. Under certain circumstances this subgroup of patients can be treated conservatively after IPAA even with preservation of the ileal pouch.
Disclosure of Interest: None declared

P1626 PREDICTING SURGERY AT THE MOMENT OF DIAGNOSIS OF CROHN'S DISEASE IS POSSIBLE. PROPOSAL OF A PREDICTIVE MODEL

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Introduction: It is estimated that 80% of patients with Crohn's Disease (CD) will required a surgery anytime during their lives. However, few studies to determine predictors of surgery at the precise moment of diagnosis have been performed. We aimed to identify predictive factors for surgery at the moment of diagnosis and to propose a predictive model for that outcome, able to guide therapeutic decisions.
Aims & Methods: Unicentric, retrospective, case-control study of CD patients: 71 cases with previous abdominal surgery for CD and 205 non-operated CD controls. Demographic, clinical, laboratorial, and endoscopic data and Montreal classification at the moment of diagnosis were collected. Statistical analysis was performed using SPSS software, version 22.0.
Results: There were no differences between groups regarding gender (p = 0.984) or family history (p = 0,970). Smoking habits were more common in cases (p = 0.003). Concerning Montreal classification, L3 location was more common in cases (p < 0.001) e B1 behaviour was less frequent (p < 0,001); no differences were found on age at diagnosis (p = 0.142), upper gastrointestinal tract involvement (p = 0.122) or perianal disease (p = 0.264). At the moment of diagnosis, while abdominal pain and oral manifestations were more common in cases (p = 0.006 and p = 0.046, respectively), no significant differences were found in the remaining symptoms or extraintestinal manifestations. At the moment of diagnosis, anemia (p < 0,001), leucocytosis (p < 0.001), thrombocytosis (p < 0.001) and increased ESR (p = 0.002) and CPR (p < 0.001) were significantly more frequent in cases. Multivariate analysis established B2 or B3 behaviour (OR = 0.728, p = 0.013), L3 location (OR = 3.01, p = 0.016), haemoglobin value (OR = 0.728, p = 0.013) and leukocyte count (OR = 1.24, p = 0.001) as predictive factors for surgery at the moment of diagnosis. These factors were included in a predictive model for surgery ($P_{(cirurgia)} = 1/(1 + e^{-[-1.692 + 1.1xL3 + 3.09xB2/B3 - 0.317xHb(g/dL) + 0.214xLeuc(x103n/\mu L)]}$)), with a specificity of 93.5%, a sensitivity of 71.4%, a positive predictive value of 76.9%, and a negative predictive value of 91.6%.
Conclusion: At the moment of diagnosis, behaviour and location of CD and haemoglobin and leukocyte values, when integrated in the proposed predictive model, allow, with high specificity, identification of patients potentially requiring surgery. In these patients, the use of more aggressive medical therapies should be considered to avoid or at least defer a surgical outcome.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 09:00-14:00
OTHER LOWER GI DISORDERS III - HALL 7

P1627 SPECIFIC BACTERIAL SEQUENCES DETERMINATION IN FECES IDENTIFIES HIGHER COLORECTAL CANCER RISK SUBGROUP AMONG LYNCH SYNDROME CARRIERS

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Introduction: Cancer risk in Lynch Syndrome (LS) carriers is variable and may depend upon the involved gene. However, starting at early ages, LS non-affected carriers follow an exhaustive surveillance through colonoscopy in order to detect pre-neoplasic lesions or CRC in early stages. Thus, it is crucial to find a key biomarker that reflects CRC development risk. It has been shown that bacterial communities in the colonic mucosa of CRC patients differ from healthy individuals and intestinal microbiota has been proposed as a

determining agent in the development and progression of CRC along its stages. Recent data from our research group showed that a set of specific phylotypes determined in intestinal biopsy from CRC patients presented a high relatedness with CRC risk.

Aims & Methods: We aimed at defining a microbiological signature in stool sample capable of determining CRC risk in LS carriers.

We designed a preliminary retrospective study to analyze intestinal microbiota in feces of individuals with different profile of CRC risk: LS carriers (n = 30) who had a colonoscopy in the Digestive Department of Hospital Universitari Dr. Josep Trueta.

Detection of specific phylotypes was performed through q-PCR of 16S rDNA bacterial sequences. The quantification of specific bacteria sequences was expressed in q-PCR cycle threshold (Ct). Ratios for the different sequences identified were calculated.

Results: Ratios were calculated for LS carriers with (high-risk group, n = 15) and without (low-risk group, n = 15) adenomatous polyps in their last colonoscopy. Cut-off values were defined (14.02, 24.76, 21.42 and 22 ct values respectively for four bacterial sequences) and specific patterns for 16S rDNA were identified. Low-risk group presented elevated levels of 16S rDNA (Ct values under cut-off) in front of high risk-group that presented low levels. The analytical performance of the CRC risk estimation was 80% and 100% respectively for sensitivity and specificity.

Conclusion: Changes of specific microbiological signatures in feces of LS carriers may depict those carriers harboring lesions. These preliminary results outline a new non-invasive approach to identify high-risk LS carriers. But, the potential of this tool needs validation in larger studies.

Disclosure of Interest: M. Serra Pagès Shareholder: GOODGUT, Directorship(s): GOODGUT, J. Brunet: None declared, E. Darder: None declared, M. Pineda: None declared, G. Capellà: None declared, A. Bahí: None declared, J. García-Gil Consultancy: GOODGUT, Shareholder: GOODGUT, X. Aldeguer Consultancy: GOODGUT, Shareholder: GOODGUT, V. Piñol: None declared

P1628 SPECIFIC BACTERIAL DETERMINATION IN FECES RELATED TO COLORECTAL NEOPLASIA: A NOVEL NON-INVASIVE SCREENING TEST?

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Introduction: Colorectal cancer (CRC) is the second leading cause of cancer death in Europe and in United States, and is the most frequently diagnosed cancer in Europe, with over 400,000 new cases and 200,000 deaths in 2008.

These data reflect that preventive measures need to be taken. The most effective and economic measures to reduce CRC incidence and mortality are CRC risk screening test, thus an improvement of the sensitivity from actual screening methods would be helpful. For this reason, we think it is crucial a better understanding of the CRC etiology to find a key biomarker that could be used for CRC screening.

The genetic basis and natural history of CRC are well defined, considering that less than 5% of CRCs are hereditary, and majority are sporadic CRC (patients with no personal or family history of colonic neoplasm). The etiology of this disease is still unknown, although a multifactorial origin in which endogenous and exogenous factors are actively involved in tumor development is suspected. These factors are: age, tobacco, personal history of inflammatory bowel disease, diet, lifestyle, and more recently microbiota.

Lately, it has been shown that bacterial communities in the colonic mucosa of CRC patients differ from healthy individuals and the intestinal microbiota has been proposed as a determining agent in the development and progression of CRC along its stages.

Recent data from our research group showed that a set of specific phylotypes determined in intestinal biopsy from CRC patients presented a high relatedness with CRC risk.

Aims & Methods: We aimed at defining a microbiological signature in stool sample capable of being use as screening test.

We designed a preliminary retrospective study to analyze intestinal microbiota in feces of healthy individuals (n = 15) and CRC patients (n = 15) who had a colonoscopy in the Digestive Department of Hospital Universitari Dr. Josep Trueta.

Detection of specific phylotypes was performed through q-PCR of 16S rDNA bacterial sequences. The quantification of specific bacteria sequences was expressed in q-PCR cycle threshold (Ct). Ratios for the different sequences identified were calculated.

Results: Ratios were calculated for healthy individuals (n = 15) and CRC diagnosed (n = 15) at colonoscopy. Cut-off values were defined (22, 16.56, 22.97 and 19.24 ct values respectively for four bacterial sequences) and specific patterns for 16S rDNA were identified. Healthy group presented elevated levels of 16S rDNA (Ct values under cut-off) in front of CRC group that presented low levels. The analytical performance of the CRC risk estimation was 80% and 100% respectively for sensitivity and specificity.

Conclusion: Changes of specific microbiological signatures in feces depict CRC neoplasia. These preliminary results outline a novel non-invasive approach to screening CRC. The potential of this tool needs validation in larger studies.

Disclosure of Interest: M. Serra Pagès Shareholder: GOODGUT, Directorship(s): GOODGUT, X. Aldeguer Consultancy: GOODGUT, Shareholder: GOODGUT, A. Bahí: None declared, J. García-Gil Consultancy: GOODGUT, Shareholder: GOODGUT, V. Piñol: None declared

P1629 THE INFLUENCE OF CELL WALL PROPERTIES OF LACTOBACILLI AND BIFIDOBACTERIA STRAINS ON THE PHAGOCYTIC CELLS FUNCTIONAL ACTIVITY

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Introduction: Probiotics have strong potential to develop healthy diets and integrated approach for immunity-related diseases management. The cell wall of probiotic bacteria is a dynamic entity, depending on many components and plays an essential role in many aspects of modulating immune response [1]. The cell wall elasticity impacts on beneficial effects of probiotic strains have not been sufficiently studied.

Aims & Methods: The aim of this study was to investigate the effect of lactic acid bacteria (LAB) and bifidobacteria strains on phagocytic system cells functional activity and immunoregulatory cytokines synthesis *in vitro* in regards to the bacteria surface properties as cell walls elasticity using atomic force microscopy (AFM).

Methods: We conducted experimental studies on Balb/c line mice 18-20 g weight using lyophilized strains of LAB – *L. acidophilus* IMV B-7279, *L. casei* IMV B-7280, *L. delbrueckii* subsp. *bulgaricus* IMV B-7281 and bifidobacteria – *B. animalis* VKL, *B. animalis* VKB. We evaluated the viability of probiotic cultures via monitoring of their growth. We cultivated the macrophages received from the peritoneal cavity of mice by common method individually with the strains of LAB and bifidobacteria. We estimated the impact of LAB and bifidobacteria strains on the functional activity of peritoneal cavity macrophages using the conventional methods of study oxygen-dependent bactericidal activity, nitric oxide production, their effect on the immunoregulatory cytokines. We used AFM scanning to estimate bacteria cell walls elasticity.

Results: All strains had a stimulating effect on the functional activity of macrophages and ability to produce NO/NO_2 *in vitro*. Lactobacilli strains increased the production of IL-12 and IFN-γ *in vitro*. The AFM demonstrated different degree of the cell walls elasticity in various strains of LAB and bifidobacteria. Among lactobacilli the most elastic cell wall was found in *L. delbrueckii* subsp. *bulgaricus IMV B-7281*, and among bifidobacteria – in *B. animalis VKL*, which induced the considerable activation of the phagocytes. Probiotic strains survival in the macrophages depended on the elasticity of bacterial cell walls and on the time of their joint cultivation.

Conclusion: LAB and bifidobacteria strains stimulate immunomodulatory cytokines and active oxygen and nitrogen oxides compounds production in macrophages. Strains with a more elastic cell wall according to AFM data demonstrated higher resistance to intracellular digestion in macrophages and higher level of their activation. AFM might be considered as a fast and accurate method to assess parameters of probiotic strains cell wall to predict their immune-modulatory properties.

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Disclosure of Interest: None declared

P1630 UNDERDETECTION OF GASTROENTERITIS IN PRIMARY CARE PATIENTS

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Introduction: Dutch primary care practice guidelines promote selective use of faeces testing for bacterial and parasitic enteropathogens in patients suspected of gastroenteritis (GE), based on clinical assessment (1). As clinical differentiation between bacteria and parasites is difficult, selective testing may be a source of underdetection of enteropathogens (1).

Aims & Methods: This study quantified the number of undetected patients with one or more enteropathogens in primary care patients suspected of GE as a consequence of the present guideline. In the first week of every month between July 2012 and June 2013 we randomly collected faecal samples of – at least – the first 100 routine primary care patients. A multiplex qPCR assay was performed for all patients for detection of five bacterial (*Salmonella* spp., *Shigella* spp., *Yersinia* spp., *Campylobacter* spp. and *Plesiomonas* spp.), three parasitic pathogens (*Entamoeba histolytica, Giardia lambiae and Cryptosporidium* spp.,) and two potentially pathogenic parasites (*Blastocystis hominis* and *Dientamoeba fragilis*). The identified enteropathogens were compared with the clinical indication for testing (request for bacteria, parasites or both) as provided by the primary care physician (PCP). Potentially pathogenic parasites were analysed separately.

Results: In all 1275 samples were collected. The mean age of included patients was 35 years (SD = 24) and 56% of the patient were female. PCPs tested both bacteria and parasites in 541 (42%) patients. Selective testing was performed in 734 (58%) patients, of which 343 (27%) were tested for bacteria only and 391 (31%) for parasites only. Of the 734 selectively tested patients 39 (36%) of the total 108 patients positive for one or more enteropathogens were undetected due

to the selection made by the PCP. When potentially pathogenic parasites were included, 140 (36%) of the total 402 patients positive for one or more enteropathogens were undetected.
Conclusion: In this study the etiological diagnosis of GE was missed in 36% of the primary care patients due to preselected faecal testing by PCPs. If this underdetection represents clinically relevant underdiagnosis needs to be established.

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Disclosure of Interest: None declared

P1631 SHIGA TOXIN PRODUCING ESCHERICHIA COLI IN GASTROENTERITIS IN PRIMARY CARE

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Introduction: Gastroenteritis (GE) with Shiga-like toxin producing *Escherichia coli's* (STECs), including enterohaemorrhagic *E. coli* (EHEC), can cause serious complications including haemorrhagic colitis, haemolytic-uremic syndrome and death. Therefore, the Centers for Disease Control and Prevention (CDC) recommend screening of patients with community acquired diarrhoea for STEC. In Europe STEC screening is gradually being introduced in standard care. However, the incidence of GE caused by STEC in European primary care is unknown.
Aims & Methods: The aim of this study was to determine the incidence of STEC in Dutch primary care patients suspected of GE. In the first week of every month between July 2012 and June 2013 we randomly collected – at least – the first 100 faecal samples of patients suspected of GE. The RIDA®GENE *E. coli* Stool Panel I multiplex qPCR (R-Biopharm AG, Germany) was used for detection of Shiga-toxin 1 and 2 genes and the intimin (EAE) gene, after validation with positive (n = 80) and negative (n = 20) control strains, as well as preselected positive and negative stool samples (n = 75 each). The cumulative incidence for STEC with 95% confidence interval (CI) was calculated.
Results: In all 1275 samples were collected. The mean age of included patients was 35 years (SD = 24) and 56% of the patient were female. The RIDA®GENE *E.coli* Stool Panel I kit showed 100% sensitivity and specificity in the validation. STEC was found in 14 patients (1.1%, 95% CI: 0.5-1.7%), of which 6 (0.5%, 95% CI: 0.1-0.9%) were EHEC. STECs were more often detected in summer (June-September) (n = 9, 64%), with a peak incidence in August (n = 5). In none of the STEC positive patients other relevant bacteria or parasites (*Salmonella* spp., *Shigella* spp., *Yersinia* spp., *Campylobacter* spp., *Plesiomonas* spp., *Entamoeba histolytica, Giardia lambiae* and *Cryptosporidium* spp.) were found.
Conclusion: The prevalence of STEC in faecal samples of primary care patients suspected of GE was 1.1%. In all positive samples STEC was the only detected relevant enteropathogen. Although screening on STECs seems most relevant in the summer period, the clinical relevance of STEC infections in primary care needs to be determined before further decisions can be made on future screening.
Disclosure of Interest: A. Schierenberg: None declared, M. Nipshagen: None declared, J. Alphenaar: None declared, B. Broekhuizen: None declared, P. Bruijning-Verhagen: None declared, S. van Delft: None declared, M. Deege: None declared, M. Kolader: None declared, M. Bonten: None declared, N. de Wit: None declared, J. Kusters Conflict with: R-Biopharm AG supported the study by providing the RIDA®GENE E. coli Stool Panel I kits. We declare no conflict of interest.

P1632 ADHERENCE TO GENERAL PRACTICE DIAGNOSTIC GUIDELINES FOR GASTROENTERITIS IN THE NETHERLANDS

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Introduction: Dutch primary care guidelines for gastroenteritis (GE) advice to reserve diagnostic faeces testing (DFT) for: ill patients with fever, frequent watery or bloody/mucosal stools, patients with comprised immunity or increased transmission risk (1). Compliance with current guidelines is unknown. Laboratories recently replaced traditional culture is by user-friendly and fast molecular PCR-based techniques, with potential impact on testing practices in primary care.
Aims & Methods: To determine the adherence to the Dutch primary care guideline for DFT in patients with GE and evaluate the impact of PCR introduction. A before-after cohort study in 1000 primary care patients receiving DFT was performed. Clinical data were extracted from the electronic medical patient records and a random selection (2 samples, n = 500) was made from the before (conventional DFT, 2010-11) and after period (PCR, 2013). For each episode the GP's reason for DFT was extracted and their management assessed by two researchers on its accordance with the Dutch guideline (1). The proportion of adherence was calculated and group differences of patient characteristics were tested using the chi-square and Mann-Whitney U tests. Multivariate logistic regression was performed investigating the influence of PCR with adjustment for population differences between the periods.
Results: In 88% of the patients a reason for testing was specified, most frequent were symptom duration of > 10 days and a recent visit to the (sub)tropics. Guideline adherence for DFT was 17% overall; 16% under conventional testing and 18% under PCR. Patients tested according to the guideline were significantly older, more often female, had more contacts per episode, comorbidities and acid related disorder drug use (Table 1). The use of PCR did not seem an independent predictor of guideline adherence (OR = 1.2, 95% CI = 0.8-1.8).
Table 1: Patient characteristics and reasons for DFT (numbers are percentages, unless specified otherwise).

Patient Characteristics/ DFT reason	Adherence (17)	Non-adherence (83)	Total
Age, mean (SD)[#]	45,3 (25,1)	32,2 (23,9)	34,5 (24,6)*
Gender, Female[#]	64	55	57*
Contacts per episode, mean (SD) [#]	4 (2,8)	3,7 (2,4)	3,4 (2,5)*
Intestinal comorb.	19	9	11*
Cardiovascular comorb.	13	5	6*
DM	13	4	6*
Acid rel. disorder drug use	43	23	26*
Guideline criteria†: Sick Patient/Immunocomp. patient/Increased transmit. risk			6/9/3
Non-guideline criteria: Duration ≥ 10 days/Recent visit (sub)tropics			26/17
Any reason specified by GP			88

[#]Included in multivariate regression, [†]Reason presence signifies "adherence", *$p < 0.05$.

Conclusion: Adherence to the Dutch primary care guideline for DFT in primary care patients with GE is low and DFT is predominantly driven by motives that are not specified in this guideline. The introduction of PCR testing did not influence guideline adherence. Evaluation of the current guideline regarding DFT is needed to ensure proper management of primary care patient with GE.

Reference

1. Brühl PhC, et al.. *Huisarts Wet* 2007; 50(3): 103–13.

Disclosure of Interest: None declared

P1633 CLOSTRIDIUM DIFFICILE INFECTION IN COUNTY DURHAM HOSPITALS: A CHANGING CLINICAL PROFILE OVER 5 YEARS

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Introduction: *Clostridium difficile* infection (CDI) continues to pose a significant challenge to all hospitals in the United Kingdom, despite significant improvements to antibiotic prescribing and new drugs to treat it. Its incidence in the ageing population contributes to significant morbidity and mortality as does its association to patients with multiple co-morbidities[1]. County Durham represented an area of high CDI about a decade ago, and since then significant improvements in the rational use of antibiotics together with a multi-disciplinary approach to hospital acquired infections have resulted in a reduction of the annual incidence of the disease. In this report we describe the changes to clinical practice and outcomes of CDI in this region over a period of 5 years.
Aims & Methods: An annual review of all CDI patients was carried out over two 12 month periods, June 2010- May 2011 and April 2012- October 2013 using a standardised proforma and all cases recorded on the Microbiology and Infection Control Databases. The patients included all hospital attributable cases which are nationally reported as post-48 hour infections. A number of paramters including patient demographics, severity of CDI, antibiotics implicated in the development of CDI, outcomes, mortality and recurrence were studied in both time periods.
Results: The incidence in County Durham in 2008-2009 was one of the highest reported in the North East - 232 cases (74.4/100,000 bed days). By 2010 this incidence fell to 70 cases (23/100,000 bed days). In 2013, 75% of CDI patientes were diagnosed inthe hospital, and 75% were over the age of 75 years. 39/71 patients responded to initial treatment, and the remaining patients needed esclation of treatment. 39% pts died with in 3 months of their diagnosis, with 70% deaths occurring in hospital. Different parameters were studied including mortality and whilst there had been a significant reduction in the over-all incidence of CDI in the region, the mortality remained unchanged (25% in 2010-11 vs 24.7% in 2012-13). The results are as follows:

Parameter	2010-11	2012-13
Mean Age	75.5	76.8
CDI in community	38%	25%
CDI in hospital	62%	75%
Recurrence	7%	17%
28-day Mortality	**25%**	**24.7%**

Conclusion: Most of our CDI cases occur in the elderly, with 75% pts being over the age of 75years. There is a higher recurrence rate in 2012-13 (17%) compared to 2010-11 (7%), which is a cause for concern. Despite improvements in treatment, the all cause 28-day mortality remained unchanged and this is a challenge to healthcare professionals to find better ways of treating elderly patients.

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P1634 PROCALCITONIN LEVELS CAN BE USED TO DISCRIMINATE BETWEEN INFLAMMATORY AND NON-INFLAMMATORY DIARRHEA

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Introduction: The objective of this study is to determine if the level of procalcitonin can be used to differentiate between inflammatory diarrhea and non-inflammatory diarrhea in patients with acute infectious diarrhea or acute gastrointestinal infection.

Aims & Methods: This was a retrospective case-control study based on medical records from a single tertiary medical center located in Daejeon, Republic of Korea. The records of 1,176 patients who presented with abdominal pain, fever (≥37.8℃), and diarrhea between March 2011 and February 2015 were reviewed, and 514 patients were selected. The eligible patients had undergone abdominal computed tomography (CT) or colonoscopy within 3 days and blood sampling on the day of admission. The selected patients were divided into two groups on the basis of their abdominal CT or colonoscopy findings: group A, the inflammatory diarrhea group (n = 370), and group B, the non-inflammatory diarrhea group (n = 144). We then compared the clinical and laboratory characteristics of these two groups.

Results: White blood cell (WBC), absolute neutrophil count (ANC), blood urea nitrogen (BUN), C-reactive protein (CRP), and procalcitonin levels were significantly higher in group A (inflammatory diarrhea) patients than group B (non-inflammatory diarrhea) patients (11.05 ± 0.30 vs. 8.76 ± 0.29 ($P < 0.05$), respectively, 9.19 ± 0.26 vs. 6.64 ± 0.27 ($P < 0.05$), respectively, 19.1 ± 0.65 vs. 16.21 ± 1.1 ($P < 0.05$), respectively, 5.52 ± 0.23 vs. 3.06 ± 0.31 ($P < 0.05$), respectively, and 2.47 ± 0.17 vs. 0.58 ± 0.12 ($P < 0.05$), respectively). Multivariate analysis revealed that procalcitonin level on admission was the most important predictor of inflammatory diarrhea (OR 1.321, $P < 0.05$). Receiver operating characteristic analysis results also showed that procalcitonin had the highest area under-the-curve value (0.81; 95% confidence interval 0.79–0.83; $P < 0.05$) for distinguishing inflammatory diarrhea from non-inflammatory diarrhea. At a cut-off level of 0.797 mg/dL, procalcitonin had a sensitivity of 87.03% and a specificity of 68.75%.

Conclusion: Procalcitonin as a diagnostic marker of inflammatory diarrhea was superior to the other inflammatory markers and clinical characteristics we evaluated in this study. A patient's procalcitonin level on admission may aid clinical decision-making, for example initiating empiric antibiotics therapy and/or performing additional clinical tests.

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Disclosure of Interest: None declared

P1635 WE ARE NOW CONFRONTED BY YEAR-TERM INFECTION CHANGES, REQUIRING A PARADIGM SHIFT, BOTH EPIDEMIOLOGICALLY AND IN TERMS OF TREATMENT

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Introduction: An increasing awareness of the etiology of sporadic and outbreak cases of viral gastroenteritis has transformed the traditional dichotomous view that *Norovirus* causes epidemic viral gastroenteritis in older children and adults whereas *Rotavirus* causes diarrhea in infants and young children. We previously reported that 14.3% of adult diarrhea was caused by group A *Rotavirus* infection (*Lancet*, 357, 9272, 2001). Thereafter other viruses such as *Astrovirus*, *Adenovirus*, *Norovirus*, and *Enterovirus* have turned out to be also responsible for gastroenteritis. However acute gastroenteritis seemed to be gradually changed.

Aims & Methods: We recruited consecutive 768 patients (M/F; 387/371, median age; 35) acute sporadic diarrhea in adult, during the four years from 2011-2014. Referring to virus, *Astrovirus*, *Adenovirus*, *Norovirus*, and enteric pathogenic bacteria were examined by conventional stool culture. We used commercially – available immune-chromatography assay kits (QUICKNAVI-NORO™, Otsuka Pharmaceutical Co., Ltd Tokyo, Japan, and BD Rota/Adeno Examan Stick™, Becton and Dickinson Co., Franklin Lakes, NJ) for virus check. Cosinor method was tried to analyze seasonality of infection.

Results: Viral infection was confirmed at the rate of 56.4% (429/760), and bacteria was 24.0%(184/760) in sporadic acute gastroenteritis. Co-infection between virus and bacteria was extraordinary high.

Conclusion: Viral infection is approximated with a cosine curve with a period of 12 months. However Rotavirus and Adenovirus is getting decreased. Norovirus infection is getting increased. Co-infection between virus and virus or virus and bacteria is unexpectedly frequent such as we reported two years ago at this meeting. Campylobacter species are becoming dominant among bacteria pathogens. *Vibrio parahemolyticus* due to raw fish eating was dominant for long time, however during the 4 years we daiganosed only 2 case. We speculate this paradigm shift of intestinal infection appears from induction of Rotavirus vaccination, profile change of intestinal microbiota, and dietary change such as "fish to meat."

Disclosure of Interest: None declared

P1636 CONSUMED BY THE CONSUMPTION: ONGOING DELAYS IN DIAGNOSING INTESTINAL TUBERCULOSIS. 61 PATIENTS IN EAST LONDON

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Introduction: Intestinal tuberculosis (ITB) is rare but on the rise. The diagnosis is frequently delayed. Clinical presentation tends to be non-specific and often mimics inflammatory bowel disease (IBD), malignancy or less sinister conditions (eg. appendicitis, gastroenteritis). In light of the TB resurgence in urban, high-immigration areas in developed nations, prompt recognition of ITB is vital to avoid complications and death. We present the largest case series of patients with ITB in Europe.

Aims & Methods: Retrospective study of 61 consecutive ITB patients from 2008-2014 at two East London hospitals, identified using the London TB Register. Electronic records were searched for demographics, symptom duration, site of ITB, details of diagnostic confirmation and patient outcomes. Statistical analysis was done using χ^2, Fisher exact & Mann-Whitney U tests ($\alpha = 0.05$).

Results: Male:female ratio was 40:21. Mean age was 34.6 (range 13-82) years. 93% were born outside the UK, mostly from TB-endemic areas (Indian subcontinent: 88%, sub-Saharan Africa: 9%). 3% had confirmed HIV. 25% had previous pulmonary TB. Time from symptom onset to ITB diagnosis varied from < 1 week to 30 years (mean 59.4 weeks).

Main sites of ITB involvement were the small bowel (52%) or ileocaecum (44%). 3% had appendiceal TB. 26% had colonic TB (31% right colon only). Virtually all patients – except the 8% with isolated perianal TB – had cross-sectional imaging; presumptive diagnosis of ITB was made on radiology in 31%. In the other 69%, ITB was confirmed on positive histology and/or microbiology (28/61 each). 8/10 IGRAs performed were positive. 17 patients underwent endoscopy, confirming TB in 76%. Nearly one-third of patients underwent diagnostic surgery (14 had laparoscopy, 5 had laparotomies).

The total cohort was divided into Group A: ITB diagnosed on index visit to our centres with ITB-related complaint (n = 23) and Group B: ITB diagnosed later than index visit (n = 38). Group B were more likely to have previously been administered treatment for other diagnoses ($p = 0.002$), particularly IBD ($p = 0.007$). Group B had higher rates of perianal TB (4/5), strictures (18% v 9%) and obstruction (13% v 0%). 1 patient died in Group B, none in Group A. Unexpectedly, overall Group A appeared to have more severe disease on diagnosis. Group A were more likely to have perforations (17% v 11%) and intra-abdominal collections or intestinal fistulae (35% v 16%). They were also more likely to be hospitalised when ITB diagnosis was made ($p = 0.019$), undergo laparotomy ($p = 0.025$), have more surgical complications (intra-operative perforation, wound dehiscence, adhesions) ($p = 0.04$), and longer length of hospital stay that visit (mean 19.4 v 7 days). Patient delay in presentation to our centres did not influence outcomes between groups (difference in symptom duration pre-index visit, $p > 0.1$).

Conclusion: ITB is curable but morbidity and mortality remains high due to late diagnosis. The differential needs to be considered early in patients with abdominal complaints and high index of suspicion for TB to establish prompt diagnosis and treatment.

Disclosure of Interest: None declared

P1637 ENDOSCOPIC AND CLINICAL CHARACTERISTICS OF AMEBIC COLITIS IN JAPANESE PATIENTS: WITH SPECIAL REFERENCE TO DISEASE LOCATION

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Introduction: Amebiasis is a major cause of death from parasitic disease worldwide. In the developed countries, however, amebic infection could be overlooked because of a relatively lower incidence as well as nonspecific endoscopic findings, and travelling to endemic areas and sexual contacts are predominant risks for infection. The endoscopic findings include various patterns, possibly making the exact diagnosis difficult.
Aims & Methods: Our aim is to elucidate the endoscopic and clinical characteristics of amebic colitis in Japanese patients. This is a retrospective observational study. Twenty consecutive Japanese patients who were diagnosed as amebic colitis in our hospital were included. Clinical, endoscopic (19 colonoscopy, 1 sigmoidoscopy), parasitological, histological findings, and clinical outcome were reviewed. Sex, age, risk of infection, disease locations, and the presence of concomitant diseases were also recorded.
Results: This study included 20 patients (male 95%, mean age 45.6 years), 80% of which had symptoms (mucous and bloody stool 60%, diarrhea 25%, fever 15%, abdominal pain 15%). Travels to endemic areas and sexual transmission were determined in 60% and 25%, respectively. Colonoscopic findings included aphthous ulcers (75%), superficial ulcers (65%), and inflamed mucosa (62%). Among 19 patients who underwent colonoscopy, the disease location was the right colon alone (proximal to the splenic flexure) 25%, the left colon alone (including rectum) 32%, and both 42%. The age at diagnosis was higher in patients without left colon involvement than in patients with left colon involvement (mean 54.8 vs. 42.3, $p < 0.05$). In 80% of patients parasitological confirmation was demonstrated using mucosal biopsy (55%) and/or stool examination (30%), while in 20% of patients both of them were negative, leading the diagnosis by additional serological tests (20%). Concomitant diseases included inflammatory bowel disease 15%, human immunodeficiency virus (HIV) infection 15%, and pseudomembranous colitis 5%. After all patients received metronidazole (mean 1,470 mg daily for 10-15 days), only one patient had relapse (the retreatment was successful).
Conclusion: Endoscopic diseased segments are often restricted to the right colon, especially in the aged patients with amebic colitis. Thus colonoscopy but not sigmoidoscopy is mandatory when clinical and endoscopic features are suggestive of amebic colitis even in the developed countries. Concomitant infections including HIV should also be considered.
Disclosure of Interest: None declared

P1638 HIGHER FECAL HEMOGLOBIN DETECTED IN OLDER PATIENTS WITH MORE SEVERE C. DIFFICILE INFECTION

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Introduction: *C. difficile* infection (CDI) rates continue to increase and cause poor outcome for patients over 65 years with comorbid disease. Patients with mild or severe disease may require a different treatment regimen to prevent relapse, while exposing carriers to antibiotics may cause infection. Previous studies have linked higher fecal lactoferrin levels with severe CDI including presence of stool toxin, increased white blood cell count, older age, ribotype 027 infection and poor outcome. Fecal hemoglobin is a biomarker for blood in stool and has been correlated with colorectal cancer and mucosal damage. Hypervirulent strains express toxins that lead to inflammation and bleeding in the lining of the colon. Measuring hemoglobin in stool may provide an additional biomarker for determining mucosal damage. Currently, the levels of fecal hemoglobin in patients with more severe CDI has not been critically evaluated.
Aims & Methods: The levels of fecal hemoglobin in severe CDI was evaluated. Severe CDI was defined in toxin positive samples with lactoferrin levels $\geq$100 μg/g faeces. Stool samples collected from patients suspected of CDI were included. Toxin was detected using tissue culture with neutralization (TC). Presence of toxigenic *C. difficile* was confirmed with a combination of bacterial culture and TC. Lactoferrin (LF) was measured using a commercial quantitative enzyme-linked immunoassay (EIA) and a cutoff of 7.25 μg/g was considered positive. Hemoglobin was detected using a monoclonal-based EIA and results were reported as μg/g. Stool consistency was determined using the Bristol Stool Scale 1 to 7 (liquid).
Results: A total of 209 fecal samples were submitted from patients with a mean age and stool consistency of 55 years and 6, respectively. A total of 16% ($N \pm 34$) had toxigenic CDI and 12% ($N \pm 24$) were positive for stool toxin. In the TC+ group, 85% were positive for LF and 35% had levels over a higher cutoff $\geq$100 μg/g to indicate more severe CDI. The mean hemoglobin levels were higher (770 μg/g vs. 610 μg/g; $p = 0.0085$) for the TC+ vs. TC- groups and for the TC+ $\geq$100 μg/g LF compared to the TC+ $<$ 100 μg/g LF groups (830 vs. 220; $p = 0.0013$). When stratified by age, 67% of TC+ LF $\geq$100 μg/g patients were older than 65 years and had a mean hemoglobin level significantly higher compared to younger patients (1081 vs. 329 μg/g). There was no difference in stool consistency among most of the diagnostic groups except the older patient group with TC+ and $\geq$100 μg/g LF (Bristol stool score 7).
Conclusion: Older patients with severe CDI as defined by the presence of stool toxin and LF over $\geq$100 μg/g had significantly higher levels of fecal hemoglobin. Future studies are needed to evaluate the utility of hemoglobin in stool as an aid in assessing severe CDI.
Disclosure of Interest: L. Chen Conflict with: employee of TechLab, S. Doyle Conflict with: employee of TechLab, J. Boone Conflict with: employee of TechLab, D. Lyerly Conflict with: employee of TechLab

P1639 DEVELOPMENT OF A CLINICAL RULE TO PREDICT HOSPITAL ONSET-HEALTHCARE FACILITY ACQUIRED CLOSTRIDIUM DIFFICILE INFECTION: THE ERASE & CLEAN OFF CDI STUDY

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Introduction: *Clostridium difficile* (CDI) infections have been difficult to control and prevent in hospitalized patients. One possible contributor to stable or increasing CDI rates is that many at-risk patients do not have individual prevention or treatment measures adopted until after CDI develops. A pilot project was performed to develop a prediction rule for patients who develop hospital onset-healthcare facility associated (HO-HCFA) CDI. If a simple rule can be developed to predict this disease, future research may be able to institute prevention strategies in at-risk patients.
Aims & Methods: This study took place at an urban hospital with 237 beds, 12,000 annual admissions and an annual ED census of 80,000 visits. This was a retrospective case-control study of patients $\geq$ 18 years old admitted between January 1, 2012, and December 31, 2013. Clinical features of patients with HO-HCFA were compared to controls who were admitted to the hospital on the same date. Logistic regression and recursive partitioning were used to create models for predicting HO-HCFA based on (1) initial ED and (2) all (ED plus inpatient) features. Receiver operating characteristic curves were compared between rules using the method of Delong (area under the curve [AUC]). Rules with a significantly greater AUC were retained. If the AUC did not differ between rules, those rules with significantly greater sensitivity and specificity (McNemar's test) were retained. If AUC and sensitivity/specificity did not differ, the rule with the least number of clinical variables was retained.
Results: There were 105 patients with HO-HCFA after excluding recurrent cases. There were 210 patients without HO-HCFA that served as controls. Recursive partitioning resulted in the optimum rule with five ED based clinical features predictive of HO-HCFA: **E**rrant immune system - 3 points, **R**esident of assisted living facility – 10 points, **A**lbumin low – 4 points, **S**ixty years old or older – 3 points, **E**pisode of CDI in the past – 12 points, (mnemonic **ERASE)**. A cutoff of $>$ 4 total **ERASE** points yielded a rule that was 65% sensitive (55-74%, 95% CI) and 81% specific (76-86%, 95% CI) for predicting HO-HCFA. Logistic regression (including inpatient plus initial features) resulted in the optimum rule using inpatient plus ED features with eight clinical weighted features associated with HO-HCFA designated by the mnemonic **CLEAN OFF–CDI: C**DI history – 14 points, **L**ives in assisted living facility – 9 points, **E**levated WBC count ($>$ 8800 cells/mm^3) - 3 points, **A**ntibiotic use during admission – 3 points, **N**exium like medicine [proton pump inhibitor] use during admission – 5 points, **O**peration during admission – 4 points, **F**asting blood sugar high (history of diabetes) **-** 2 points, and a **F**aulty immune system – 4 points. A cut off of $>$ 10 points yielded a rule that was 81% sensitive (72-88%, 95% CI) and 81% specific (75-86%, 95% CI) in predicting HO-HCFA.
Conclusion: Clinical prediction rules were created based on ED-based information and inpatient plus initial features to predict which patients will develop HO-HCFA. Prospective validation in larger diverse settings is required to confirm the utility of these rules. If confirmed, these findings may be used in the future to predict who will develop HO-HCFA and institute more comprehensive measures to prevent this disease.
Disclosure of Interest: None declared

P1640 CLINICAL FEATURES AND OUTCOMES OF CYTOMEGALOVIRUS COLITIS: RETROSPECTIVE REVIEW

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Introduction: Cytomegalovirus (CMV) colitis occurs predominantly in immune compromised patients. However, cases of severe CMV colitis are also described in the immunocompetent patients. The aim of this study was to investigate the clinical feature and outcome of CMV colitis.
Aims & Methods: We retrospectively reviewed the medical records of 106 patients who were diagnosed with CMV colitis by immunostaining for CMV antibodies or CMV-Polymerase chain reaction (PCR) test, based on the histological examination of tissue, obtained by colonoscopic biopsy or surgical resection.
Results: The patients infected with CMV colitis had comorbidities including cardiovascular disease ($n = 26$, 24.5%), diabetes mellitus ($n = 22$, 20.8%), chronic renal failure or end stage renal disease (ESRD) ($n = 11$, 10.4%), and sepsis ($n = 13$, 12.3%). Forty nine of patients (49/106, 46.2%) had inflammatory bowel disease (IBD). The most common presenting symptom was hematochezia ($n = 45$, 42.5%) and other symptoms were diarrhea ($n = 27$, 25.5%) and abdominal pain ($n = 18$, 17.0%). Sixty of patients (60/106, 56.6%) were treated with antiviral agent (ganciclovir). The mean period of antiviral agent treatment was 15.9 ± 8.7 days. The symptoms of twenty eight patients (28/106, 26.4%) were resolved without antiviral agent treatment. Eleven of patients (11/106, 10.4%) had to undergo colectomy due to worsened condition of colitis

(pan colitis, uncontrolled bleeding, and perforation). The associated risk factors for colectomy were steroid-using patients ($p = 0.021$) and underlying sepsis ($p = 0.005$).
Conclusion: CMV colitis in patients with recent steroid use or with septic condition were associated with poor outcome including colectomy.
Disclosure of Interest: None declared

P1641 IN PATIENTS WITH CLOSTRIDIUM DIFFICILE ASSOCIATED DIARRHEA IN RUSSIA: IDENTIFICATION OF HYPERVIRULENT STRAIN

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Introduction: *C. difficile* is an etiological factor of antibiotic-associated diarrhea (AAD) in 15–25% of cases. According to published data, outbreaks of nosocomial infection caused by strain *C. difficile* NAP1 (North American pulsed-field type 1) type BI PCR ribotype 027 have been reported in Europe and the USA. This new strain was shown to be resistant to fluoroquinolones and displayed genetic mutations in a toxin regulator gene (tcdC), causing higher expression of toxins A and B; it produced a binary toxin (CDTa+CDTb).
Aims & Methods: To discover the frequency of strain *C. difficile* BI/NAP1/027, during a 10-months period, all cases of AAD and CDI in a multi-specialty hospital were recorded. CDI was diagnosed by the identification of toxins *C. difficile* A and B using the EIA test system "Xpect *C. difficile* Toxin A/B" (Oxoid/Remel, USA) in fecal samples. Then 50 positive diarrheal fecal samples were examined with an automatic PCR real-time multiplex– the GeneXpertDX (Cepheid, USA) to detect genes of cytotoxin B, a binary toxin (cdtA and cdtB genes), and a deletion in the tcdC gene (attributed to BI/NAP1/027).
Results: 130 fecal samples of patients with AAD were collected for the research. 62 patients (47,7% of cases) had a positive toxin assay. During the observation, three CDI outbreaks lasting from 7 till 14 days were declared in the hospital, and some sporadic cases were registered. The average age of the CDI patients was 61 ± 14 years. The average time between the patient's admission and CDI was 10 ± 5.7 days. The duration of the CDI episode was $7{,}5 \pm 3.5$ days. All patients were treated either with metronidazole or vancomycin, or with both medical drugs. More often, this complication developed in the pulmonary (18), surgical (13) and intensive care (10) units. The risk of developing CDI in the early post-surgical period was significantly higher: among 35 patients that were in the early postsurgical period, 26 had a positive fecal test for *C. difficile* toxins (95% CI OR 1.265 – 7.290, $p = 0.013$). Two patients within 6 months prior to this hospitalization had AAD (*C. difficile* assay was not conducted). There was not a single case when pseudomembranous colitis was considered the attributable cause of death. Four patients died during the CDI episode, but the cause of death was another disease. According to the results of the PCR, one case revealed a false positive result from the EIA system «Xpect C.difficile Toxin A/B». The other 49 samples were positive for the cytotoxin B encoding genes. The deletion in the tcdC gene, attributed to strains BI/NAP1/027, and the binary toxin gene were absent in all samples. Thus, the sensitivity of the EIA was 100%, and its specificity was 98%. The follow-up period for all patients after CDI was 9 months. No recurrence of the infection was registered.
Conclusion: During a 10-months observation in a multi-specialty hospital in St.Petersburg, CDI was identified in 47.7% of cases of AAD. There were no cases of the hypervirulent strain BI/NAP1/027 and no deaths due to CDI or recurrent CDI. EIA is shown to be a sensitive and specific test for the diagnosis of CDI.
Disclosure of Interest: None declared

P1642 CLINICAL STUDY OF 32 PATIENTS WITH ANTIBIOTIC-ASSOCIATED HEMORRHAGIC COLITIS

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Introduction: Antibiotic-associated hemorrhagic colitis causes bloody diarrhea and abdominal pain after taking antibiotics, and reveals characteristic endoscopic findings. Recently, *Klebsiella oxytoca* is described as a cause of antibiotic-associated hemorrhagic colitis.
Aims & Methods: This is a retrospective chart review for patients who visited our hospital. Patients underwent diagnostic colonoscopy, and who received a diagnosis of antibiotic-associated hemorrhagic colitis. Total 32 patients with Antibiotic-Associated Hemorrhagic Colitis were identified among those who visited our institution between October 2000 and April 2015. Demographics and clinical courses of these patients were examined. In addition, we analyzed the prevalence of *Klebsiella oxytoca*.
Results: There were 13 male and 19 female patients, with a median age of 49.7 years old (range: 17-81 years old). Of these patients, 11 patients (34.4%) had underlying clinical conditions: 6 (18.8%) had hypertension, 4 (12.5%) had hyperlipidemia, 2 (6.3%) had diabetes mellitus, 2(6.3%) had chronic liver injury, 1 (3.1%) had nephrotic syndrome. Chief complaints of these all patients were bloody diarrhea and abdominal pain. Causative antibiotics were penicillins in 22 (68.8%) patients, cephalosporins in 4 (12.5%) patients, quinolones in 3 (9.4%) patients, macrolides in 1 (3.1%) patient and Fosfomycin in 1 (3.1%) patient. Duration until onset after taking causative antibiotics were 5.6 ± 2.4 days. Colonoscopy revealed segmental hemorrhagic colitis with rectal sparing in all patients. Colitis was almost localized in the right colon. Endoscopic findings were mucosal edema, mucosal hemorrhage and mucosal redness. In stool culture, 17 (58.6%) of the 29 patients who underwent stool culture were positive for *Klebsiella oxytoca*. All the 32 patients achieved clinical remission with conservative treatment and needed 4.0 ± 1.2 days till. clinical remission.
Conclusion: Antibiotic-associated hemorrhagic colitis was seen in relatively younger population who didn't have underlying clinical conditions. Causative antibiotics were mostly penicillins, cephalosporins and quinolones. Colitis was almost localized in the right colon. *Klebsiella oxytoca* was detected in most patients with antibiotic-associated hemorrhagic colitis.
Disclosure of Interest: None declared

P1643 THE DETECTION OF COLORECTAL NEOPLASTIC LESIONS IN ASYMPTOMATIC HIV-INFECTED SUBJECTS DURING SCREENING COLONOSCOPY

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Introduction: The incidence of non-AIDS defining cancer has increased with prolongation of life expectancy of HIV-infected patients. Previous studies from western countries have suggested that higher incidence of colonic adenoma in patients with HIV infection compared with the general population. However, little is known about the risk of adenoma in HIV-infected patients compared with the general population in Asia.
Aims & Methods: We conducted a prospective cross-sectional single-center study to determine the prevalence of colonic neoplasm in 200 HIV-infected patients and age- and sex- matched 200 uninfected subjects. All subjects underwent screening colonoscopy. Colorectal neoplasm included adenoma, early or advanced adenocarcinoma, and other tumors. Lifestyle habits, medications, co-morbidities, HIV-related factors and human papillomavirus (HPV) infection were assessed before colonoscopy. To evaluate the effects of HIV infection on colorectal neoplasm, adjusted odds ratio (OR) was estimated by multivariate logistic regression.
Results: Between HIV infected and non-infected subjects, no significant difference was noted in the prevalence of adenoma ($n = 28$ vs 30, $P = 0.78$). Multivariate analysis adjusted by alcohol, smoking, NSAIDs, low-dose aspirin, and diabetes mellitus showed that HIV infection is not associated with increased risk of adenoma (adjusted OR [95%CI], 1.08 [0.60-1.95], $P = 0.80$). Between HIV infected and non-infected subjects, no significant difference ($p > 0.05$) was noted in the prevalence of early adenocarcinoma ($n = 2$ vs $n = 1$), advanced adenocarcinoma ($n = 0$ vs $n = 2$), malignant lymphoma ($n = 1$ vs 0), carcinoid tumor ($n = 0$ vs $n = 1$), and lipoma ($n = 0$ vs $n = 2$). Colorectal Kaposi's sarcoma was more common in HIV-infected patients ($n = 6$ vs 0, $P = 0.03$). Among HIV-infected patients, advancing age was an independent and significant risk factor for adenoma (adjusted OR [95%CI], 1.09 [1.05-1.13], $P < 0.01$). CD4 count, HIV-RNA, history of antiretroviral treatment, and oncogenic HPV infection were not risk factors for adenoma.
Conclusion: HIV infection was not identified as risk for colorectal adenoma and adenocarcinoma in Asian HIV-infected patients. However, it should be noted that 14% of asymptomatic HIV-infected patients had adenoma and its risk increased with age. Thus, HIV-infected patients should not miss screening opportunities for colorectal adenoma as well as other HIV-related malignancies.
Disclosure of Interest: None declared

P1644 UNDERSTANDING THE EPIDEMIOLOGY AND CLINICAL SIGNIFICANCE OF LATERALLY SPREADING TUMORS: A META-ANALYSIS

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Introduction: Although the large flat colorectal neoplasms – also known as laterally spreading tumors (LSTs) – are considered to be important contributors to postcolonoscopy colorectal cancers, their frequency and significance for post-polypectomy surveillance are unclear. We performed a meta-analysis to examine the prevalence, and their endoscopic and histopathologic subtypes of LSTs in population-based studies.
Aims & Methods: We conducted a systematic search in PubMed, Cochrane Library and Scopus through all published articles (English language) until October 2014 (PRISMA methodology). Eligible studies were those reporting both population size and total number of patients with at least one LST and/or the total number of detected LSTs. We calculated pooled prevalences (95% confidence intervals (CI)) of LSTs, using random effects models.
Results: Of the 2362 studies identified, 120 were selected, of which 17 were population-based (7 European, 7 Asian, 3 American). The definitions employed for a LST varied considerably across studies: the most common definition used was 'a neoplasm with laterally growing appearance and at least 10 mm in size'. Nine of the 17 studies used the term 'LST', seven 'large flat colorectal lesion' and one an equivalent term (nodule aggregating tumor). Six of the 17 studies included both the population size and the total number of LST patients and were used in the prevalence analysis; pooled estimates for the LST prevalence were 0.67% (**Table**). Five of the 17 studies also reported the total number of patients with at least one neoplasm; pooled estimates showed a LST prevalence of 3.1% (CI: 2.4-3.8%) in these studies. Ten of the 17 studies additionally reported on the proportion of LSTs of all lesions found; pooled estimates of these data showed a LST prevalence of 2.53% (CI: 1.66 – 3.41%). Of all LSTs, 60.8% (CI: 50.7-70.8%) were of granular subtype and 39.2% (CI: 29.2-49.3%) of nongranular subtype. One study reported a predominance of nongranular LSTs.

Histopathology of LSTs included adenomas with low-grade dysplasia (61.3%, CI: 52.1-70.6%), adenomas with high-grade dysplasia (24.5%, CI: 18.3-30.7%), invasive cancer (8.2%, CI: 4.7-11.7%) or hyperplastic polyps (15.9%, CI: 8.5-13.3%). Patients with LSTs were predominantly males (56.8%, CI: 54.1-59.5%); mean age at LST diagnosis was 64.2 years. Overall, substantial heterogeneity was found across studies (maximal I^2: 95%).

Table 1: Pooled data (mixed model). *Number of LSTs derived from figures, only largest lesion per patient mentioned

Author (year)	Number of LST patients	Total number of patients	Prevalence (%) [95% CI]
Zhao (2014)	259	38050	0.68 [0.60, 0.77]
Reinhart* (2013)	354	52521	0.67 [0.61, 0.75]
Martinez (2012)	24	1234	1.94 [1.25, 2.88]
Rotondano (2011)	254	27400	0.93 [0.82, 1.05]
Chiu (2009)	53	12731	0.42 [0.31, 0.54]
Tantau (2008)	14	3856	0.36 [0.20, 0.61]
Total			0.67 [0.50, 0.84]

Conclusion: The prevalence of LSTs in population-based cohorts ranges from 0.36% to 1.95%. Such variability can be partially explained by differences in definitions applied. A universal nomenclature for LSTs is a necessary first step to clarify their biologic behavior and significance for post-polypectomy surveillance.

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P1645 HEPATITIS B INFECTION AS A RISK FACTOR FOR ADVANCED COLONRECTAL POLYP AND CANCER

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Introduction: Hepatitis B virus infection cause cirrhosis and hepatocellular carcinoma but is also etiologically linked to several extrahepatic medical condition. Several studies have probed the existence of HBV in some extrahepatic organs and tissues. HBV is also associated with extrahepatic malignancy and may be oncogenic. However, the association of HBV infection and advanced colorectal polyp and cancer has not been investigated.

Aims & Methods: A retrospective case-control study with 130 HBV infection patients(114 CHB infection, 26 LC Patients, 31 HBV treatment) and 130 healthy controls matched for age, sex. First, we investigate each group different incidence of colorectal polyp especially of advanced polyp and cancer. And the associations between advanced colorectal polyp and HBV infection were explored with multivariate logistic regression analysis.

Results: HBV patients had a higher rate of colorectal polyp, advanced colorectal polyp, colon cancer than healthy group (OR: 6.29, 95%CL: 3.651-10.859; OR: 1.31, 95%CL: 1.193~1.446; OR: 1.066, 95% CL: 1.020-1.114). And HBV infection patients had a more polyps and size is larger than healthy group (0.04 ± 0.089 vs 1.81 ± 0.184, $p < 0.001$, 0.084 ± 0.0152, 0.447 ± 0.0423 $p < 0.001$). Of the HBV patients, 111/130 had detectable HBV DNA and HBV DNA detection was a significant risk factor for colon polyp, advanced poly-p.($p < 0.001$, OR 56, $p = 0.008$). Furthermore, advanced colorectal polyp and cancer is detected only HBV DNA detection patients (31/111, 8/111). And multiple logistic regression analysis also show association of HBV DNA and advanced colon polyp ($p = 0.004$)

Conclusion: The HBV infection was positively associated with advanced colorectal polyp and colon cancer, especially for HBV DNA detectable patients. But HBV infection treatment was not show association with colorectal polyp. Further prospective studies are warranted to confirm this relationship.

Disclosure of Interest: None declared

P1646 ALCOHOLIC LIVER DISEASE IS ASSOCIATED WITH AN INCREASED RISK OF ADVANCED COLORECTAL NEOPLASM

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Introduction: Although alcoholic liver disease (ALD) may affect the incidence or progression of colorectal neoplasia through liver metabolism of alcohol, innate immune response, and genetic alterations, little is known about the association between ALD and colorectal neoplasia.

Aims & Methods: The aim of this study was to investigate whether ALD is associated with the increased risk of advanced colonic neoplasm. We analyzed 118 consecutive patients with ALD who underwent colonoscopy between January 2000 and December 2013. For each case, age- (±5 years) and sex-matched controls were identified from patients with non-alcoholic fatty liver disease and healthy controls. Clinical data were retrieved from medical records by evaluating colonoscopic, pathologic, and radiologic findings.

Results: Of the 118 patients with ALD, six (5.1%) had colon cancer and 18 (15.3%) had advanced colonic adenoma. A case-control study showed that the odds for detecting advanced colorectal neoplasm among ALD patients without decompensated liver cirrhosis (LC) were approximately 10.1 times greater than in the age- and gender-matched healthy controls (odds ratio [OR], 10.10; 95% confidence interval [CI], 3.64–28.01; $P < 0.001$). Age was an independent risk factor for detecting advanced colonic neoplasm in patients with ALD (OR, 1.08; 95% CI, 1.03–1.14; $P = 0.002$).

Conclusion: The yield for detecting advanced colonic neoplasm was significantly higher in patients with ALD than in healthy controls. Screening for colorectal neoplasm using colonoscopy is strongly warranted in ALD patients without decompensated LC or those who consider liver transplantation.

Disclosure of Interest: None declared

P1647 COLORECTAL CANCER IN INFLAMMATORY BOWEL DISEASE- IS SURVEILANCE WORKING?

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Introduction: The burden of colorectal cancer (CRC) in inflammatory bowel disease (IBD) is currently unclear. Recent studies suggest the magnitude of risk may be considerably lower than previous estimates raising questions surrounding current surveillance protocols. However, studies that use IBD surveillance cohorts to identify cases may underestimate the burden of disease with substantial number of cases arising in patients that fall outside current surveillance parameters. Our aim was to identify all cases of CRC arising in patients with IBD in a single geographic locality in a recent timeframe and analyse factors affecting diagnosis with particular reference to current UK surveillance recommendations.

Aims & Methods: Patients with IBD who developed CRC in a 5-year period from between 2010 and 2015 were identified from a fully maintained database of all CRC cases diagnosed in our locality. This was cross-referenced with histology reports and endoscopy reports from the same period. Case notes were reviewed with data on demographics, disease, presentation, diagnosis, CRC surveillance, cancer stage and outcomes collected and analysed.

Results: 672 cases of CRC were identified in the study period of which 17 (2.5%) arose in patients with IBD (10 UC: 6CD: 1 IBDU). 16 cases were adenocarcinomas with 1 anal squamous cell carcinoma in a patient with long-standing fistulating perianal Crohn's disease. 6/17 cases (35%) were screen detected in asymptomatic patients undergoing regular surveillance. 4/17 (24%) were interval cancers identified in patients prior to their next scheduled surveillance. The remaining 7/17 (41%) were identified in patients who were not participating in a screening programme. 4 of these cases fell outside current screening parameters with the further 3 cases arising in patients who had ceased surveillance (average age 87; range 84-93). Surveillance in the interval cancers did not adhere to published guidelines in 3 out of 4 cases. 5/6 (83%) screen detected cases were classified as Duke's A or B, compared with 5/11 (45%) of the non-screen detected cases.

Conclusion: The burden of CRC in patients with IBD is significant accounting for 2.5% of all cancers in the study period. Screen detected cancers were identified at an earlier stage than non-screen detected cancers, though 41% of cases arose in patients that would not currently qualify for screening in the UK. Screening did not adhere to guidelines in 75% of interval cancers. These results support the concept of a surveillance programme though reinforce the importance of meticulous high quality colonoscopy and adherence to guidelines to improve outcomes.

Disclosure of Interest: None declared

P1648 RATE OF DETECTION OF SERRATED LESIONS IN PROXIMAL COLON BY SIMULATED SIGMOIDOSCOPY

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Introduction: Screening for colorectal cancer by sigmoidoscopy benefits from the fact that distal findings predict the risk of proximal advanced neoplasms. Not all sigmoidoscopy trials have been observed a reduction in CRC-specific mortality. Major criticism of sigmoidoscopy trials is its lower ability to detect APN respect to colonoscopy. Moreover, proximal tumors may be due to the

serrated pathway. No long data about rate of proximal serrated lesions detected with sigmoidoscopy strategies has been published.
Aims & Methods: To determine the rate of detection of proximal serrated lesions by simulated sigmoidoscopy in a population based multicenter, nationwide, randomized controlled trial.
Methods: Asymptomatic individuals aged 50-69 years were eligible for a randomized controlled trial designed to compare colonoscopy and fecal immunochemical test (Colonprev study). Sigmoidoscopy yield was simulated from results obtained from the colonoscopy group, according to the criteria proposed in the UK Flexible Sigmoidoscopy Trial for colonoscopy referral. The main outcomes were first, rate of detection of proximal serrated lesions defined as sessile serrated polyp or hyperplastic polyp of any size (SP + HP) and secondly, proximal serrated polyp of any size or hyperplastic polyp ≥ 10mm (SP + HP10), both proximal to splenic flexure.
Results: Proximal serrated lesions (SP + HP) were observed in 329 of 5059 (6.5%) individuals, whereas proximal serrated polyp of any size or hyperplastic polyp ≥ 10mm (SP + HP10) were detected only in 88 subjects (1.7%). pSP + HP and pSP + HP10 were detected in 47 subjects (0.9%) and 16 subjects (0.3%), in the sigmoidoscopy simulation (odds ratio for sigmoidoscopy 0.13; 95% CI 0.09-0.18; $p < 0.0001$ and 0.17; 95% CI 0.1;-0.29, $p < 0.0001$, respectively. The number of individuals needed to refer for colonoscopy to detect one pSP + HP and one pSP + HP10 was 7 (95% CI 5-9) and 20 (95% CI 12-32), respectively. Sensitivity of sigmoidoscopy for pSP + HP was lower in women, from 14.3% in men aged 60-69 years to 3.9% in women aged 50-59 years. Sigmoidoscopy did not detect any of the 11 and 18 women's, aged 60-69 and 50-59 years, respectively, with a pSP + HP10.
Conclusion: Sigmoidoscopy–based strategies detect fewer individuals with proximal serrated lesions. Performance of sigmoidoscopy was lower in women, especially those aged 50-59 years.
Disclosure of Interest: None declared

P1649 LOWER RISK OF HIGH-RISK ADENOMA (HRA) AND COLORECTAL CANCER (CRC) AMONG PATIENTS WITH A PREVIOUS NEGATIVE RESULT FROM A FECAL IMMUNOCHEMICAL TEST (FIT) FOR COLORECTAL CANCER. DATA ON SECOND ROUND SCREENING

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Introduction: Screening for colorectal cancer by FIT is based on consecutive rounds to detect precursor lesions or CRC in early stages. Data on consecutive rounds of FIT screening are limited and based mostly on small population studies.
Aims & Methods: We assessed the final data regarding positivity predictive values (PPVs) for high-risk adenomas (HRA), low-risk adenomas (LRA) and CRC among patients with a previous negative result from a FIT.
Methods: Data were collected from 2 rounds of FIT screening in average-risk persons (50 to 70 years old). The PPV for HRA and CRC were compared among the first-round (FR group) participants and second-round (SR group) participants with a previous negative FIT result. We also evaluated those patients participant in the second round not previously participants in first round (first screening in the second round) (FS group). Definitions: HRA: advanced adenoma or three or more adenoma
Results: The rate of positive results from FIT was significantly superior in the first vs. second round screening (6.2% vs. 4.7%, $p < 0.0001$) and very similar to the FS group (6.4%, $p < 0.32$, respect to FR). Data comparing all participants in the FR, SR and FS groups who tested FIT positive and were eligible for colonoscopy were compared (4182 vs. 2281 vs 1323 colonoscopy studies performed, respectively). A significant decrease in the PPV was observed for CRC between the FR and SR (6.3% to 3.3%; $p < 0.0001$) and similar to the FS group (6.3% to 6.7, $p < 0.65$, respect to FR). A significant decrease in the PPV for HRA were observed between FR vs SR (41.2% to 33.2%; $p < 0.0001$) but also respect to the FS group (36.0%, $p < 0.001$, respect to FR). There were no significant differences in stages (I + II vs. III + IV) of CRC detected in the three groups (31.4%, 30.6%, and 22.6, respectively for stage III + IV). Proximal location of colorectal adenocarcinoma was significantly diferent between three groups (18.6%, 29.7% and 27.0%, for FR, SR and FS groups, respectively, $p < 0.014$).
Conclusion: In our population-based CRC screening program the rate of positive results from FIT decrease after a first round, and PPVs of FIT for HRA and CRC are significantly lower among second-round participants who tested negative in the first round. No differences were observed in CRC stage but a significantly more proximally location of CRC on second round screening for CRC were observed.
Disclosure of Interest: None declared

P1650 METHYLATION ANALYSIS OF COLORECTAL PRECURSOR LESIONS WITH BRAF MUTATIONS AND THEIR NORMAL BACKGROUND MUCOSA

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Introduction: Sessile serrated adenomas (SSAs), which are characterized by their preferential locations in the proximal colon and frequent *BRAF* mutation, are thought to be precursor lesions of colorectal cancer with microsatellite instability (MSI) and CpG island methylator phenotype (CIMP), while other serrated lesions including traditional serrated adenomas (TSAs) also exhibit frequent *BRAF* mutation.
Aims & Methods: To clarify the molecular and clinicopathological characteristics of serrated lesions, we assessed DNA methylation of cancer-associated genes in a cohort of *BRAF*-mutant precancerous lesions including hyperplastic polyps, TSAs, and SSAs with or without dysplasia (n = 106) and adjacent normal colon tissues (n = 83) from 94 individuals.
Results: Prevalence of CIMP-positive lesions was significantly lower in sigmoid colon and rectum as compared to other bowel subsites including cecum, ascending, transverse and descending colon (sigmoid-descending colon junction was defined as a demarcation point). In addition, a number of cancer-associated genes showed higher methylation levels in the proximal colon lesions than in the distal colon ones when the sigmoid-descending colon junction was used as a boundary line. In contrast, no significant difference in the methylation levels was observed in the normal background colonic mucosa of the *BRAF*-mutant lesions along the bowel subsites.
Conclusion: Levels of DNA methylation in the *BRAF*-mutant colorectal lesions were strongly associated with their locations and histology, suggesting the presence of distinct carcinogenic pathways. In contrast, no significant difference of methylation in the normal background mucosa indicates the lack of epigenetic field defect (field cancerization).
Disclosure of Interest: None declared

P1651 MOLECULAR SUBTYPE OF COLORECTAL CANCER IN JAPANESE PATIENTS

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Introduction: Carcinogenesis of colorectal cancer has been studied in detail. As a result, it has come to be known that colorectal tumors had various genotypes. Recently, some groups have proposed molecular subtyping of colorectal cancer, however, there has not been established classification yet. Among molecular markers, microsatellite instability (MSI), CpG island methylator phenotype (CIMP), and KRAS/BRAF gene mutations are the most important markers. Here, we report a clinicopathologic features based on the molecular subtyping in Japanese colorectal cancer patients.
Aims & Methods: We consecutively selected 576 colorectal cancer patients who underwent surgical resection at the Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital from January 2008 to December 2010 after obtaining informed consent. Patients with inflammatory bowel disease or a known history of familial adenomatous polyposis and Lynch syndrome were excluded. If patient was resected two or more colorectal tumor, a tumor which was more advanced was selected for analysis.
According to Phipps et al. (*Gastroenterology* 2015), tumor samples were classified into 5 subtypes based on combinations of tumor markers: type 1 (MSI-H, CIMP-positive, positive for *BRAF* mutation, negative for *KRAS* mutation); type 2 (MSS or MSI-L, CIMP-positive, positive for *BRAF* mutation, negative for *KRAS* mutation); type 3 (MSS or MSI-L, non-CIMP, negative for *BRAF* mutation, positive for *KRAS* mutation); type 4 (MSS or MSI-L, non-CIMP, negative for mutations in *BRAF* and *KRAS*); and type 5 (MSI-H, non-CIMP, negative for mutations in *BRAF* and *KRAS*).
Results: Among the 576 colorectal cancer patients that we were able to obtain colorectal cancer and corresponding normal tissues during the study period, the distribution of the 5 types were 1.6% in type 1, 1.0% in type 2, 22.4% in type 3, 46.2% in type 4, and 3.0% in type 5, respectively. Median age were 71 in type 1, 76 in type 2, 68 in type 3, 67 in type 4, and 60 in type 5, respectively. Female were 75% in type 1, 66.7% in type 2, 47.6% in type 3, 39.4% in type 4, and 66.7% in type 5, respectively. In type 1 and type 2, all cases were colon cancer, and in type 3 and type 4, left-side cases were frequencies. While frequencies of poorly differentiated adenocarcinoma and mucinous carcinoma were high in type 1 and type 2, those were low in type 3 and type 4. 3-year survival rate were 71.4% in type1, 25.0% in type 2, 82.1% in type 3, 88.3% in type 4, 100% in type 5, respectively. Most of type 2 patients did not show chemotherapy response, and were poor prognosis.
Conclusion: Each colorectal cancer subtype demonstrated different clinicopathological features.

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P1652 OBESITY AND COLORECTAL ADENOMA: IS THE ASSOCIATION MEDIATED BY SPARC (OSTEONECTIN)?

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Introduction: Obesity is a risk factor for colorectal cancer and adenoma but the causal mechanisms have not been fully elucidated. SPARC is a matricellular protein with pleiotropic functions implicated in obesity related metabolic dysfunction. SPARC levels are increased in obesity and are predominantly secreted by adipose tissue in the obese. Its role in obesity-related colorectal carcinogenesis has not been studied.
Aims & Methods: We aim to determine whether the association between obesity and adenoma is related to SPARC levels.
A cross-sectional study was performed. Outpatients (45-70 years) undergoing colonoscopy were recruited in accordance with STROBE guidelines. Clinical, anthropometric data, physical activity levels and venous samples were obtained prior to colonoscopy. Serum SPARC levels were measured using ELISA-based assay (USCN Human Osteonectin Elisa Kit). Correlation analysis and multivariate logistic regression was used to quantify the association between SPARC and BMI, and SPARC and adenoma respectively.
Results: 124 subjects were studied (Table). SPARC levels were modestly correlated with BMI (correlation coefficient 0.31 [0.06-0.53]). SPARC levels were significantly associated with adenoma status (OR 1.84 [1.24-3.15], p = 0.0079) after correcting for potential confounders on multivariate logistic regression.

	Colonoscopy		
VARIABLE	Normal (CONTROL) (n = 94)	Adenoma (CASES) (n = 30)	TOTAL (n = 124)
Age, (yr)	0057.0 (10.0)	0060.0 (7.0)	0058.0 (10.5)
Male Gender, N (%)	47 (50.0)	18 (60.0)	65 (52.4)
Chinese race	0085 (90.4)	0028 (93.3)	0113 (91.1)
BMI	0023.4 (4.6)	0024.6 (5.9)	0023.7 (4.6)
Obese, N (%)	0015 (16.0)	0008 (26.7)	0023 (18.5)
Charlson comorbidity Index Category 0, N (%)	0076 (80.9)	0026 (86.7)	0102 (82.3)
Ever Smoker, N (%)	0012 (12.8)	0007 (23.3)	0019 (15.3)
High physical, N (%) activity	0047 (50.0)	0011 (36.7)	0058 (46.8)
SPARC Levels (ng/ml)	0125.6 (106.3)	0858.6 (1174.3)	0169.2 (864.9)

Conclusion: Serum SPARC levels are associated with colorectal adenoma after correction for confounders.
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P1653 CIRCULATING STEM AND PROGENITOR CELLS IN PATIENTS WITH BENIGN AND MALIGNANT COLORECTAL NEOPLASMS

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Introduction: Various populations of stem cells (SCs) have been the subject of intense research in translational oncology. The number of very small embryonic/epiblast like stem cells (VSEL-SCs - small $CXCR4^+CD34^+CD133^+$ population of Lin^-CD45^- cells) mobilized into peripheral blood (PB) increases in active inflammatory bowel disease (1) and in patients with pancreatic cancer (2). Higher numbers of circulating VSEL-SCs and mesenchymal stem cell (MSCs) were detected in pancreatic cancer patients. This trafficking of bone marrow stem cells (BMSCs) was associated with significantly elevated C5a and C5b-9/MAC levels together with sphingosine – 1 phospate (S1P) concentrations detected in plasma of cancer patients, and seemed to be executed in a SDF-1 independent manner.
Aims & Methods: We became interested if stem cells were also mobilized into peripheral blood in patients with colonic adenomas (CA) and colorectal cancer (CC). Therefore we recruited 19 patients with CA, 19 patients diagnosed with CC and 10 healthy individuals into this study. All patients underwent colonoscopy and were classified according to endoscopic, pathologic and clinical criteria. Peripheral blood samples were collected, and by employing fluorescence-activated cell sorting (FACS) the numbers of i) VSELs-SCs, ii) Mesenchymal SCs (MSC), iii) Endothelial Progenitor Cells (EPC) and iv) Hematopoietic SCs (HSC) were counted and/or isolated. Plasma levels of complement cleavage fragments, activation of coagulation and fibrinolysis, C-reactive protein as well as level of various chemokines were measured by ELISA: C5a, zonulin, plasmin-anti-plasmin (PAP) and thrombin-anti-thrombin (TAT), stromal derived factor - 1 (SDF-1), vascular endothelial growth factor (VEGF) and hepatocyte growth factor (HGF).
Results: In contrast to our previous data showing increase of circulating stem and progenitor cells including VSELs and MSCs, no increase in circulating stem and progenitor cells was found in patients with colorectal adenomas and cancer. While in our previous study mobilization of stem cells correlated with level of C5a, in patients with CC the level of C5a was low. Higher plasma levels of zonulin (marker of intestinal permeability) and HGF were observed in patients with cancer. No statistical difference was observed in PAP, TAT, SDF-1, VEGF and clonogenic assays in both groups of patients.
Conclusion: Mobilization of stem cells into peripheral blood depends on type of malignancy. Lack of mobilization of stem cells in patients with colorectal adenomas and cancer correlated with lack of activation of complement cascade. The role of intestinal permeability requires further investigation.

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P1654 TGF-B1 INDUCES RESISTANCE TO APOPTOSIS BY SUPPRESSING P53 EXPRESSION IN COLORECTAL CANCER CELLS LACKING FUNCTIONAL TYPE II TGF-B RECEPTOR

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Introduction: Transforming growth factor β (TGF-β) has paradoxical and context dependent effects on cell survival and proliferation. In normal tissues, TGF-β1 inhibits cell proliferation through binding to type II TGF-β receptor (TGF-βRII) and type I TGF-β receptor (TGF-βRI) and regulating cell cycle by induction of $p21^{Cip1}$. Conversely, in many advanced colorectal cancers, TGF-β1 is overexpressed and promotes migration and proliferation of tumor cells, although TGF-βRII/Smad signaling pathway is usually impaired due to the transcriptional repression or functional deficiency of TGF-βRII. The roles of TGF-β1 in TGF-βRII-dysfunctional colorectal cancer cells are still unknown.
Aims & Methods: We aimed to investigate the roles of TGF-β1 in TGF-βRII-dysfunctional colorectal cancer cells. We used human colorectal cancer cell lines; HCT116, Lovo and LS513, to investigate the ability of TGF-β1 to affect apoptosis and proliferation, and its association with TGF-β receptors. TGF-β1, TGF-βRII or TGF-βRI expression was knocked down by short interfering RNA, and p53 knockdown was performed by short hairpin RNA.
Results: Enzyme-linked immunosorbent assay revealed that TGF-β1 was generated in the supernatant of all cancer cells. Suppression of TGF-β1 in HCT116 (mutant TGF-βRII and wild type of TGF-βRI and p53) cells increased the expression of p53 and $p21^{Cip1}$, and reduced cell survival by increased apoptosis. In p53-deficient HCT116 cells, suppression of TGF-β1 did not affect cell survival. In Lovo (mutant TGF-βRII and wild type of TGF-βRI and p53, same as HCT116) cells, suppression of TGF-β1 also demonstrated the similar effects, whereas in LS513 (wild type of TGF-βRII, TGF-βRI and p53), it did not increase p53 expression. Stimulation with human recombinant TGF-β1 or neutralizing antibody against TGF-β1 did not cause Smad2-phosphorylation or the elevation of p53 expression in HCT116 cells. In LS513, recombinant TGF-β1 induced Smad2 phosphorylation and $p21^{Cip1}$ expression without p53 induction. Suppression of TGF-β1 did not induce significant p53 elevation in LS513 cells. However, suppression of TGF-β1 caused p53 elevation in TGF-βRII deficient LS513 cells. Moreover, suppression of TGF-β1 significantly increased the

expression of TGF-βRI in HCT116 cells. Addition of SB431542, a selective inhibitor of TGF-βRI, suppressed p53 elevation despite of TGF-β1 suppression. Consistently, suppression of TGF-βRI inhibited p53 elevation and cell apoptosis when expression of TGF-β1 was suppressed in HCT116.
Conclusion: These results indicate that in TGF-βRII-dysfunctional colorectal cancer cells, endogenous TGF-β1 has the potential to suppress p53 expression via reduced TGF-βRI expression, leading to resistance to apoptosis.
Disclosure of Interest: None declared

P1655 SURVEILLANCE COLONOSCOPY IN PATIENTS WITH SERRATED LESIONS AT BASELINE

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Introduction: Serrated lesions of the colon comprise of a group of heterogeneous lesions with distinct histological features. The large serrated polyps, in particular, are associated with advanced colonic neoplasia and possibly higher risk of colorectal cancer.[1,2] However, there is a paucity of data on the optimal surveillance interval for patients with different serrated lesions of the colon.
Aims & Methods: We aim to determine the polyp and adenoma detection rate on surveillance colonoscopy in patients with different serrated lesions.
We identified patients who were diagnosed to have serrated lesions during colonoscopy in our hospital between January 2008 and June 2011. Patients with concurrent or past history of colorectal cancer were excluded. Patients were categorized according to their baseline lesions: serrated adenoma (SA), large ($\geq$10mm) serrated polyps (LSP) and medium-sized (5-9mm) hyperplastic polyps (MHP) without concomitant or past history of adenoma. Patients with SA and LSP (SA + LSP group) were grouped together for analysis because of the small number of patients in these groups. The proportion of patients and the time to recurrent colonic polyps/adenoma on surveillance colonoscopy between the two groups (SA + LSP vs MHP) were compared.
Results: 98 patients (24 SA, 9 LSP and 65 MHP) were included for analysis. Surveillance colonoscopy was completed in 65 (66.4%) patients (20 SA, 7 LSP and 38 MHP) with a total of 75 colonoscopy performed. The median age of the patient in the SA + LSP group was significantly older than the MHP group (64.3 years, range 34-86 vs 55.8 years, range: 26-89; $p = 0.023$). The median time of surveillance colonoscopy was 40.7 and 44.3 months in SA + LSP group and MHP group respectively ($p = 0.332$). The proportions of patients with recurrent colonic polyps (including serrated lesions and adenoma) on surveillance colonoscopy were 63.0% and 36.8%, respectively (SA + LSP group vs MHP group) ($p = 0.038$). There was also a significant difference on the time to polyps recurrence between the two group, with a lower rate in the MHP group (Log Rank; $P = 0.006$). The adenoma detection rate on surveillance colonoscopy for SA + LSP group and MHP group were however comparable (29.6% and 28.9%; $p = 0.952$). Amongst those who have recurrent polyps, 41.2% and 35.7% of patients developed serrated lesions in SA + LSP group and MHP group respectively.
Conclusion: Patients with baseline SA and LSP have a significantly higher polyp recurrence rate on surveillance colonoscopy. However, the adenoma detection rate on surveillance colonoscopy was similar. These findings provide new data when deciding on the optimal screening interval for patients with different baseline serrated lesions.

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P1656 MECHANISM OF PROKINETICIN RECEPTOR 2 IN COLON CANCER

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Introduction: Prokineticin-1 (PROK1) is thought to be involved with cell invasion through the intermediary of prokineticin receptor 2 (PK-R2), that is one of the Prokineticin-1 receptors. We report a function via PROK1-PK-R2 signaling in vitro.
Aims & Methods: 1: Four colon cancer cell lines (DLD1, HCT116, SW620 and HT29) were analyzed for PROK1 and PK-R2 protein expressions. 2: Two colon cancer cell lines (DLD1 and HT116) stimulated with PROK1 protein, were observed for 24 hours using "Olympus Fluoview 10i-w", for the presence of change in cell movement. Furthermore, we measured the moving distance of five cells in non-stimulated group and PROK1 stimulated group, compared using the U test of Mann-Whitney. 3: The expression of PROK1 and PK-R2 protein was assessed in 325 colorectal cancer tissues by immunohistochemical staining using anti-PROK1 antibody and anti-PK-R2 antibody. We investigated the relation between PROK1 and PK-R2 expression and clinicopathological factor. The association of PROK1 and PK-R2 expression with serosal invasion, lymphatic invasion, venous invasion, lymph node metastasis, peritoneal metastasis, and hematogenous metastasis was assessed by cross-tabulation, and statistical significance was determined by the c^2 test. Life-table analysis was performed using Kaplan-Meier technique and outcomes from different groups of patients were compared by the log rank test.
Results: 1: The expression of PROK1 and PK-R2 protein was detected in four colon cancer cell lines. 2: The PROK1 stimulated group, compared to non-stimulated group is a highly deformation of cells, and observed increased motility. The average of the moving distance of the cells of DLD1 was 380.96 pixel in non-stimulated group, in PROK1 stimulated group was 581.50 pixel. The average of the moving distance of the cells of HCT116 was 286.29 pixel in non-stimulated group, in PROK1 stimulated group was 400.90 pixel. Both cell lines showed a significant extension of the moving distance of the cells in PROK1 stimulated group. 3: Group1, positive both PROK1 and PK-R2, was 117 cases. Group2, positive either PROK1 or PK-R2, but not both, was 109 cases. Group3, negative both PROK1 and PK-R2, was 99 cases. According to the clinicopathological examinations, the frequency of Group1 was significantly higher in cases with lymphatic invasion, venous invasion, lymph node metastasis and hematogenous metastasis. The prognosis for patients with Group1 were significantly worse than the other groups.
Conclusion: Colon cancer cell lines stimulated with PROK1 protein, showed enhancement of moving distance and deformation and motility of cells. Signaling cascade thought PROK1/PK-R2 was suggested likely to be involved in metastasis, especially cell invasion.
Disclosure of Interest: None declared

P1657 USE OF SOMATIC MUTATIONS IN BRAF AND KRAS AS MOLECULAR MARKERS OF RISK IN SERRATED POLYPS

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Introduction: Serrated polyps comprise a heterogeneous group of lesions. The reliable classification and their molecular profile are important to implement a surveillance and screening approach.
Aims & Methods: We aimed to study BRAF and KRAS mutations and CpG island methylator phenotype (CIMP) in the DNA of polyps in order to determine molecular and histological differences and the prognostic value of these markers in patients with serrated polyps. We performed a retrospective study with patients recruited between 2007and 2009 with at least one surveillance colonoscopy. A total of 994 polyps from 313 patients were collected for histological and molecular analysis. We analyzed KRAS and BRAF mutations in the DNA of all these polyps, and CIMP in 404 polyps from 103 patients. Mutation analysis for KRAS (codons 12 and 13) was performed by DNA sequencing and BRAF mutation (V600E) using allelic discrimination. CIMP was examined by MS-MLPA, considering CIMP-positive when 5 out of 8 markers were methylated.
Results: Adenomas were the main lesion (68%, n = 676), being 0.8% of them mutated for BRAF, 11% for KRAS and 1.1% CIMP-positive. A total of 318 (32%) polyps were classified as serrated lesions: 265 (83.3%) were hyperplastic polyps (HPs), 47 (14.8%) sessile serrated polyps (SSP) and 6 (1.9%) traditional serrated adenomas (TSA). Of the serrated polyps, 39.7% of them showed BRAF mutation, 20.3% KRAS mutation and 12.8% CIMP. Considering only serrated polyps, we found BRAF mutation in 39.4% of HPs and in 40.8% of SSP and KRAS mutations in 18.7% of HP and in 28.6% of SSP. There were no differences in the morphology, size and location of the serrated polyps depending on the BRAF mutational status, while KRAS mutation was predominantly present in rectum-sigmoid ($p = 0.014$). Serrated polyps were found in 104 patients at baseline colonoscopy. The mutational status of BRAF did not predict the finding of advanced adenomas or serrated lesions at follow-up. However the presence of somatic mutations in KRAS in serrated polyps at baseline predicts advanced lesions at follow-up. Patients with somatic BRAF mutation in polyps at baseline do not show a higher proportion of advanced adenomas or large (> 1cm) or proximal serrated polyps at follow-up (BRAF mutation: 34.5% vs no-BRAF mutation 45.9%; $p = 0.35$). Regarding KRAS, there is a higher proportion of advanced adenomas or advanced serrated polyps when serrated polyps at baseline showed KRAS mutation (60.9% vs 30.2%; $p = 0.016$).
Conclusion: We found a low frequency of somatic BRAF or KRAS mutations in serrated polyps. The presence of BRAF or KRAS mutation was not associated with location, size or histology in serrated polyps. Patients with KRAS mutations in serrated polyps show a higher risk of new advanced lesions in follow-up colonoscopies.
Disclosure of Interest: None declared

P1658 THE RELATIONSHIP BETWEEN PROXIMAL COLONIC DISTRIBUTIONS OF ADVANCED POLYPS AND THOSE OF INVASIVE CANCER

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Introduction: Colorectal polyps with advanced pathology (adenoma with high-grade dysplasia; HGD or intramucosal cancer) are considered to be precursor lesions developing into invasive cancer. In the present study we aimed to evaluate the relationship between the distributions of colorectal polyps with advanced patholgy and those of invasive cancers with a special attention to proximal location.
Aims & Methods: The study included 1064 patients (mean age 66.1+-10.2yr, M:F = 2.07:1) having colorectal polyps with advanced histology which were

colonoscopically resected in our hospital. The percentages of proximal location (proximal to the splenic flexure) of the lesions were assessed with regard to age (younger than 65 yr or 65 yr of age or older), gender (male or female), number (single or multiple), size (less or more than 10mm), shape (polypoid or non-polypoid), and histology (HGD or cancer). 629 patients with invasive colorectal cancer (mean age 70.4+-11.1yr, M:F = 1.41:1) resected by surgery were also investigated the percentages of proximal distribution with regard to age and gender.

Results: The percentages of proximal polyp location were 24.7% of 457 non-elderlys and 36.6% of 607 elderlys ($p < 0.001$), and 29.2% of 718 males and 36.1% of 346 females ($p < 0.05$), disclosing significant proximal shift of the lesions in older and female patients. 29.4% of 930 patients with single lesion and 46.3% of 134 with multiple lesions ($p < 0.005$), revealed proximal extension in those with multiple lesions compared to single lesion. 31.9% of 464 patients with small lesion and 31.2% of 600 with large lesion, demonstrating no difference in distribution according to size. The percentage of proximal location was significantly higher in 221 patients with non-polypid lesion than 843 with polypoid lesion (51.1% vs 26.3%) ($p < 0.0001$). In contrast it was significantly lower in 475 patients with intramucosal cancer than 589 with adenoma of HGD (24.6% vs 35.3%) ($p < 0.005$), disclosing negative association of proximal shift with pathological progress. The percentages of proximal invasive cancer location were 24.2% of 265 non-elderlys and 38.5% of 364 elderlys ($p < 0.001$), and 24.4% of 369 males and 43.8% of 260 females ($p < 0.0001$), respectively. Significant proximal shifts in older and female patients were also observed in those with invasive cancer similar to the patients having pathologically advanced polyps. The logistic regression analysis revealed that older age (OR 1.72; 95%CI, 1.25-2.38, $p < 0.001$), non-polypoid shape (OR 3.56; 95%CI 2.46-5.15, $p < 0.0001$) were independent risk factors of proximal shift in patients with advanced polyps, and older age (OR 1.88; 95%CI, 1.32-2.69, $p < 0.001$), female gender (OR 2.25; 95%CI 1.60-3.17, $p < 0.0001$) in those with invasive cancers.

Conclusion: Proximal shifts in older and female patients were observed in both of those with colorectal advanced polyps and those with invasive cancers. Among risk factors for proximal shift in patients having pathologically advanced polyps non-polypoid appearance was a most significant factor, although number, size, and pathological progress from HGD to cancer were not influencing factors for proximal shift.

Disclosure of Interest: None declared

P1659 THE GROWTH PATHWAY AND THE PATHOLOGICAL FEATURES OF DEPRESSED-TYPE COLORECTAL CARCINOMAS

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Introduction: Advanced colorectal carcinomas were conventionally considered to develop from sessile-type "polyps". And it has been maintained as the mainstream of development of cancers in colorectum.

But recently advances in endoscopic technology and diagnostic ability have revealed the existence of many depressed-type carcinomas, which have a growth pathway different from "*adenoma-carcinoma sequence*".

Aims & Methods: The aim is to clarify the pathological features of depressed-type colorectal carcinomas compared with flat- and sessile-type. A total of 23725 colorectal neoplasms excluding advanced carcinomas were resected endoscopically or surgically in our Center from April 2001 to November 2014. Of these, 961 lesions were T1 carcinomas. According to the morphological/development classification, 226 lesions (23.5%) were depressed-type, 325 lesions (33.8%) were flat-type and 409 lesions (42.6%) were sessile-type. We analyzed the pathological features of these lesions.

Results: The rate of submucosal invasion in all the lesions was 64.0% in depressed-type, 3.7% in flat-type and 3.0% in sessile-type. Within under 5mm in diameter, that was 11.3%, 0.02% and 0.05% respectively. In T1 carcinomas, the rate of lymphovascular permeation was 63.7% in depressed-type, 33.5% in flat-type and 38.6% in sessile-type, that of tumor budding was 68.1%, 45.8% and 52.6%, and that of poorly differentiated adenocarcinoma was 16.4%, 11.1% and 15.2% respectively. Within lesions smaller than 20mm in size, the rate of nodal metastasis was 10.3%, 2.9% and 7.6%, respectively. The rates of these pathological factors and nodal metastasis were significantly higher in the depressed-type lesions. On the other hand, the rate of adenomatous component was 6.6%, 44.0% and 51.1%, respectively. This was significantly lower in depressed-type lesions, suggesting that they emerge directly from the normal epithelium without going through the adenoma stage.

Conclusion: Growing downward even when they are small in size, depressed-type colorectal neoplasms hardly had adenomatous component and harbor higher risk of lymphovascular permeation, tumor budding and nodal metastasis. It suggests that they follow a growth "*De Novo* pathway", different from the "adenoma-carcinoma sequence." Therefore it is important to give a careful consideration to the development and progression of colorectal cancers.

Disclosure of Interest: None declared

P1660 CLINICAL OUTCOMES OF FOLLOW-UP COLONOSCOPIC SURVEILLANCE FOR PATIENTS WITH SESSILE SERRATED ADENOMAS

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Introduction: Sessile serrated adenomas (SSAs) are known to be precursors of colorectal cancer (CRC). The proper interval of follow-up colonoscopy for SSAs is still being debated.

Aims & Methods: The purpose of this study was to determine the proper interval of colonoscopic surveillance in patients with SSAs.

This study retrospectively reviewed the medical records of patients who diagnosed as SSAs at colonoscopy and received one or more follow-up colonoscopies. Clinicopathologic characteristics of SSAs detected at initial and follow-up colonoscopies were analyzed.

Results: From 2007 to 2011, 152 SSAs and 8 synchronous adenocarcinomas were identified in 138 patients. The mean age of patient was 56.4 years and 60% were male. SSAs were located in a right colon (proximal to the hepatic flexure) in 68.4%. In 8 synchronous adenocarcinomas, The T stage of 5 cases were pTis, and the others were more than pT1. 2 cases of cancer were treated with colectomy and the others were treated with snare polypectomy. At the first follow-up (the mean interval from initial colonoscopy: 20.2 months) 27 SSAs were identified in 138 patients. 66.7% of SSAs were located in a right colon. At the second follow-up (the mean interval from the first follow-up: 21.4 months), 6 SSAs were identified in 65 patients, 66.7% of SSAs were located in a right colon. At the third and fourth follow-up (the mean interval: 15.9 and 18.2 months), 21 and 11 of each patient received colonoscopy, and no SSAs were detected. The mean size of SSAs at initial, first and second follow-up endoscopy were 7.9 ± 5.1, 9.9 ± 5.6 and 8.5 ± 1.8mm, respectively. The difference of size was not statistically significant (ANOVA, *p-value*: 0.335). The size of SSAs detected with synchronous adenocarcinoma was 9.25 ± 8.75mm and the others were 8.13 ± 5.01mm. The difference of size was not statistically significant (t-test, *p-value*: 0.554). During follow-up colonoscopic surveillance, no cancer was detected.

Conclusion: Biennial colonoscopic surveillance might be enough to detect metachronous CRC in patients with SSAs. During follow-up colonoscopies in patients with SSAs, we should inspect right colon more carefully.

Disclosure of Interest: None declared

P1662 COLORECTAL SCREENING BY USING TOTAL COLONOSCOPY FOLLOWING FECAL IMMUNOCHEMICAL TESTS IN JAPANESE ALCOHOLIC MEN AND THE DETERMINANTS OF THEIR COLORECTAL NEOPLASIA

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Introduction: Alcohol consumption increases the risk of colorectal adenoma and cancer. The fecal immunochemical test (FIT) is a widespread screening method for colorectal neoplasia. However, appropriate screening methods for high-risk alcoholics have not been evaluated.

Aims & Methods: Total colonoscopic screening was performed in 1006 Japanese alcoholic men (462 FIT-positive and 544 FIT-negative). Advanced neoplasia was defined as neoplasia $\geq$10 mm, villous or tubulovillous adenoma, high-grade adenoma, or carcinoma.

Results: The detection rates of non-advanced adenoma, advanced neoplasia, and intramucosal or invasive carcinoma were 38.7%, 39.4%, and 9.7%, respectively, among the FIT-positive group, and 33.5%, 10.7%, and 2.2%, respectively, among the FIT-negative group. Advanced neoplasia, especially carcinoma, was much more frequently detected in the distal colon than in the proximal colon among the FIT-positive group. The multivariate odds ratios (ORs) (95% confidence interval) for non-advanced adenoma and advanced neoplasia were 2.81 (2.05-3.86) and 9.30 (6.29-13.76), respectively, for the FIT-positive group (vs. negative); 1.67 (1.39-2.01) and 1.82 (1.45-2.30), respectively, according to age (per +10 years); and 1.57 (1.08-2.28) and 1.86 (1.16-3.00), respectively, according to current smoking status (vs. non-smokers). The multivariate OR for advanced neoplasia was significant (1.61 [1.03-2.52]) according to the presence of a markedly enlarged mean corpuscular volume (MCV $\geq$ 106 fl vs. $<$106 fl). Genetic polymorphisms of alcohol dehydrogenase1B and aldehyde dehydrogenase-2 did not affect the risk of colorectal neoplasia.

Conclusion: In conclusion, the detection rate of advanced colorectal neoplasia was extremely high among FIT-positive alcoholics but was high even among FIT-negative alcoholics. An older age, smoking, and an enlarged MCV were predictors of the detection of advanced colorectal neoplasia.

Disclosure of Interest: None declared

P1663 ASSOCIATION BETWEEN COLORECTAL CANCER AND SOCS1 -1478CA/DEL GENE POLYMORPHISM

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Introduction: Suppressor of cytokine signaling 1 (SOCS1) is a prototype molecule of SOCS family. Alterations in SOCS1 expression have been reported in human cancers and there are some studies suggesting that SOCS1 might act as a tumor suppressor in carcinogenesis. In the present study, we aimed to evaluate the association of SOCS1 promoter -1478CA/del gene polymorphism detected in DNA isolated from tissues of patients with colorectal cancer (CRC) with histopathological characteristics and survival.

Aims & Methods: For the study, we retrospectively enrolled 53 patients with resected colon due to CRC and 23 control subjects with no systemic illness. SOCS1- 1478CA/del gene polymorphism was determined using Polymerase chain reaction -Restriction fragment length polymorphism (PCR-RFLP) methodology. These results were evaluated in relation to histopathological features and survival results and analyzed statistically. A p value equal to or less than 0.05 was considered significant.

Results: Neither control subjects nor CRC group showed a significant association with SOCS1 -1478CA/del gene polymorphism ($p = 0.248$). SOCS1 -1478CA/del gene polymorphism was not significantly associated with histopathological features either. However, in the overall survival (OS) analysis, those patients with del/del allele were found to have a 3.9-fold greater risk of mortality compared to those with CA/CA allele ($p = 0.05$). Progression-free survival (PFS) was also significantly different in such patients ($p = 0.05$).

Conclusion: The present study examining the association of SOCS1 -1478CA/del gene polymorphism with CRC showed that CRC patients with del/del allele had both significantly shorter PFS and OS versus those with CA/CA or CA/del allele.

Disclosure of Interest: None declared

P1664 WHY ARE WE MISSING SERRATED POLYPOSIS SYNDROME PATIENTS?

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Introduction: Serrated polyposis syndrome (SPS) is a new and under recognised colorectal cancer (CRC) predisposition syndrome. Previous studies reported miss-rates of SPS diagnosis varying from 40 to 82% (1,2). Since SPS patients and their first degree relatives have an increased risk of CRC, early recognition is important.

Aims & Methods: We aimed to determine the miss-rate of SPS during follow-up and determine reasons for missed diagnosis. We retrospectively identified patients diagnosed with ≥ 1 colorectal polyp or carcinoma detected at our center between 1986 and 2013 using the nation-wide pathology registry. A cumulative polyp count was scored for adenomatous and serrated polyps per patient. Size and location of serrated polyps were recorded to assess if patients fulfilled the WHO criteria for SPS (2010). Based on the available diagnosis in the patient files, miss-rate and 95% confidence interval (CI) were calculated.

Results: We randomly assessed 4500 patients of which 1804 (40.1%) had ≥ 1 serrated polyp. Nineteen patients fulfilled the WHO criteria with a median number of 24 serrated polyps (range 5-59) and 2 adenomas (range 0-21). In four patients no prior SPS diagnosis was made, leading to a miss-rate of 21.0% (95%CI 2.1-38.1). Duration of follow-up varied from 2 to 16 years in these missed cases. In three out of these four patients familial CRC was diagnosed instead of SPS. These patients were under strict follow-up with surveillance intervals ranging from 1 to 6 years. The diagnosis in the other patient was probably missed because the majority of serrated polyps had been removed before the formulation of the WHO criteria for SPS in 2000 and the pathology reports were not easily available. Of the patients diagnosed with SPS only one had a delay of 2 years before diagnosis, however, the surveillance interval (every 2 years) was adequate. A fifth patient fulfilling the SPS criteria was diagnosed with Lynch syndrome based on a MSH2 mutation, and as such was not marked as a missed case.

Conclusion: The miss-rate for diagnosis of SPS is significant, even during longer follow-up with repeated colonoscopies. Failure to recognize SPS was the result of not systematically applying the WHO criteria or the unavailability of older pathology reports to the clinician. Awareness of this CRC predisposition syndrome needs to be raised to lower the miss-rate of SPS.

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P1665 THE MANAGEMENT FOR COLORECTAL DIMINUTIVE ADENOMATOUS POLYPS USING PIT PATTERN CLASSIFICATION

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Introduction: It is now available to estimate histological feature of colorectal lesions using magnifying chromo-endoscopy (pit pattern (PIT) classification). In regard to diminutive (≦5mm) adenomatous polyps (DAPs), it has been reported that the prevalence of advanced histological features was low. However diminutive invasive cancer has been found. We basically permit to left untreat and follow up DAP with type IIIL PIT and resect ones with type IIIs, IV or V PIT in routine colonoscopy.

Aims & Methods: The aim of this retrospective study was to assess our management DAPs using PIT classification. The study subjects were patients over 30 years who were referred for initial total colonoscopy were followed up for more than 3 years between April 2001 and March 2014. Exclusion criteria was patients who had the lesions > 5mm in size and/or with type IIIs, IV, ? PIT left untreated at initial treatment, and those who have a history of familial adenomatous polyposis, Lynch syndrome, Advanced colorectal cancer, Inflammatory bowel disease and cololectomy.

They were classified into three groups according to the findings and treatment of initial colonoscopy: Group A, patients whose DAPs with type IIIL PIT were left untreated as semi-clean colon group.; Group B, patients whose all neoplastic polyps including DAPs were resected as clean colon group.; Group C, patients without any adenomatous polyp as internal control group. As a primary outcome measure, the cumulative incidence of index lesions (ILs) at follow-up colonoscopy analyzed among the three groups. The ILs diagnosed during follow-up colonoscopy was defined as follows: large adenomatous polyp ≧10 mm, high grade dysplasia (intra mucosal cancer), and invasive cancer. We evaluation the incidences of invasive cancers.

Results: A total of 4602 patients were enrolled in our study. 1439 patients classified into Group A, 1112 in Group B, 2051 in Group C. ILs were detected in 136 patients (9.4%) in Group A, 116 (10.4%) in Group B, and 40 (2.0%) in Group C, respectively. Invasive cancers were detected in 12 patients (0.8%) in Group A, 12 (1.1%) in Group B, and 9(0.4%) in Group C, respectively. There was no significant difference between Group A and Group B in incidences of ILs and invasive cancer. In regard to Group C, it was significant lower than Group B and Group C in incidences of them.

Conclusion: Removing DAPs with type IIIL PIT did not decrease an incidence of ILs and invasive cancers, significantly. DAPs with type IIIL PIT could be allow to left untreated and followed up.

Disclosure of Interest: None declared

P1666 TUMOR LOCATION IN COLORECTAL CANCER (CRC) DETECTED BY CRC SCREENING USING IMMUNOLOGICAL FECAL OCCULT BLOOD TEST (FIT) WITH TWO-DAY METHOD

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Introduction: According to the Japanese colorectal cancer (CRC) screening guideline, a 2 days stool sampling method by immunological fecal occult blood test (FIT) is widely accepted for over 40-year-old males and females. On the contrary, the role of flexible sigmoidoscopy in population-based screening has been recognized once again, based on the evidence that the UK Flexible Sigmoidoscopy Screening Trial recently provided high-level evidence that flexible sigmoidoscopy results in a substantial reduction in CRC mortality and incidence.

Aims & Methods: The purpose of this study was to investigate tumor location in colorectal cancer (CRC), which were detected by CRC screening using immunological fecal occult blood test (FIT). For 6 years (from April 2007 to March 2012), 719,079 participants, who were over 40-year-old, were screened for colorectal cancer with one of FITs, the OC-SENSOR (Eiken, Japan). A cut-off value of 100ng/mL was adopted.

Results: Colorectal cancer (CRC), which were detected by 2-day method with FIT, were 1,289 cases in number. The cancer detection rate was 0.0179%. Further examination revealed the proportion of CRC for R/C: 392(30.4%), S/C: 416(32.4%), D/C: 57(4.4%), T/C: 130(10.1%) and A + C/C: 294(22.8%).

Conclusion: Our results by 2-day method with FIT showed that over 1/3 of CRC might be missed on flexible sigmoidoscopy screening. We concluded that CRC screening using FIT with two-day method might be more adequate.

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Disclosure of Interest: None declared

P1667 STUDY ON THE CUT-OFF VALUE OF FIT SCREENING (2007-2012)

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Introduction: According to the Japanese colorectal cancer (CRC) screening guideline, a 2 days stool sampling method by immunological fecal occult blood test (FIT) is widely accepted for over 40-year-old males and females. It is demanded that CRC screening is carried out effectively, so one of the effective screening is to decide an appropriate cut-off value.

Aims & Methods: The aims of this study is to analyze the appropriate cut-off value. So the cut-off values were analyzed with positive rate, cancer detection rate, positive predictive value (PPV), invasive cancer detection rate and PPV of the invasive cancer for 719,075 (Males: 299,275 and Females: 419,804) CRC participants (2007-2012) with FIT-2days method. The cut-off value was analyzed in 100, 110, 120, 130, 140, 150, 200ng/mL. The comparative verification with the chi-squared test was used for reference to the cut-off value 100ng/mL.

Results: Positive rates fell significantly both males and females according to increasing cut-off values. Cancer detection rates also fell significantly over 150ng/mL for males and females (males: 0.255%–0.228% and females: 0.126%–0.110%). PPV rose significantly over 140ng/mL for females, and over 130ng/mL for males (males: 2.84%–3.22% and females: 2.10%–2.47%). Invasive cancer detection rates fell significantly at 200ng/mL just for females. PPV of the invasive cancer also rose significantly over 140ng/mL for females, over 130ng/mL for males (males: 1.43%–1.67% and females: 1.16%–1.42%).

Conclusion: As for the cancer detection rate for both males and females with the cut-off value 140ng/mL, there was no difference compared to the cut-off value 100ng/mL. In addition, PPV rose over cut-off value 130ng/mL in males, so we thought cut-off 130ng/mL was an appropriate value by this study. In this study, we targeted CRC examinee over 40 years old. Also we analyzed 50-74 years old, it became an equivalent result.

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P1668 SIMETHICONE TO IMPROVE BOWEL PREPARATION QUALITY DURING COLONOSCOPY WITH POLYETHYLENE GLYCOL PLUS ASCORBIC ACID: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Low-volume PEG-Asc has been proved to be similarly safe and effective as traditional 4 L PEG. However, PEG-Asc produce lots of bubble and endoscopists feel discomfort during colonoscopy. The study on adding antiforming agent such as simethicone with PEG-Asc methods are lacking.

Aims & Methods: The aim of this study was to compare PEG-Asc and PEG-Asc with simethicone in the aspect of bowel preparation quality and compliance of endoscopist. Single center, randomized, observer-blinded study was performed from July 2014 to September 2014. Total 200 out-patients were prospectively enrolled. We used the Boston Bowel Preparation Scale and Bubble score for evaluation of bowel cleansing. To investigate the compliance of endoscopists, a questionnaire for water shooting count and withdrawal time was performed. Also, patients completed questionnaires about the symptoms associated with the preparations to assess their tolerability before the colonoscopy.

Results: One hundred patients received PEG-Asc and 100 patients received PEG-Asc with simethicone. There were no significant differences between 2 groups in the aspect of completion of preparation, cecal intubation time, success rate and overall preparation quality. In consideration of better preparation quality, the PEG-Asc with simethicone group showed superior cleansing results over the PEG-Asc group (6-9 Boston scale score: 100% vs 84%, 3 bubble score: 95% vs 54%, $p < 0.05$). From the perspective of practitioners, PEG-Asc with simethicone group was less suffer from bubble which disturbed the lens. The mean count of water shooting for cleansing lens was significantly lower and withdrawal time of colonoscope was less in PEG-Asc with simethicone group compared to PEG-Asc group (1 vs. 10, 15.02 ± 10.10 vs. 17.83 ± 14.80min, $p < 0.05$). PEG-Asc with simethicone caused fewer gastrointestinal symptoms (ex. abdominal fullness, colicky pain, general discomfort) than PEG-Asc.

Conclusion: According to our data, PEG-Asc plus simethicone has comparably effective and better tolerable for patient and endoscopist. Therefore, a combination of PEG and simethicone appears to be a standard method for bowel preparation.

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P1669 RELATIONSHIP BETWEEN ONCO-RELATED MIRNAS AND COLORECTAL TUMORS

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Introduction: Accumulating data indicate that some microRNAs (miRNAs or miRs) function as tumor suppressors or oncogenes in cancer development. The certain miRNAs (miR-143, -145, -34a, -7) were differently expressed in the samples between the tumor and the paired non-tumorous samples in the same patient in colorectal tumors.

Aims & Methods: We examined the expression of these miRNAs in 131 sporadic exophytic adenomas or early cancers, 52 sporadic flat elevated adenomas or early cancers, and 77 type 2 cancer to clarify the relationship between the expression of the miRNAs and the endoscopic morphological appearance in the colorectal tumors. To validate the function of these miRNAs in cell growth, we used the endogenous or inhibitor miRNA for transfection of the human colon cancer DLD-1 cells.

Results: The expression levels of miR-143, -145, and -34a were significantly reduced in most of the exophytic tumors compared with those in the flat elevated ones. In type 2 cancers, the miRNA expression profile was very similar to that of the exophytic tumors. The expression levels of miR-7 were significantly up-regulated in some flat elevated adenomas compared with those in exophytic adenomas. The cell growth of DLD-1 cells was significantly inhibited in a dose-dependent manner at 48 h after the transfection with endogenous miR-143,-145, or -34a or inhibitor of miR-7.

Conclusion: These findings indicated that the expression of onco-related miRNA associated with the morphological appearance of colorectal tumors and miRNA may be a hopeful candidate as an RNA medicine for the treatment of colorectal tumors.

Disclosure of Interest: None declared

P1670 IMMUNOHISTOCHEMICAL ANALYSIS OF LYMPHOVASCULAR INVASION IN RECTAL NEUROENDOCRINE TUMORS COMPARED WITH HE STAIN

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Introduction: Rectal neuroendocrine tumors measuring ≤ 10 mm in diameter (RNETs ≤ 10 mm) rarely metastasize, thus those are usually treated by endoscopic resection (ER). Recently, lymphovascular invasion (LVI) has been considered to be an important predictor for nodal metastasis after ER [1,2]. However, little is known about the accurate detection rate of LVI in RNETs ≤ 10 mm evaluated by immunohistochemical analysis.

Aims & Methods: The aim of this study is to demonstrate the actual detection rate of LVI in RNETs ≤ 10 mm using D2-40 and Elastica van Gieson (EVG) stain. We retrospectively reviewed 100 consecutive RNETs ≤ 10 mm in 96 patients treated by ER between November 2000 and March 2015 at 5 hospitals in Japan. In addition to HE stain, lymphatic invasion was evaluated using D2-40 stain, and venous invasion was evaluated using EVG stain. The detection rate of LVI using D2-40 and EVG stain was compared with that using HE stain. We analyzed clinical outcomes in 75 patients who were followed for 24 months or more. The study protocol conformed to the ethical guidelines of the Helsinki Declaration, and our institutional review board approved the study.

Results: Of the 96 patients, the median age of patients was 61 years (range 27–84) with a preponderance of male ($n = 63$). Of the 100 RNETs ≤ 10 mm, 11 were located in the upper rectum and 89 were located in the lower rectum. The median tumor size was 5.0 mm (range 1.0–10.0). R0 resection was achieved in 71 lesions, Rx in 16, and R1 in 13. The median SM depth was 2000 μm (range 400–5500). In all the tumors, the mitotic count was very low, and grading was based on the Ki-67 index. 8 tumors demonstrated a Ki-67 index of 3%–4%; there were 92 Grade 1 RNETs and 8 Grade 2 RNETs. Using HE stain alone, we detected lymphatic invasion in 7.0% and venous invasion in 4.0% patients. Using D2-40 and EVG stain, lymphatic and venous invasion was detected in 19.0% and 47.0% patients, respectively. Finally, the detection rate of LVI using D2-40 and EVG stain was significantly increased compared with that using HE stain (56.0% vs. 9.0%). Among the tumor size $>$ 5mm vs. $\leqq$5mm, the rate of LVI with the size $>$ 5mm was significantly higher (71.4%) than that (47.7%) $\leqq$5mm. Among Grade 1 vs. Grade 2 RNETs, the rate of LVI was 57.6% (53/92) vs. 37.5% (3/8); there was no significant difference observed. During the

median follow-up period of 42 months (range 12.5-184.1 months), no metastasis or recurrence was detected. There were no deaths due to RNETs.
Conclusion: Compared with HE stain, D2-40 and EVG stain proved to significantly increase the detection rate of LVI in RNETs ≤ 10 mm. Therefore, the application of D2-40 and EVG stain is considered to be indispensable for RNETs ≤ 10 mm after ER. Further prospective studies are required to clarify the clinical role of LVI evaluated by D2-40 and EVG.

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Disclosure of Interest: None declared

P1671 INTENSIVE FOLLOW-UP AFTER CURATIVE SURGERY FOR COLORECTAL CANCER

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Introduction: The purpose of intensive postoperative surveillance programs after curative surgery for colorectal cancer (CRC) is to detect asymptomatic recurrences, with the premise that an important rate will be potentially eligible for curative resection, improving the survival. We have implemented a surveillance program for patients with CRC, AJCC stages II-III, after curative surgery, lasting five years, with periodic clinical assessment, carcinoembryonic antigen (CEA), cancer antigen 19-9 (CA19,9), computed thorax, abdomen and pelvis tomography (CT) and colonoscopy.
Aims & Methods: Primary outcome: rate of surgical treatment of recurrence with curative intent; secondary outcomes: colorectal cancer mortality, time to detection of recurrence, survival after treatment of recurrence with curative intent, clinical characteristics associated with unresectability of recurrence and diagnostic accuracy of the surveillance model. Cohort study, single center. All patients with CRC on the intensive surveillance program between 03/2008 and 01/2015, with at least one determination of any of the methods and a monitoring visit, were included. Statistical analysis was performed with SPSS v20.0, using chi-square test, a multivariate regression model and survival analysis with Kapplan-Meier log-rank test; p value < 0.05 was considered statistically significant.
Results: 404 patients were evaluated; 59.6% male; mean age = 65 ± 10 years; site of tumor: rectum: 50.7%, colon: 49.3%; AJCC classification: stage II: 43.8%, stage III: 56.2%; Average time of follow-up = 37 months (1-79). Recurrence rate: 12.9% (n = 52), mostly detected in the first 3 years (88.4%), due to elevation of tumor markers: 46.2%, CT: 40.4%, colonoscopy: 7.7%, symptoms: 5.8%; Site of recurrence: metastatic: 86.5%, locoregional: 13.5%; Twenty-one patients underwent curative resection. Clinical factors associated with unresectable recurrence were age > = 70 years (p = 0.022), and site of tumor-colon (p = 0.033). CA 19,9 elevation was the only altered surveillance test associated with unresectability (p = 0.024). After recurrence: average time of follow-up = 15 months (1-49), 2-year survival: 95.2% if curative surgery was performed *vs* 59.9% for unresectable recurrence (Kapplan-Meier log-rank, p = 0.016). Overall rate of cancer-specific mortality: 2.2% (n = 9). This surveillance model had good diagnostic accuracy for detection of recurrence (AUC 0.885).
Conclusion: The benefit of this intensive postoperative surveillance program is demonstrated by the number of patients undergoing curative surgery of recurrence (40.3%), with an impact on survival.
Disclosure of Interest: None declared

P1672 COLORECTAL CANCER STAGE IV AT DIAGNOSIS - THE LAST FRONTIER?

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Introduction: Surgical resection with curative intent in patients with metastatic colorectal cancer (mCRC) on diagnosis has impact on survival and should be offered whenever possible. However, preoperative predictors of survival are needed, to better select patients.
Aims & Methods: To evaluate the overall survival (OS) and the treatment morbidity/mortality and to determine possible predictors of surgical resection with curative intent in patients with mCCR on diagnosis. Retrospective, single-center study. Patients with mCRC on diagnosis, assessed in multidisciplinary group between 06/2008 and 12/2013, and whose treatment and follow-up occurred in the same institution were included. Statistical analysis was performed with SPSS v20.0, using chi-square test, T-student test, a multivariate regression model and survival analysis with Kapplan-Meier log-rank test; p value < 0.05 was considered statistically significant.
Results: 181 patients were evaluated, 56.4% male; mean age = 65 years (28-94); Charlson comorbidity Index = 8.78 ± 1.75; average CEA and CA 19.9 on diagnosis: 30.8ng/mL (1-20412) and 34.5ng/mL (1-1516684); site of tumor: colon: 57.5%, rectum: 42.5%. Stage: cM1a: 67.4%, cM1b: 32.6%. Metastatic site: liver: 55.7%, disseminated disease: 28.7%, lung: 7.2%, peritoneum: 5%, lymph nodes: 2.8%, other: 0.6%. Treatment: palliative chemotherapy (CT): 26%, palliative radiotherapy (RT): 5%, symptomatic therapy: 5.5%, palliative surgery +/- CT +/- RT: 38.1%, curative surgery +/- CT +/- RT: 25.4%; Treatment complications: 27.1%. Postoperative mortality: 4.6%. Global OS at 3 and 5 years: 26.4% and 10.7%. The OS at 3 and 5 years was significantly higher in the group of patients who underwent curative surgery: 68.4% and 32.5%, compared with the group of patients with unresectable disease: 10.7% and 2.7%, (Kapplan-Meier log-rank, p < 0.001). Average time of follow-up = 33 months (14-82). The clinical factors associated with unresectable disease were: CEA on diagnosis > = 5 (p < 0.001), age > = 70 years (p = 0.005) and M1b disease (p < 0.001).
Conclusion: This study demonstrates that, even in mCCR, surgical curative resection is associated with prolonged survival. Age > = 70 years and CEA > = 5 at diagnosis are possible predictors of poor prognosis and their prospective validation in a therapeutic decision model could help on the selection of surgical candidates.
Disclosure of Interest: None declared

P1673 ENDOSCOPIC MUCOSAL RESECTION WITH CAP IS SUPERIOR TO ENDOSCOPIC SUBMUCOSAL DISSECTION IN COMPLETE RESECTION OF RECTAL NEUROENDOCRINE TUMORS

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Introduction: Recently, rectal neuroendocrine tumors (NETs) are found more frequently on screening colonoscopy. Most of rectal NETs are located in deep mucosa and/or submucosa. Therefore, conventional endoscopic mucosal resection (EMR) has a likelihood of incomplete resection. There are several method of treatment for rectal NETs: conventional EMR, EMR with a cap (EMR-C), EMR with a ligation device (EMR-L), and endoscopic submucosal dissection (ESD). In this study, we compare the effectiveness of EMR-C and ESD in resection of rectal NETs.
Aims & Methods: 118 lesions of 114 patients with rectal NETs which was resected by EMR-C or ESD were included in this study. All patient received EMR-C or ESD at Pusan National University Yangsan Hospital between June 2009 and July 2014. Endoscopic complete resection rate, histologic complete resection rate, procedure time, and adverse events in the EMR-C (n = 63) and ESD (n = 50) groups were analyzed.
Results: Mean (standard deviation [SD]) tumor size was 4.60 (1.63) mm in the EMR-C group and 7.53 (3.04) mm in the ESD group (P < 0.001). Complete resection was performed in all group. Histologic complete resection rate of EMR-C group(92.1%) was significantly greater than that of ESD group (77.4%) (P = 0.041). Mean procedure time was longer in the ESD group (14.03 [7.21] min) than in the EMR-C group (3.81 [1.15] min) (P < 0.001). Histologic complete resection rate was similar in both tumor diameter ≤ 5 mm (EMR-C, 93%; ESD, 100%; P = 0.442)and in cases of 5 mm < tumor diameter ≤ 10 mm (EMR-C, 83%; ESD, 72.0%; P = 0.504).
Conclusion: EMR-C is simple, faster, and more effective in resction of rectal NETs, when compared with ESD, and may be preferable for resection of small rectal NETs.
Disclosure of Interest: None declared

P1674 ULTRAVIOLET-C ENHANCES CISPLATIN-INDUCED DOWNREGULATION OF RECEPTOR TYROSINE KINASES IN HUMAN COLON CANCER CELLS

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Introduction: Receptor downregulation is the most prominent regulatory system of receptor tyrosine kinase (RTK) signal attenuation and a critical target for therapy against colorectal cancer that are highly dependent on RTKs including epidermal growth factor (EGF) receptor (EGFR) and erbB2 (HER2). Platinum-containing anti-cancer drugs such as cisplatin are widely used for patients with various types of cancers. We have recently reported that ultraviolet-C (UV-C) irradiation induces the removal of EGFR from cell surface that can protect colon cancer cells from oncogenic stimulation of EGF, resulting in cell cycle arrest by desensitization of EGFR, which exerts oncogenic signaling in colorectal cancer.
Aims & Methods: In this study, we investigated the combination effect of low dose cisplatin and low dose UV-C on cell growth and apoptosis in several human colorectal cancer cells (SW480, DLD-1, HT29 and HCT116) using cell proliferation assay, BrdU incorporation assay, Western blot analysis and fluorescence microscopy study.
Results: The combination inhibited cell cycle and colony formation indicating the suppressive effect on cell proliferation, while either cisplatin or UV-C alone had little effect. We also observed that the combination induced apoptosis in these cells. To clarify its mechanism, we focused on receptor tyrosine kinases (RTK) and found that the combination caused the downregulation of EGFR as well as HER2. In fluorescence microscopy study and quantification analysis for cell surface EGFR, UV-C caused transient internalization of the EGFR but with time EGFR recycled back to the cell surface, while cisplatin did not affect its

localization. Moreover, the combination caused persistent internalization of the EGFR, indicating that cisplatin inhibits the recycling of the internalized EGFR induced by UV-C, which results in the lasting ubiquitination of the EGFR.
Conclusion: These results suggest that the combination use of cisplatin and UV-C synergistically leads anti-cancer effect by down-regulating RTK. Our present findings could provide evidence of a possible combination therapy against human colorectal cancer.

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P1675 CLINICOPATHOLOGICAL FEATURES AND LONG-TERM OUTCOME AFTER THE THOROUGH TREATMENT FOR RECTAL NEUROENDOCRINE TUMORS (R-NETS), ANALYSIS OF 304 CASES IN SINGLE CENTER

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Introduction: In clinicopathological characteristics for rectal neuroendocrine tumors (R-NETs), we have previously reported that venous invasion as well as tumor size and lymphatic invasion has indicated high malignant potential to metastasize to lymph node[1)]. The pathological assessment after initial resection and surveillance method is not established.
Aims & Methods: The purpose of this study is to revaluate the risk factors for lymph node metastasis including our up data, moreover to analysis long-term outcome after treatment go through our strategy. We investigated a total of 304 patients diagnosed R-NETs between January 1979 and May 2013 at cancer institute hospital. We used endoscopic ultrasonography (EUS) to measure tumor diameter and to estimate the depth of invasion. We pursued the initial therapeutic strategy according to clinical malignant potential, and we decided whether or not we achieved complete resection with investigating pathological features. We performed endoscopic treatment for patients with R-NETs based on the following criteria: tumor diameter less than 11 mm, no lymph node metastasis and no invasive lesion to muscularis propria determined by EUS, computed tomography (CT) or magnetic resonance imaging (MRI). If the case didn't meet these criteria, it underwent surgical treatment with radical lymph node dissection. Pathological malignant potential was evaluated especially with mitotic rate and MIB-1 index, lymphovascular invasion (lymphatic or venous invasion). We recommend annually check by colonoscopy and abdominal CT or abdominal ultrasonography to not only recurrence lesions also synchronized colorectal tumors, and we don't have period definition. We evaluated outcome of patients followed up by the above-mentioned strategy and surveillance.
Results: We evaluated 304 R-NETs that was excluded multiple type NETs. In 34 cases with more than 11mm in diameter, 19cases (55.9%) were found lymph node metastasis, the muscularis propria invasive lesion found it 9 of 12 cases (75%). In lymphovascular invasion (lymphatic or venous invasion) there were 20 of 8 cases (34%) found lymph node metastasis, it was significant high frequency. In the feature of central depression found it 7 of 37 cases (19%). There were 118 R-NETs those were identified and Grading, the cases of 113 were classified to Grade1 that lymph node metastasis was found in 9 (8%). In 5 cases were classified to Grade2, and found it was 1 case (20%). In median follow-up period was 60 months (range; 24 to 237) there were no patients with recurrence lesion with any examination after underwent our treatment strategy.
Conclusion: In our hospital, the treatment strategy of R-NETs is getting a good long-term outcome with being enforced of evaluating clinicopathological features. In surveillance method, because R-NETs is a slow growing tumor, we have to recommend maintain periodic examination as much as possible.

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P1676 A HUMANIZATION AND AFFINITY MATURATION OF AN ANTI-CD24 MONOCLONAL ANTIBODY TARGETING GASTROINTESTINAL CANCERS

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Introduction: Background: CD24 is a cell-surface heavily glycosylated GPI-anchored mucin-like protein. We have shown that CD24 is a valid target in gastrointestinal (GI) malignancies. Anti-CD24 mAb treatment induces a significant growth inhibition of CRC and PC cells, in a time- and dose-dependent manner *in vitro* and *in vivo* (*Gastro* 2006, *Clin Can Res* 2007, *Can Res* 2008). Affinity maturation is an important process in optimizing therapeutic antibodies. Affinity-matured antibodies can exhibit increased biological efficacy, and allow reduced dosage with less toxic side effects.
Aims & Methods
Aim: To develop mature humanized anti-CD24 monoclonal antibodies (mAbs) and to evaluate their efficacy alone and/or in combination with standard chemotherapy for CRC and PC.
Methods: Edman-degradation, cDNA synthesis, sequence and computational analysis (Ig-blast) were performed to reveal the entire DNA sequence of a murine anti-CD24 mAb (SWA11). Replacement of the Fc with the human IgG1 resulted in a mouse-human chimera. A human donor (Ig-blast) was chosen as a scaffold human Ab for grafting critical sequences of the murine antibody into it leading to the generation of humanized Ab derivatives. Sequence analysis of the CDR loops was the base for library designing. Affinity maturation was performed in two steps; CDR walking (two-step selection) and by using phage display technique
Results: *In vivo* antibody targeting and accumulation within a CD24 positive tumor and its excess clearance was clearly demonstrated using direct imaging. Combinatorial phage-displayed antibody libraries with varying degrees of diversity at randomized positions from which high-affinity antibodies can be selected were created. A chosen matured clone was isolated and showed higher binding strength ($1.8x10^{-8}$), compared to the parental murine and humanized Abs ($3.3x10^{-8}$ and $4.2x10^{-8}$). The matured antibody showed selective recognition and binding to the CD24 antigen, as demonstrated by antigen-based and whole-cell ELISA and FACS analysis. It stability was enhanced following the maturation process, as demonstrated by *in vitro* stability test. The antibody lost only 16% of its activity after 23 days in 37°C. Combined treatment with standard chemotherapeutic agents and natural products, such as monoterpenes (terpinen-4-ol), showed significant reduction in cell viability (90% cell death).
Conclusion: Targeting CD24 may be a promising treatment for GI malignancies in combination with chemotherapy and natural agents. The resulted matured fully humanized anti-CD24 mAb is more effective than the murine parental Ab.
Disclosure of Interest: None declared

P1677 COLORECTAL CANCER WITH SYNCHRONOUS UNRESECTABLE LIVER METASTASES. WHICH IS THE BEST TREATMENT?

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Introduction: The optimal treatment strategy of patients affected by colorectal cancer with unresectable liver metastases (mets) is at present undefined. There are 2 main therapeutic options:
1) surgical excision of the primary tumour followed by first line CT to downsize liver mets
2) first line-chemotherapy (CT) to stabilize/downsize the disease followed by removal of primary tumor and further post operative CT to downsize liver mets.
Aims & Methods: Aim of the study is to analyze the safety and effectiveness of the therapeutic strategies in a group of patients treated in one Institution.
A retrospective analysis of a prospectively collected database was conducted. All patients affected by colorectal cancer with synchronous unresectable liver mets treated between January 2003 and October 2012 in this Institution were included. Patients more than 80 years old, presenting peritoneal carcinosis or severe medical morbidities and a follow up shorter than 2 years were excluded. Primary endpoint was overall survival in both groups, estimated with Kaplan-Meyer methods; secondary endpoints were rate of liver mets resection after CT, influence of CT regimens and morbidity in both groups.
Results: 148 patients were included, with a median follow up of 45.5 months (range 24.4-126.1). Baseline characteristics were similar in both groups, even if patients older than 65 were more often operated on (60.3% vs 41.2%; $p = 0.01$), while patients with extrahepatic disease were more frequently treated with CT. 85 patients (57.4%), were treated with I line CT (Group 1), whereas 63 (42.6) with surgical excision of primary tumor (Group 2). In group 1, 34/85 patients underwent colorectal resection (6 in the emergency setting, 4 for occlusion and 2 for perforation during CT administration). 42/63 patients in group 2 were treated with CT after surgery of the primary tumor. Overall survival was not significantly different: 16.2% in Group 1 and 17.6% in Group 2 ($p = 0.174$), but statistical significance was reached comparing patients who underwent colorectal resection in both groups with who did not ($p = 0.025$) Rate of liver mets surgery was higher in Group 2: 19/63 (30.2%) vs 17/85 (20.0%) ($p = 0.056$). CT regimen were similar, but anti VEGF and EGFR monoclonal antibodies were more often used in Group 1 (53.8% vs 22.5% $p = 0.014$); CT regimen was more frequently stopped for progressive disease in Group 1 patients (53.8% vs 22.5% $p = 0.014$). Age, Grading, Lymph node ratio < 0.28, post surgical CT, CT suspension, liver mets surgery, and liver mets ablation were identified as prognostic factors at univariate analysis. Only age > 65 and lack of liver mets surgery were confirmed at multivariate analysis. Further multivariate analysis on operated patients in both groups (97 who underwent colorectal resection) and on patients treated with CT in both groups (127) revealed that post surgical CT, low lymph node ratio and age < 65 were predictive of better survival.
Conclusion: With the limits of a retrospective analysis the study shows that both treatment strategies are equally effective. Age > 65 and Lymph node ratio > 0.28 are predictive of worse outcome. Monoclonal antibodies are probably not so useful in this kind of patients.
Disclosure of Interest: None declared

P1678 TARGETED COLORECTAL CANCER SCREENING IN TYPE 2 DIABETES PATIENTS AND HIGH CARDIOVASCULAR RISK PATIENTS – FIRST INTERIM RESULTS OF CZECH MULTICENTER PROSPECTIVE STUDY

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Introduction: The Czech Republic belongs to the countries with the highest colorectal cancer (CRC) incidence all over the world. In several studies, metabolic syndrome (MS), especially diabetes mellitus type 2 (DM2) and ischemic heart disease (IHD), was found to be associated with development of colorectal neoplasia. There is absence of prospective studies focused on association between these metabolic diseases and colorectal neoplasia in the Czech population.

Aims & Methods: To investigate the prevalence of colorectal neoplasia (advanced adenomas and cancers) in individuals with high metabolic risk factors - DM2 and cardiovascular risk (SCORE > 10%). Prospective, multicenter study is planned to run since January 2013 until December 2015 with 2,000 individuals involved; 1,000 in the target group (metabolic risk) and 1,000 in the control group. All individuals (aged 45–75 years) from the screening population (asymptomatic, without family or personal history of colorectal neoplasia) have been examined by colonoscopy (possibly after positive FIT) at eight high quality colonoscopy centers. All participants underwent blood biochemical tests and filled the questionnaire regarding lifestyle. The interim data are presented, including both crude and adjusted (odds ratio, OR, by logistic regression, including age, sex and previous FIT+) comparisons.

Results: 1344 individuals have been examined until April 2015. Complete data have been recorded in 774 individuals; 433 men (56%) and 341 women (44%); mean age 60 years. There were 379 individuals (49%) enrolled in the target group and 395 (51%) in the control group. There has been higher prevalence of adenomas in the target group (47%; 95% CI 42-52%) in comparison to the control group (31%, 95% CI 27-36%), adjusted OR 1.36, p = 0.08. Similarly, the advanced adenomas prevalence was higher in the target group (18%; 95% CI 14-22%) than in the control group (8%; 95% CI 5-11%), adjusted OR 1.90, p = 0.01. There were no statistically significant differences found in cancer prevalence.

Conclusion: Metabolic risk factors (cardiovascular; diabetes mellitus type 2) are significantly associated with prevalence of advanced colorectal neoplasia in the Czech population. These results may help to identify the colorectal cancer high risk individuals and can be used in personalized CRC screening program modification.

Project was supported by the Czech Ministry of Health grant NT 13673.

Disclosure of Interest: None declared

P1679 COLORECTAL CANCER SCREENING IN THE CZECH REPUBLIC – IS THE TRANSITION TO POPULATION BASED PROGRAM EFFECTIVE?

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Introduction: The organized non-population-based National Colorectal Cancer (CRC) Screening Program in the Czech Republic has been running since year 2000. It was focused on asymptomatic individuals aged 50 years with no upper age limit. The target population coverage was continuously increasing and reached the level of 27% in year 2013. In 2014, the transition to population-based setting was realized by personalized mail invitations of program non-participants in specific age range. The preliminary data from the first round are presented.

Aims & Methods: To assess the increase of target population coverage, volume of preventive colonoscopies (FIT+colonoscopy and screening colonoscopy) and colorectal neoplasia detection after initiation of organized targeted invitation (comparison of years 2013 and 2014). All non-participants (no prior colonoscopy in last 5 years and no FOBT in last 3 years; no CRC previously diagnosed) from screening population (aged 50 – 70 years), were invited by mail to immunochemical fecal occult blood test (FIT) or screening colonoscopy. In case of FIT positivity, the colonoscopy was performed. The invitation was centrally organized, using the database of health insurance companies.

Results: In year 2014, there were 1,500,897 individuals (53% of all CRC screening target population) invited to FIT or colonoscopy, with 14% response. According to preliminary results, this resulted in coverage increase by 6 percent points in comparison with year 2013 (33% in year 2014). This has influenced the increase of number of detected adenomas (by 41%) and cancers (by 19%) detection in year 2014 (detailed results in the table) according to the Colonoscopy Registry.

	Year	Colonoscopy (numbers)	Adenomas (numbers)	%	Cancers (numbers)	%
FIT+ colonoscopy	2013	21,973	8,757	39.9%	817	3.7%
	2014	28,655	11,692	40.8%	950	3.3%
Screening colonoscopy	2013	4,965	1,361	27.4%	49	1.0%
	2014	9,258	2,596	28.0%	81	0.9%
All preventive colonoscopies	2013	26,938	10, 118	37.6%	866	3.2%
	2014	37,913	14,288	37.7%	1,031	2.7%

Conclusion: The transition to population-based Colorectal Cancer Screening Program in the Czech Republic was effective. It resulted in the improvement of target population participation followed by increase in colorectal neoplasia detection.

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Disclosure of Interest: None declared

P1680 LONG-TERM OUTCOMES AFTER ENDOSCOPIC RESECTION FOR SUBMUCOSAL INVASIVE COLORECTAL CARCINOMA

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Introduction: Endoscopic resection (ER) for early colorectal carcinoma has been recently performed more and more often. Only little, however, is known about the long-term outcomes after ER for submucosal (SM) invasive colorectal carcinoma.

Aims & Methods: The aim of this study was to evaluate long-term outcomes after ER for SM invasive colorectal carcinoma. We retrospectively analyzed all consecutive patients with SM colorectal carcinoma that underwent ER at NTT Medical Center Tokyo through January 2000 and December 2012. Our treatment strategy followed the Japanese Society for Cancer of the Colon and Rectum (JSCCR) guideline, in which cases meeting all the following conditions were recommended for ER, because they have a low risk for lymph node metastasis and local recurrence: (i) negative vertical margin, (ii) invasion depth of less than 1000μm, (iii) well and moderately differentiated adenocarcinoma, (iv) no lymphatic or vascular invasion, (v) budding grade 1. The patients were retrospectively divided into the following three groups: patients that underwent ER alone and met the guideline criteria (Group A), patients that underwent ER plus additional surgery because they did not meet the guideline criteria (Group B), and patients that underwent ER alone although they did not meet the guideline criteria (Group C). We collected data on patients' characteristics and pathological features of resected cancers, and investigated the clinical courses.

Results: ER was carried out for 217 SM colorectal carcinomas (134 males, 83 females, mean age 65.4yr). 142 cancers were located in the colon (right colon 68, left colon 74) and 75 were located in the rectum. Macroscopically 88 (41%) and 129 (59%) were protruded and laterally spreading tumors, respectively. Pathologically 136 (63%) and 81 (37%) were well and moderately differentiated adenocarcinomas, respectively. There were 86 cases (40%) in Group A, 108 (50%) in Group B, and 23 (10%) in Group C. The median follow-up periods in Group A, B, and C were 45.3, 47.3 and 58.3 months, respectively. In Group A, there was no case of recurrence during the follow-up period. In Group B, lymphatic metastasis was found in 9 cases (8.3%) at the time of additional surgical resection. The recurrence rate after the additional surgery was 0.9% (1/108). That case developed lymph node metastasis 11 month after ER, and then underwent additional salvage surgery. In Group C, the recurrence rate during the follow-up period was 13% (3/23; $P < 0.01$ compared with Group B). Two cases and one case presented with local recurrence and liver metastasis, respectively. In one local recurrence case, multiple lymph node and liver metastases also developed rapidly after the salvage surgery. Two cases of three died in the 20 and 57 month after the ER. In these two cases, the tumors were pathologically moderately differentiated adenocarcinoma at the time of ER.

Conclusion: Our results suggest that the criteria for additional treatment after ER presented in JSCCR guideline are appropriate. Once tumor recurrence occurs, it is often very difficult to control disease progress. Therefore, in patients failing to meet the guideline criteria, we recommend additional surgery as far as possible, because of the high rate of recurrence.

Disclosure of Interest: None declared

P1681 IMPACT OF INDIVIDUALIZED CHEMOTHERAPY FOR ADVANCED COLORECTAL CANCER (CRC) BASED ON COLLAGEN GEL DROPLET-EMBEDDED DRUG SENSITIVITY TEST (CD-DST)

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Introduction: The leucovorin (FOL) and fluorouracil (5-FU) plus oxaliplatin (*l*-OHP; FOLFOX) or FOL and 5-FU plus irinotecan (SN-38; FOLFIRI) are widely used as first-line chemotherapy in the treatment of advanced colorectal cancer (CRC). However, second-line chemotherapy must be abandoned in certain cases due to disease progression, adverse effects or high medical cost in clinical setting. Therefore, the most effective regimen should be selected as first-line chemotherapy. We reported that individualization of first line treatment was possible using the collagen gel droplet-embedded culture drug sensitivity test (CD-DST) (UEGW 2014 P1538).

Aims & Methods: In this prospective study, we explored the overall survival (OS) of the CRC patients treated with individualized first-line chemotherapy based on CD-DST. Between Mar. 2008 and Mar. 2015, we obtained tumor specimens from 108 CRC patients without preoperative chemotherapy. CD-DST was performed and the growth inhibition rate (IR) was determined by incubation for 24 h with 5-FU and *l*-OHP (6.0 and 3.0 μg/ml, respectively) and 5-FU and SN-38 (6.0 and 0.2 μg/ml, respectively). The cumulative distribution of IR values under each condition was evaluated on the basis that the clinical response to FOLFOX and FOLFIRI is equivalent (approximately 50%). [1] All patients were divided into 4 cohorts: FOLFOX and FOLFIRI responders (super responders), FOLFOX responders, FOLFIRI responders, and poor responders. [2] From the point of view that there is no choice other than FOLFOX or FOLFIRI in clinical setting, all patients were divided into 3 cohorts: FOLFOX recommended, FOLFIRI recommended, and both regimens recommended. First-line regimens were selected by the attending physician. OS of the treated CRC patients were evaluated Kaplan-Meier method.

Results: There were 35 patients with unresectable CRC with chemotherapy. [1] In 4 cohorts, the median survival time (MST) of super responders (n18) and poor responders (n13) was 1,128 and 810 days, respectively. [2] In 3 cohorts, FOLFOX was recommended, FOLFIRI was recommended, and both regimens were recommended in 19, 15, and 1 patients, respectively. In first-line treatment, the MST was 960 days in 24 patients with recommended regimen and 430 days in 11patients without recommended regimen ($p = 0.054$). For poor responders, the corresponding MST values were 810 and 244 days ($p = 0.014$).

Conclusion: Individualized first-line therapy with the CD-DST may improve the prognosis of patients with unresectable CRC, especially in poor responders.

Reference

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P1682 CLINICAL, HISTOLOGICAL AND MOLECULAR RISK FACTORS FOR CANCER RECURRENCE IN PATIENTS WITH STAGE II COLON CANCER

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Introduction: The assessment of risk factors of cancer recurrence in patients with stage II colon cancer (CC) is crucial for identifying the patients at higher risk of recurrence who are likely to benefit from adjuvant chemotherapy. Although some of these factors have been proposed, the data are controversial and there is still need for new and more reliable predictive factors. Our aim was to study the clinical, histological and molecular features associated with 3-year disease-free survival (DFS) in a series of consecutive patients with stage II CC treated in three regional digestive oncology centers.

Aims & Methods: Clinical and histological data of all patients after curative surgery for stage II CC, treated in three institutions from 2001 until 2009, for whom at least 3-year follow-up data were available, were collected retrospectively. Additionally, histological samples were obtained and prospectively tested for microsatellite instability using fluorescent PCR amplification. Cox proportional hazards regression models were used to compute p values, hazard ratios (HRs), and 95% confidence intervals (CIs).

Results: Among 195 patients studied (median age 76 years, range 23-97 years, men 55%), 37 (18.9%) received adjuvant chemotherapy. Twenty-two patients (11%) had disease recurrence during the 3-year period following diagnosis. No significant association was found between the risk of recurrence and age, sex, degree of tumor differentiation, the presence of venous, lymphatic or perineural invasion at histology, adjuvant chemotherapy or the MSS status. On univariate analysis, obstruction or tumor perforation at diagnosis, T4 tumor status and low (<12) number of lymph nodes examined were clinically significant risk factor for recurrence, while anemia and right colon localization were associated with a lower risk of recurrence. On multivariate analysis, only low number of lymph nodes (HR = 3.81 {95% CI: 1.19-12.19}, $p = 0.02$) and T4 status (HR = 5.49, {95% CI: 1.06-28.43}, $p = 0.04$) were significantly associated with a higher risk of 3-year recurrence.

Conclusion: In our study, only T4 status and low number of lymph nodes were independent prognostic factors for 3-year DFS. In consequence, these patients should be considered for adjuvant chemotherapy.

Disclosure of Interest: None declared

P1683 LONG-TERM OUTCOMES AND PROGNOSTIC FACTORS OF RECURRENCE IN T1 COLORECTAL CARCINOMAS

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Introduction: Although the recurrence of T1 colorectal cancers is relatively rare, some cases do develop even after surgery. However, their prognostic factors remain obscure, and there is little evidence regarding long-term outcomes.

Aims & Methods: Our aim is to clarify the prognostic factors for recurrence of T1 colorectal carcinomas, reviewing their long-term outcomes. We analyzed the associations between recurrence and various clinicopathological features (age, gender, tumor size, location, morphology, degree and depth of submucosal invasion, lymphatic infiltration, vascular infiltration, tumor budding, histologic type, and lymph node metastasis) in 792 patients with T1 colorectal carcinomas resected at our unit from April 2001 to December 2012. Patients were followed up until December 2014 over a median follow-up period of 51.4 months. Of these, 544 lesions were resected surgically including additional colectomy after endoscopic resection, and 168 lesions were endoscopic resections only. Cox regression analysis was used to calculate hazard ratios for recurrence or distant metastasis.

Results: One case developed local recurrence in 69.4 months after endoscopic resection. Distant recurrences were found in eight cases, of which five cases were after surgical resections and three cases were after endoscopic resections. Of the nine lesions in total, five cases were rectal carcinomas, and four cases were depressed type of the lesion. As for pathological factors, all cases were submucosal massively invasive carcinoma. Five cases had lymphatic infiltration, and four cases had vascular infiltration. Three cases had poorly differentiated carcinomas. Only the attribution of rectum was revealed to be a significant prognostic factor of recurrence in Cox regression analysis ($p = 0.036$, HR = 4.54).

Conclusion: Even after surgical resections, some lesions develop recurrences. More careful surveillance is recommended, especially for rectal carcinomas.

Disclosure of Interest: None declared

P1684 ALTERED LEVELS OF CORTISOL IN HAIR IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Stress is considered an important component in the pathophysiology of Irritable Bowel Syndrome (IBS). Long term Hypothalamus Pituitary Adrenal (HPA)-axis activity can be studied by measuring cortisol in hair.

Aims & Methods: We investigated whether hair cortisol concentrations (HCC:s) and self-reported stress differentiate IBS patients from non-IBS controls by means of a case control study. Subjects aged 18-65 years, with a known IBS diagnosis and active symptoms, identified in the patient medical register of 10 selected Swedish primary health care centres (PHCs), were invited. The control group comprised other patients at these PHCs, with a similar age and sex distribution, who had sought care for other complaints not associated with gastrointestinal (GI) symptoms and with no earlier GI diagnoses. Hair samples were collected from 381 IBS-patients and 450 non-IBS controls. HCCs were measured using a competitive radioimmunoassay. Questionnaires including self-reported perceived stress (PSS) and Rome III criteria were completed by 296 IBS patients and 375 non-IBS controls. We had access to all participants' medical records and the material was checked thoroughly in both groups. Due to non-completions of questionnaire, steroid treatment, IBS diagnoses in the controls, other GI diagnoses, two old age and one patient's will to drop-out, 169 Rome III-fulfilling IBS patients and 316 patients without gastrointestinal complaints were available for analysis. Due to non-normal distributions, HCCs were log transformed before statistical analysis and also divided into quintiles. Multiple regression analyses were used to adjust for potential confounders among relevant background variables.

Results: IBS patients had significantly ($p = 0.022$) lower HCCs (median = 16.3 pg/mg, IQR = 26.9 pg/mg) compared to controls (median = 22.8 pg/mg, IQR = 29.1 pg/mg). There was also a significant difference ($p = 0.001$) in the distribution of cortisol quintiles between IBS- and non-IBS-patients. The highest proportion of IBS patients (30.2%) were found in the lowest cortisol quintile. The opposite was seen in non-IBS patients, where the smallest proportion (14.2%) was found in the lowest quintile. PSS was higher among IBS-patients with a mean (SD) total score of 25.3 (SD = 8.0) compared to the non-IBS patients 21.4, (SD = 7.5) ($p < 0.0001$). After taking other factors into considerations in multiple regression models of HCCs and PSS, only quintiles of HCCs stayed significantly related to IBS ($p < 0.005$). There was a weak negative correlation between HCCs and PSS in the study group as a whole ($r = -0.109$, $p = 0.019$).

Conclusion: IBS patients had lower HCCs than non-IBS patients and IBS patients were over-represented in the lowest quintile of cortisol. These results could indicate a possible suppression of the HPA-axis activity in a considerable proportion of IBS patients. Self-reported stress was higher in IBS-patients compared to non-IBS patients, but the correlation between HCC and PSS was poor, indicating that they in fact reflect different aspects of stress in IBS.

Disclosure of Interest: None declared

P1685 INHIBITION OF DEFECATORY URGE PROVOKED BY RECTAL BALLOON DISTENSION FACILITATES COGNITIVE CONTROL IN HEALTHY VOLUNTEERS

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Introduction: A recent study (Tuk et al 2011) showed that as the bladder fills people increasingly inhibit their motor impulse to void, and that this is associated with improved performance on cognitive control tasks requiring inhibition of automatic responses.
Aims & Methods
Aims: To investigate the effect of defecatory urge provoked by rectal distension on cognitive control in healthy subjects.
Methods: Twenty-two healthy volunteers were intubated with a rectal balloon. After a 15-min adaptation period, a stepwise (4mmHg/30sec) isobaric distension procedure was performed using a barostat. Perceived intensity of urge to defecate was rated on a visual analogue scale (VAS) after 15sec in each distension step. Moderate and severe urge thresholds were derived for each subject to define 3 "urge conditions": no urge (balloon deflated), moderate urge (VAS $\geq$ 41), and severe urge (VAS $\geq$ 81). Next, during each of the 3 urge conditions (in counterbalanced order), subjects performed the Stroop task as a measure of cognitive control. This task includes 3 types of stimuli, incongruent color naming (color words written in font of a different color), congruent color naming (color words written in font of the same color), or "word naming" stimuli (color words written in black), presented 10 times each during each urge condition. In response to the stimuli, subjects needed to press one of 3 keys with colors corresponding to the color of the font (in both color naming trials) or the meaning of the color word (in word naming trials) as quickly as possible. Linear mixed models [3 (urge condition) x 3 (Stroop stimulus) within-subject 2-way ANOVA] were used to analyze reaction times (RT). The urge condition*Stroop stimulus interaction effect was the effect of interest, followed by planned comparisons of the difference in RT between incongruent color naming (task requiring cognitive control over an automatic response) on one hand and congruent color naming and word naming (automatic response tasks) on the other, between Stroop conditions. A larger difference in the no urge compared to the other two conditions would confirm our hypothesis of increased cognitive control during inhibition of defecatory urge.
Results: The difference in RT between incongruent color naming and word naming in the no urge condition (85 $\pm$ 29 msec) was higher than in the moderate (-6 $\pm$ 30) and severe (-7 $\pm$ 35) urge conditions (both $p < .002$). The difference between incongruent color naming and congruent color naming trials in the no urge condition (181 $\pm$ 35 msec) was also numerically higher compared to both the medium (141 $\pm$ 36) and high (158 $\pm$ 42) urge conditions, but these differences were not significant ($p = .23$ & .50, respectively).
Conclusion: In line with earlier findings on voiding urge, inhibition of defecatory urge provoked by rectal balloon distension facilitates cognitive control in healthy volunteers. This may be explained by "spillover" of inhibitory processes from one domain to the other due to a common neural mechanism underlying inhibitory processes. Further, these findings provide proof of concept for an influence of gut-brain signals on cognitive processes, which may be relevant for Irritable Bowel Syndrome.
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P1686 PREVENTION OF INTESTINAL HYPERPERMEABILITY BY PROTEASOME TARGETING IN STRESS-INDUCED AND POST-INFLAMMATORY MICE MODELS OF IRRITABLE BOWEL SYNDROME

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Introduction: An impaired gut barrier leading to visceral hypersensitivity and immune disorders have been described in irritable bowel syndrome (IBS). The ubiquitin-proteasome system (UPS) could be involved in the alteration of the colonic barrier observed in IBS via the degradation of tight junction proteins. We aimed to investigate the role of UPS in gut barrier regulation in two mice models mimicking IBS: the water avoidance stress model (WAS) and a post-inflammatory model (post-TNBS).
Aims & Methods: Both models were performed in C57BL/6 male mice (n = 8-10/group); WAS model was induced by placing mice on a small platform in a tank of water during 1 hour per day during 10 consecutive days. Control mice were placed on the same platform without water. Post-inflammatory model was obtained with an intra-colonic instillation of TNBS (0.5mg) at day 1, before a 28-day follow-up. Colonic permeability, inflammatory response and UPS activities and composition were measured. In additional experiments, mice received injections of a selective proteasome inhibitor (PR-957) or we used knock-out mice for β2i proteasome subunit.
Results: In WAS mice, a significant increase of fecal pellet output (1.5 fold change, $p < 0.05$), of mucosal pro-inflammatory cytokine (IL-1β, TNFa and CXCL-1) mRNA levels and of myeloperoxidase (MPO) activity was found. Colonic permeability also increased (1.5 fold change, $p < 0.05$) while expression of tight junction proteins, occludin and ZO-1, was reduced. While pro-inflammatory cytokine mRNA levels were restored to control levels at day 28 in post-TNBS mice, colonic permeability remained higher (3 fold change, $p < 0.05$) with a significant decrease in claudin-1 expression. In both models (WAS at day 10, post-TNBS at day 28), we observed an increase of proteasome trypsin-like activity and of inducible β2/constitutive β2 subunit expression ratio (1.5 and 3 fold change in WAS and post-TNBS mice, respectively, both $p < 0.05$). Moreover, intestinal hyperpermeability was blunted by i.p. injection of selective proteasome inhibitor (PR-957) in post-TNBS and WAS mice and knock-out mice for β2i subunit exhibited a significant decrease in intestinal permeability and fecal pellet output during WAS.
Conclusion: In conclusion, proteasome system is altered in the colonic mucosa of IBS mice models with an increased trypsin-like activity. Intestinal hyperpermeability was prevented by inhibition of proteasome or deletion of β2i subunit in mice suggesting that UPS may be involved in the occurrence of IBS symptoms.
Disclosure of Interest: None declared

P1687 ADENOSINE RECEPTORS IN INFLAMMATION ON RAT COLON PREPARATIONS. ARE THEY INVOLVED IN THE ANTI-INFLAMMATORY ACTION OF STW 5?

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Introduction: The purine nucleoside adenosine, which is involved in a variety of physiological functions, regulates immune and inflammatory responses and acts as a modulator of gut functions. Although it is present at low concentrations in the extracellular space, stressful conditions, such as inflammation, can markedly increase its extracellular level up to micromolar range. By activation of different receptor subtypes adenosine is able to induce anti-inflammatory or pro-inflammatory impacts. The current study examined the impact of adenosine A2A receptors (A2AR) and adenosine A2B receptors (A2BR) to regulate contractility in untreated and inflamed rat colon preparations using a specific A2AR agonist (CGS 21680) and an A2BR antagonist (PSB-1115) on acute inflammation in rat colon preparations. Further it focused on interactions of the multi-herbal drug STW 5 with A2AR as a possible mechanism of the protective effect of STW 5 in gastrointestinal disorders.
Aims & Methods: Inflammation was induced by intraluminal instillation of 2,4,6-trinitrobenzene sulfonic acid (TNBS). Contractions were measured isometrically in an organ bath set up. Gene expression was determined using RT-PCR. Radio ligand binding assays (competition experiments) were carried out with rat brain homogenates. Morphological changes were estimated after van Gieson staining.
Results: All four adenosine receptor subtypes were expressed in untreated colon preparations. Activation of A1, A2B, and A3 receptor with specific agonists reduced the acetylcholine (ACh, 10μM)-induced contractions, while activation of A2BR enhanced it. After incubation with TNBS morphological damages in colonic mucosa and muscle walls were detectable followed by reduced ACh-contractions. The TNBS-mediated decrease of ACh-contractions as well as the morphological damages were partially normalized by co-incubation of TNBS with CGS 21680 (10μM) or with PSB 1115 (100μM). The same effects with smaller intensity were found for STW 5 (512 μg/ml) in female but not in male colon preparations. These results are in accordance with ligand binding studies indicating that STW 5 interact with the A2AR.
Conclusion: Anti-inflammatory mechanisms and cell protective actions of STW 5 are partly due to the interaction with adenosine receptors. The results give a clear-cut correlation with symptom improvements in clinical trials and therby highlight the relevance of STW 5 as a therapeutic approach in IBS.
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P1688 THE EFFECT OF GI-SPECIFIC ANXIETY AND ABUSE ON VISCERAL SENSITIVITY IN IRRITABLE BOWEL SYNDROME IS MEDIATED THROUGH SOMATIZATION

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Introduction: Psychosocial factors are associated with visceral sensitivity in FD, but in IBS evidence is limited.
Aims & Methods: We aimed to study associations between psychosocial factors and visceral sensitivity parameters in IBS. Two IBS cohorts underwent rectal barostat testing and completed questionnaires on anxiety & depression, GI-specific anxiety, somatization, and abuse history. Cohort 1 (n = 124, Rome II) underwent an ascending method of limits (AML) paradigm returning to operating pressure (OP) between distensions to measure pain threshold and pain referral area. Cohort 2 (n = 127, Rome III criteria) underwent an AML protocol

without returning to OP, random phasic distensions with pain intensity ratings, and assessment of pain ratings during 4h following a 25g lactulose challenge test.

Results: Parameters significantly associated with visceral sensory measures in bivariate analysis were included in 3-step general linear models. The 3 steps and the results are shown in Table 1.

		Step 1 Demographics & Abuse	Step 2 +Anxiety & Depression	Step 3 +Somatization
COHORT 1				
Pain threshold	*Age*	0.007	0.01	0.01
	Female gender			0.04
	Sexual abuse adult	0.001	0.007	0.007
Somatization			0.02	
Pain referral area	*Age*		0.05	0.05
	GI-specific anxiety		0.03	0.2
Somatization			0.04	
COHORT 2				
Pain threshold	*Age*	0.0001	0.002	0.002
	Sexual abuse adult	0.04	0.04	0.05
Somatization			0.5	
Pain intensity ratings (36 mmHg rectal distension)	*Female gender*	0.01	0.007	0.1
	Depression		0.04	0.2
Somatization			0.03	
Lactulose provoced pain	*Female gender*	0.005	0.008	0.3
	Physical abuse child	0.05	0.06	0.3
	GI-specific anxiety		0.03	0.2
Somatization			0.0004	

The effects of GI-specific anxiety on pain referral area (Co.1), the effect of depression on pain intensity ratings and the effects of female gender, childhood physical abuse and GI-specific anxiety on lactulose-provoked pain (Co.2) were mediated through somatization.

Conclusion: Somatization either has an independent effect on visceral sensitivity parameters, or mediates the association between psychosocial factors and these parameters.

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P1689 PSYCHOSOCIAL FACTORS ARE ASSOCIATED WITH INCREASED SYMPTOM RESPONSE TO A LACTULOSE CHALLENGE TEST IN IBS

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Introduction: Irritable Bowel Syndrome (IBS) is associated with an increased postprandial symptom response to a 25g lactulose challenge test compared to healthy controls (Le Nevé et al, AJG 2013). Psychosocial morbidity is associated with having a diagnosis of IBS and with increased symptom severity in IBS patients.

Aims & Methods: Our aim was to investigate the relationship between psychosocial status and the time course of the postprandial symptom response to this test. 204 IBS patients (Rome III) consumed a 400-ml liquid breakfast (Nutridrink, 1.5 kcal/ml, 16% proteins, 49% carbohydrates, 35% fat, gluten free, lactose <0.025 g/100 ml) combined with 25g of lactulose after an overnight fast. They completed visual analogue scales (0-20) assessing severity of five gastrointestinal (GI) symptoms (abdominal pain, bloating, nausea, gas, urgency) and overall digestive comfort before breakfast and every 15 minutes up to 240 minutes postprandially. Patients completed validated self-report questionnaires for general anxiety, GI-specific anxiety, depression and somatization. The relationship between these psychological variables and the course of GI symptom scores over time was analyzed using linear mixed models, controlling for comorbid functional dyspepsia. "Time" was included as a categorical within-subject effect, the psychological variables were included as continuous between-subject effect (in separate models to avoid multicollinearity), and the psychological variable-by-time interaction effect was also included. The main effect of the psychological variable and the interaction effect are the effects of interest.

Results: Significant main effects of both general and GI-specific anxiety, depression and somatization, indicating a shift of the intercept of the curve (i.e. at the preprandial time point), were found for digestive comfort (negative association) as well as all GI symptoms (positive association), except for gas, where only both types of anxiety showed a significant main effect. General anxiety-by-time interaction effects were found for pain ($p=0.012$), bloating ($p=0.0039$), and urgency ($p=0.048$). No significant GI-specific anxiety-by-time interaction effects were found for any symptoms. Depression-by-time interaction effects were found for pain ($p=0.046$), bloating ($p=0.0071$), urgency ($p=0.004$), and digestive comfort ($p=0.030$). Somatization-by-time interaction effects were found for bloating ($p=0.027$), and urgency ($p=0.032$). These interaction effects reflect a steeper early postprandial increase of these symptoms (decrease for digestive comfort) and slower recovery to baseline in subjects with higher levels of the respective psychosocial factors.

Conclusion: In IBS, anxiety, depression and somatization are associated with increased symptom responses to a lactulose challenge test (steeper postprandial increase in ratings to a higher maximum and slower recovery), particularly for the symptoms bloating, urgency, and, to a lesser extent, pain. These results indicate that psychosocial morbidity is relevant for symptom reporting in IBS, including symptoms after a standard nutrient challenge test.

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P1690 EFFECT OF LINACLOTIDE AS COMPARED TO PLACEBO ON RECTAL SENSORY AND MOTOR RESPONSE TO DISTENSION ASSESSED BY ELECTRONIC BAROSTAT IN HEALTHY SUBJECTS

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Introduction: Linaclotide has been recently approved for the treatment of IBS with constipation. In animal models, linaclotide was able to inhibit high-threshold afferent responses both in basal and sensitized conditions (1). Whether the reported efficacy of linaclotide in reducing abdominal pain in humans is related to a direct effect on sensory pathways is unknown.

Aims & Methods: To compare the effect of linaclotide and placebo on the rectal sensory and motor response to distension assessed by the barostat in healthy subjects.

After an overnight fast a 700 ml plastic balloon was introduced in the rectum of 10 volunteers (6 females, 32 ± 4 years) and connected to a barostat. A volume- (50 ml/2 min) and a pressure-controlled (4 mmHg/2 min) stepwise, two ramp (300 ml/min, fast and 100 ml/min, slow) and three phasic (up to 8, 16, 24 mm Hg) distensions were performed and the intra-balloon pressure then settled at minimal distending pressure (MDP)+ 2 mm Hg for 30 min before and 120 min after the oral administration of placebo and linaclotide (290 µg) in a randomized, crossover fashion. Distensions were then repeated. Rectal tone, rectal distensibility (slope of the volume-pressure and pressure-volume relationship) and volume and pressure threshold for discomfort were evaluated. During phasic distensions intensity of discomfort and pain were rated on a 100 mm visual analogue scale (VAS) and rectal distensibility calculated as ratio between volume and distending pressure. Data are expressed by mean ± SEM of the delta (Δ) between values after and before the administration of the drug and compared by means of the Wilcoxon test.

Results: The MDP and rectal tone did not differ between treatments. During volume-controlled distension, rectal distensibility (-0.02 ± 0.005 for placebo vs -0.02 ± 0.01 mmHg/ml for linaclotide, $P=0.74$) as well as volume (20 ± 11 vs 5 ± 13 ml, $P=0.19$) and pressure (1.7 ± 5 vs -4.8 ± 3.7 mm Hg, $P=0.26$) thresholds for discomfort did not differ between treatments. During pressure-controlled distension, rectal distensibility (5.5 ± 1.2 vs 2 ± 1.9 ml/mmHg, $P=0.22$) as well as pressure (-1.6 ± 2 vs 1.7 ± 1.7 mmHg, $P=0.41$) and volume (20 ± 16 vs -8 ± 33 ml, $P=0.32$) thresholds for discomfort did not differ between treatments. During fast ramp, rectal distensibility (0.005 ± 0.12 vs -0.25 ± 0.19 mmHg/ml, $P=0.30$) as well as volume (12 ± 10 vs -3.4 ± 22 ml, $P=0.68$) and pressure (-0.58 ± 3.7 vs -10 ± 4.7 mmHg, $P=0.23$) thresholds for discomfort were similar for both arms. During slow ramp, rectal distensibility (-0.30 ± 0.26 vs -0.34 ± 0.25 mmHg/ml, $P=0.49$) as well as volume (19 ± 22 vs 24 ± 18 ml, $P=0.96$) and pressure (-6.6 ± 2 vs -4 ± 3.6 mmHg, $P=0.41$) thresholds for discomfort did not differ between treatments. During phasic distensions up to 24 mmHg, rectal distensibility (-0.005 ± 1.7 vs 1.2 ± 1.5 ml/mmHg, $P=0.99$) as well as VAS scores for discomfort (2 ± 5 vs 12 ± 8 mm, $P=0.08$) and pain (3.6 ± 3 vs 8 ± 6 mm, $P=0.30$) did not differ between treatments. No effect of linaclotide vs placebo was observed also during phasic distensions up to 8 and 16 mmHg (all $P>.10$).

Conclusion: In healthy humans, acute administration of linaclotide does not affect the sensory and motor response to rectal distension. It remains to be evaluated whether linaclotide affects rectal sensitivity in patients with visceral hypersensitivity and whether it affects responses to colonic distension.

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P1691 CORTICOTROPIN-RELEASING FACTOR CHANGES THE PHENOTYPE OF MESENTERIC LYMPH NODES DENDRITIC CELLS BY REGULATION ERK1/2 SIGNAL PATHWAY IN IBS

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Introduction: Our previous research indicated that abnormal immune function of mesenteric lymph nodes dendritic cell (MLNDC) was involved in the pathophysiology of irritable bowel syndrome (IBS). However, little is known of the contribution of Corticotropin-releasing factor (CRF) to intestinal DCs and the involved signal pathway.
Aims & Methods: In this study, we try to investigate the role of CRF in the change of intestinal dendritic cell phenotype and changes in mitogen-activated protein kinase (MAPK) activity in MLNDC.
The mice mesenteric lymph nodes dendritic cells (MLNDCs) were obtained by the technique of magnetic bead sorting. Expression of CRF-R1/R2 on the surface of MLNDCs were determined by double-labeling immunofluorescence and RT-PCR. Then, MLNDCs were exposed to different concentration of CRF, the expression of MHCII and CD80 were tested by the technique of flow cytometry and western blot. IBS rat model was established by combining neonatal maternal separation (NMS) and colorectal distension and undergoing transfection with CRF -targeting siRNA by intracerebroventricular injection. According to experiments, expression of surface molecule MHC-II and CD80 on the surface of MLNDC in both groups was determined by flow cytometric analyses, and Western-blot were used to determine the expression of MHCII?CD80?p-p38?p-ERK1/2 and p-JNK in MLNDC.
Results: Both the CRF receptors (CRFR1 and CRFR2) exist on the surface of MLNDCs. CRF could increase the expression of MHC-II of MLNDCs. In vivo, visceral sensitivity was significantly higher in IBS group while lower in IBS-CRF silencing group. MLNDC from IBS group expressed high level of MHCII, however, MLNDC from IBS-CRF silencing group expressed lowered surface expression of MHCII, the expression of p-ERK1/2 in MLNDC in IBS group were higher than that in control group while significantly reduced in IBS-CRF silencing group ($p < 0.05$). However, there was no substantial difference in the protein expression of p-JNK and p-p38 between groups.
Conclusion: Our findings suggest that CRF could induce the expression of MHCII in MLNDC in IBS, which may involved in the activation of ERK1/2 signal pathway.
Disclosure of Interest: None declared

P1692 LOW SENSE OF COHERENCE IS ASSOCIATED WITH REDUCED OVERALL HEALTH IN IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: Background: Sense of coherence (SOC) is defined as a global orientation that expresses the extent to which a person has a pervasive, enduring, though dynamic feeling of confidence that life is comprehensible, manageable, and meaningful (Antonovsky, 1987). SOC is strongly correlated with performance of activities of daily living, global health status and outcome in various medical conditions. In IBS few studies have addressed the importance of SOC for health status and quality of life. As stressful life events are common symptom triggers in IBS, and SOC is associated with successful coping with stressors and better health outcome, we hypothesized that SOC is reduced in an IBS subgroup characterized by high symptom burden and reduced quality of life (QOL).
Aims & Methods
Aim: To assess SOC in a large group of patients with IBS and evaluate the association with GI and psychological symptoms, and disease-specific QOL.
Methods: We included 387 patients with IBS (mean age 37 ± 13 (mean $\pm$ SD) years; 271 females) and 58 healthy controls (31 ± 9 years; 36 females). All subjects completed the SOC scale, and the patients also completed questionnaires to assess the severity of GI (Gastrointestinal Symptom Rating Scale-IBS, GSRS-IBS) and psychological symptoms (Hospital Anxiety and Depression Scale, HAD; Visceral Sensitivity Index, VSI), as well as disease-specific QOL (IBSQOL). The 5th percentile of the total SOC score in the healthy control group was used to define low SOC.
Results: SOC was reduced in IBS vs. control subjects. This was true for the total score and the three domains comprehensibility, manageability and meaningfulness. Within the IBS group SOC was lower in females than in males ($p = 0.009$), but unrelated to age ($p = 0.3$). IBS patients with low SOC (SOC total score < 116;$n = 76$) reported more severe IBS symptoms (GSRS-IBS) than patients with normal SOC ($n = 311$): abdominal pain (4.7 ± 1.3 vs. 3.9 ± 1.4; $p < 0.0001$), bloating (5.0 ± 1.3 vs. 4.4 ± 1.4; $p = 0.002$), constipation (3.2 ± 1.8 vs. 2.7 ± 1.7; $p = 0.03$), and diarrhea (4.2 ± 1.3 vs. 3.4 ± 1.4; $p < 0.0001$). They also reported more severe depression (HAD depression: 8.7 ± 3.4 vs. 4.1 ± 3.0; $p < 0.0001$), as well as general (HAD anxiety: 12.5 ± 3.6 vs. 7.0 ± 3.9; $p < 0.0001$) and GI-specific anxiety (VSI: 49 ± 15 vs. 36 ± 16; $p < 0.0001$). Reduced disease-specific QOL was seen for all IBSQOL domains in the low SOC group, and this was especially pronounced for the domains Emotional, Mental Health and Energy (see table).

Table SOC	Low SOC (n = 76)	Normal SOC (n = 311)	p-value
Emotional	33 ± 21	56 ± 22	<0.0001
Mental health	49 ± 25	76 ± 20	<0.0001
Sleep	64 ± 24	73 ± 24	
Energy	39 ± 27	61 ± 27	<0.0001
Physical functioning	61 ± 23	75 ± 21	<0.0001
Food	54 ± 24	66 ± 21	<0.0001
Social role	50 ± 24	66 ± 23	<0.0001
Physical role	40 ± 26	61 ± 30	<0.0001
Sexual function	57 ± 28	67 ± 25	

Conclusion: A substantial proportion of patients with IBS have reduced sense of coherence, which is associated with more severe symptoms overall as well as reduced quality of life. Low sense of coherence diminishes the ability to mobilize coping resources in response to daily stressors, and therefore helping IBS patients with low sense of coherence to improve their coping skills has the potential to positively affect global health in IBS.
Disclosure of Interest: None declared

P1693 ENTERIC NEURONAL LOSS IN MOUSE COLON FOLLOWING PERMANENT OCCLUSION OF THE MIDDLE CEREBRAL ARTERY

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Introduction: Ischemic cerebral stroke is a major cause of death worldwide. In addition to the brain injury, patients are also at risk of a number of comorbidities including cardiac, pulmonary and gastrointestinal (GI) complications as well as infections and sepsis. Bowel dysfunction and constipation greatly reduce the patients' quality of life but, equally important, they represent a major risk factor in sepsis development. Intestinal dysfunction has its roots in defect nervous regulation of motility and secretion, events locally controlled by the enteric nervous system (ENS). Co-morbidity in both central and enteric neurons has been demonstrated in several neuropathologies like Parkinson's disease and prion diseases but is so far unexplored in brain damaging situations like stroke.
Aims & Methods: The aim of the present study is to investigate if the ENS is affected after ischemic cerebral stroke. Forty-one C57BL/6 mice, mean age 11.6 months underwent either left sided permanent occlusion of the middle cerebral artery (pMCAO) ($n = 30$) or sham operation ($n = 11$). The pMCAO model results in limited damage to cortical brain tissue. After 6 hours (pMCAO $n = 6$), 3 days (pMCAO $n = 12$, sham $n = 7$) or 7 days (pMCAO $n = 12$, sham $n = 4$) mice were sacrificed their GI tracts collected. Histological and immonycytochemical methods were performed to analyze intestinal remodulation, and neuronal density in colon.
Results: Mice subjected to pMCAO display mild symptoms, like transient immobility of the contralateral hind paw. Animal weight and intestinal length was unaltered between pMCAO and sham animals. Morphological and immunocytochemical analysis of the colon revealed normal morphology 6 hours and 7 days after pMCAO compared to sham. After 3 days a thickening of the mucosa was observed in the pMCAO group compared to sham ($p < 0.05$). A significant loss of both myenteric ($p < 0.01$) and submucousal ($p < 0.05$) neurons was noted in the colon after 3 days, present also at 7days in pMCAO animals compared to sham.
Conclusion: pMCAO, an experimental model simulating stroke, results in a loss of enteric, in particular myenteric colon in mice. The loss is obvious 3 days post pMCAO and a 50% loss of myenteric neurons is detected 7 days post stroke. The mechanism behind is elusive but may involve neuroimmune interactions.
Disclosure of Interest: None declared

P1694 GUT DYSMOTILITY AFTER CATECHOL-O-METHYLTRANSFERASE AND DOPAMINE TRANSPORTER GENETIC REDUCTION IN MICE: IMPLICATION IN IRRITABLE BOWEL SYNDROME PATHOGENESIS

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Introduction: Psychiatric factors have long been thought to play a primary role together with biologic factors in the onset of irritable bowel syndrome (IBS) because of the interplay between psychosocial stressors and abdominal symptoms'
Aims & Methods: Since psychiatric disorders and pain syndromes are associated to changes in catecholaminergic transmission and these conditions are both related to IBS we investigated whether genetic reduction of both catechol-O-methyltransferase (COMT) and dopamine transporter (DAT) affects gut motility and enteric nervous system (ENS) circuitries. Female DAT and COMT heterozygous ($DAT^{+/-}COMT^{+/-}$) and wild-type ($DAT^{+/+}COMT^{+/+}$) mice (12 ± 2

weeks) were genotyped by PCR. Gastrointestinal transit was assessed 30 minutes after intragastric administration of nonabsorbable fluorescein isothiocyanate labeled dextran. Isolated ileum segments were isometrically mounted in organ baths and changes in muscle tension were recorded following addition of either carbachol (0.001-100 μM), KCl (60 mM) or after electric field stimulation (EFS, 1-40 Hz) and inhibition in non-adrenergic non-cholinergic conditions (EFS = 10 Hz, 1 μM atropine, 1 μM guanethidine, in the absence or presence of 0.1 mM L-NAME). Immunofluorescence staining for the neuronal marker HuC/D, neuronal nitric oxide synthase (nNOS) and the glial marker S100beta was evaluated with confocal microscopy in longitudinal muscle myenteric plexus preparations (LMMPs). To evaluate the integrity of myenteric plexus neurochemical coding, acetylcholinesterase and NADPH-diaphorase activity and GluN1 mRNA levels were studied in LMMPs.
Results: Gastrointestinal transit was delayed in transgenic animals compared to controls (GC 5.1 ± 0.2 vs 5.7 ± 0.2, $p < 0.05$). In $DAT^{+/-}COMT^{+/-}$mouse ileum, both receptor- and KCl-mediated contractions as well as cholinergic and nitrergic responses to electrical field stimulation significantly increased. In the myenteric plexus of $DAT^{+/-}COMT^{+/-}$mice immunoreactivity to S100beta augmented while staining for acetylcholinesterase^{+} ($-18 \pm 4\%$) and NADPH-diaphorase^{+} ($-23 \pm 6\%$) diminished. Distribution of nNOS immunopositive neurons changed compared to wild-type animals. A two-fold increase of GluN1 mRNA levels was found in LMMPs obtained from transgenic mice.
Conclusion: Our study provides evidence that changes in catecholaminergic transmission due to genetic-driven COMT and DAT defective activity affects ENS architecture, neurochemical coding and function leading to intestinal dysmotility and possibly to enhanced visceral pain perception, which may underlie the development of a disease with high social and economic impact such as IBS.
Disclosure of Interest: None declared

P1695 ISCHAEMIC COLITIS VS ISCHAEMIC CARDIOVASCULAR DISEASE

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Introduction: Although there are some considerations, involving pathological and anatomical data, to clarify the perfusion deficit[1, 2], the underlying etiology of ischaemic colitis (IC) is unclear[3].
Aims & Methods: The aim of this study is the evaluation of laboratory findings, such as haematological tests and lipids, in order to compare the pathophysiology of IC with that of ischaemic cardiovascular disease (CVD).
Laboratory tests were evaluated in 56 cases of IC and the findings were compared with 44 controls with known predisposing factors (including history of thrombosis, atherosclerosis, hypertension, chronic renal insufficiency, diabetes mellitus, irritable bowel syndrome, chronic constipation, history of abdominal aorta aneurysm, history of schock and autoimmune disease) but no evidence of IC. Parameters measured were: Complete blood count, cholesterol, high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglycerides and apolipoproteins B (ApoB).
Results: The absolute lymphocyte count had a tendency to be lower in the IC group ($p = .080$) with lymphopenia ($< 1200/\mu l$) most prevalent ($\chi^2(2) = 7.925$, $p = .019$). The platelet count was higher and the mean platelet volume (MPV) lower in the IC group ($p = .0005$ and $p = .039$, respectively). HDL levels > 40 mg/dl were significantly more common in male patients than in male controls 76.9% vs 35.7% ($\chi^2(1) = 6.034$, $p = .014$), while in females, levels > 50 mg/dl tended to be more prevalent in the IC group, 60.0% vs 28.6% ($\chi^2(1) = 3.548$, $p = .060$). The values of ApoB were lower ($p = .028$) in the same group. No significant results arose from the neutrophils to lymphocytes ratio (N/L) and the rest of the parameters tested, while no difference was observed in the statins' intake between the groups.
Multivariate analysis was performed to determine the effects of HDL and ApoB in IC. Increased HDL levels were associated with an increased likelihood of exhibiting IC (OR 1.119; 95% CI 1.039-1.204) and increased ApoB levels were associated with a reduced probability of IC (OR 0.948; 95% CI 0.916-0.981). (OR: Odds ratio, CI: Confidence intervals)
Conclusion: This study suggests that the pathophysiology of IC seem to be different from that of acute CVD. Platelets in patients with IC seem to function in a different way than in CVD, while they appear to have the inflammatory bowel disease (IBD) profile and they are, possibly, activated. Furthermore, HDL and ApoB predict IC in the opposite way than they do for CVD.

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P1696 ENDOSCOPIC FINDINGS ARE SIGNIFICANT FACTOR OF CLINICAL OUTCOME IN ISCHEMIC COLITIS

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Introduction: Colonic ischemia is the most common form of intestinal ischemic injury and comprises a spectrum that ranges from transient colitis to fulminant universal colitis. The aim of this study was to explore clinical characteristics and endoscopic findings and to investigate prognostic factor of ischemic colitis (IC).
Aims & Methods: We conducted a retrospective study in single tertiary hospital. The medical records of patients who were diagnosed with IC from 2010 to 2014 were reviewed. Their clinical characteristics, laboratory results, radiological, endoscopic, histological evidence were collected and analyzed.
Results: A total 103 patients with IC were identified. Endoscopic findings were presented mucosal gangrene at 20 patients (19.4%), right colon involvement at 21 patients (20.4%) and multi-segment involvement at 64 patients (62.1%). Multivariate analyses showed that mucosal gangrene is independent risk factor of clinical outcomes such as mortality (adjusted odds ratio = 22.7), surgery (adjusted odds ratio = 89.6), ICU admission (adjusted odds ratio = 3.47). Patients were divided into two groups (the presence or absence of mucosal gangrene) Nausea/vomiting, rebound tenderness, and guarding were observed more frequently in mucosal gangrene group ($P = 0.007$, $P < 0.001$, $P < 0.001$, respectively). No differences in other clinical symptoms and signs and laboratory findings, comorbidities were observed between the two groups.
Conclusion: Endoscopic findings of mucosal gangrene in patients with IC are significant factor of clinical outcome. The initial presentations that were clinical symptoms and laboratory findings do not necessarily predict the presence or absence of gangrenous change of IC. Clinicians have to consider prompt colonoscopy for prognosis as well as diagnosis of IC.
Disclosure of Interest: None declared

P1697 DYSSYNERGIC PATTERN OF DEFECATION IS OBSERVED IN HIGH RESOLUTION ANO-RECTAL MANOMETRY IN PATIENTS WITH INCONTINENCE, CONSTIPATION AND ANAL PAIN

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Introduction: Dyssynergic pattern of defecation has been described in 22% of healthy control with high resolution (HRAM)[1] and in 67% with high definition ano-rectal manometry[2] when bearing-down in the lying position.
Aims & Methods: To determine the percentage of dyssynergic defecation pattern found in ano-rectal HRM in a group of patients. Also, to evaluate if there are any differences in the clinical and manometric parameters between the groups with normal and dyssynergic pattern in the HRM and the result of the balloon expulsion test (BET). Anal sphincter pressures, bearing down maneuver and rectal sensory thresholds were measured in 100 patients with HRAM (Given imaging). We compared data analyzed between the two groups those with normal defecatory pattern and the other with dyssynergic defecation. Also they were compared for the BET (positive: balloon expulsion time in physiological position < 2 minutes).
Results: Patients' characteristic and manometric data are expressed in the table. Dyssynergic pattern was found in 34 (34%) of the patients and in 6 (17.6%) of them the BET was negative. 5 patients in which BET was negative had constipation and 1 anal pain. All the patients with dyssynergic pattern and incontinence had normal BET. There were differences in the anal residual and in the rectal bearing down pressures between the two groups. No other significant differences in the other parameters studied were observed.
Conclusion: Dyssynergic pattern is frequently observed in patients studied with HRAM. Anal canal pressure was higher and rectal pressures lower (more negative gradient and lower defecation index) during simulated evacuation in patients with dyssynergic pattern but only a minority of them had a negative BET.

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P1698 EVALUATION OF THE EFFECTIVENESS OF BIOFEEDBACK THERAPY IN THE TREATMENT OF FUNCTIONAL CONSTIPATION AND ENCOPRESIS IN CHILDREN

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Introduction: Defecation disorders are one of the most common problems in gastroenterology. It may be caused by the organic disease or more frequently it is a functional problem. The treatment includes fiber rich diet, proper education of patient, pharmacotherapy and in some cases the biofeedback therapy. Biofeedback therapy is helpful therapeutic method for the treatment of functional constipation with pelvic floor dyssynergia and fecal incontinence (encopresis) caused by abnormal function of the anal sphincters.

Aims & Methods: The aim of the study was to assess impact of parameters of anorectal manometry and their changes during biofeedback therapy on clinical outcome in children with constipation and pelvic floor dyssynergia and to evaluate the effectiveness of biofeedback therapy in fecal incontinence (encopresis) in children. Since 2000 to 2014, 44 children (aged 7-18 years, medium 12.5 years) with constipation and pelvic floor dyssynergia and 19 patients (aged 6-18 years, medium 11 years) with symptoms of fecal incontinence caused by improper function of the anal sphincter muscle were retrospectively assessed in this study. All of them had one to four biofeedback series consisted of two to four sessions. In the first group of patients with pelvic floor dyssynergia amplitudes between extremal and basic pressure during defecation maneuver during first and last session as well as difference between them both (amplitude in first session – amplitude in last session) were compared between group with clinical improvement after last session (n = 38) vs. group with no clinical improvement (n = 6). U Mann-Whitney test was used for analysis with $p < 0.05$ regarded as significant. In the second group with encopresis, during manometric recording, the patients were required to squeeze as to prevent defecation while being given visual feedback and verbal guidance on how to reach this goal.
Results: In the first group, there were no significant difference found in amplitude in first session values [mmHg] 94, 65, 115 vs. 112, 55, 170 [median, Q1, Q3]; amplitude in last session values 36, 27, 52 vs. 41, -38, 66; as well as in difference between them both 71, 11, 124 vs. 81, 17, 109 in groups with clinical improvement after last session vs. group with no clinical improvement respectively. In the group with encopresis, the improvement in the anorectal manometry parameters was observed in 17 out of 19 patients. Subjective clinical improvement was reported by 14 out of 19 patients. 2 out of 19 patients were lost for follow up.
Conclusion: Parameters of anorectal manometry and their changes during biofeedback therapies do not contribute to clinical outcome in children with constipation and pelvic floor dyssynergia. Biofeedback therapy is effective treatment for fecal incontinence in children caused by abnormal function of the anal sphincters.
Disclosure of Interest: None declared

P1699 BOTULINUM TOXIN INJECTION – LONG TERM EFFICACY IN THE TREATMENT OF CHRONIC ANAL FISSURE

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Introduction: Chronic anal fissure is a common cause of anal pain. It is more common in young adults, with similar incidence in both sexes. Its location achieves more frequently the posterior anal commissure (90-98%). Botulinum toxin (BT) and the lateral internal sphincterotomy are reserved for refractory cases. BT is minimally invasive and safer, compared to surgery, which carries a significant risk of disturbance in anal continence. BT presents a limited period of action and its long-term effectiveness is not well known.
Aims & Methods
Aims: Evaluate the long-term outcomes and the healing success rate of BT injection in chronic anal fissure.
Methods: Observational and retrospective study, including the patients treated with BT (single injection of 20U or two injection of 10U in intersphincteric space) between 2009 and 2012. Patients were followed up at 1, 6, 12 and 24 months and were assessed for healing of anal fissure. The response was registered as complete with a total healing and relapse.
Results: Ninety-one patients were treated, with an average age of 47 years and mostly were male (54 percent). In 80% of patients the fissure was located in the posterior midline. All the patients had been treated with topical drugs. In the first month, 87% of patients showed a complete healing. The 6 month inspection revealed 3% of recurrence and an increase of healing in 2 patients (86%). The 12 month, 76% of patients had no evidence of fissure, with a relapse rate of 10%. The healing rates at 24 month and relapse were 63% and 11% respectively. The recurrence rate was 24%, and 19% of patients was carried out surgery. The treatment was well tolerated by all patients and there were no complications.
Conclusion: BT has proven to be a safe and effective therapy, with satisfactory results in the long-term treatment.

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Disclosure of Interest: None declared

P1700 THE PUBORECTAL CONTINENCE REFLEX IS NOT MEDIATED BY THE PUDENDAL NERVE AND SEEMS TO SUPPORT FAECAL CONTINENCE DURING AGEING

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Introduction: We have recently found that conscious and unconscious contractions of the puborectal muscle are required for faecal continence and that unconscious contraction is mediated by the puborectal continence reflex.
Aims & Methods: In this study we aimed to investigate whether the puborectal continence reflex is regulated by the same nerve pathway as conscious contraction of the puborectal muscle. Furthermore, we aimed to find whether unconscious and conscious contractions of the puborectal muscle are influenced by each other, by age and by gender.
We included all adult patients who underwent anorectal function tests between 2010 and 2014 at the UMCG (n = 283). In total, 189 patients were excluded, because of possible generalized nerve damage or operations in the pelvic region, after which 94 patients remained. The patients underwent three different types of anorectal function tests. First, they underwent the anal electrosensitivity test, to investigate sensory condition of the pudendal nerve. Second, they had the anorectal pressure test, to measure conscious contraction of the puborectal muscle. Lastly, they underwent the balloon retention test, to measure unconscious contraction of the puborectal muscle.
Results: We found no correlation between unconscious contraction and anal electrosensitivity ($P = .811$). In contrast, we found a correlation between conscious contraction and anal electrosensitivity ($P = .012$). Furthermore, there was no correlation between conscious and unconscious contraction ($P = .634$). Age had no influence on unconscious, nor on conscious contraction of the puborectal muscle ($P = .080$ and $P = .344$, respectively). Gender had no influence on unconscious contraction ($P = .673$). However, gender did have a significant influence on conscious contraction ($P = < .001$), since men had a significant stronger conscious contraction.
Conclusion: We conclude that the nerve pathway responsible for the puborectal continence reflex is different than the one responsible for conscious contraction of the puborectal muscle. In addition, conscious and unconscious contractions work independently of each other. The puborectal continence reflex and conscious contraction of the puborectal muscle seem to support faecal continence during ageing.
Further clinical studies are necessary to evaluate the exact nerve pathway responsible for the puborectal continence reflex.
Disclosure of Interest: None declared

P1701 ENDOSCOPIC RADIAL INCISION AND CUTTING METHOD FOR REFRACTORY STRICTURE OF RECTAL ANASTOMOSIS AFTER SURGERY

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Introduction: Benign colorectal strictures occur mainly secondary to surgical resection, the risk is up to 20%. They sometimes cause obstruction and can lead to a low quality of life even if the surgery was successful. The therapeutic options for these strictures are repetitive surgery or endoscopic treatment. The most preferred treatment is endoscopic balloon dilation (EBD) because of its less-invasiveness, safety and effectiveness. However frequent sessions are often required to fully clear the obstruction. The best treatment for benign rectal stricture has not yet been determined. Radial incision and cutting (RIC) method was a first reported by Muto et al. as a new endoscopic therapeutic modality for refractory esophageal benign strictures. RIC is superior to other dilation methods in that it achieves a certain diameter of the lumen and a long patency period. But it has not been applied to any gastrointestinal tract other than the esophagus.
Aims & Methods
Patients: Indications for RIC for rectal anastomotic stricture at our institution were as follows: 1) the stricture caused an obstruction; and 2) ten or more sessions of EBD or mechanical bougie were not effective enough to permit the passage of an ordinary endoscope (about 10 mm in diameter). Institutional review board approval was obtained for this study and written informed consent was obtained from all patients.
RIC method: As previously described, first, the stricture area was incised radially in four or more directions with an insulation-tipped (IT) knife-1 (Olympus Co., Japan). Next, the flaps formed by the radial incisions were sliced off with the IT knife-1.
Results: From January 2012 to January 2015, we experienced 11 patients with a rectal anastomotic stricture through which an endoscope could not pass. Among them, 3 patients matched the indication and we performed total of four sessions of RIC during this period. They were all male, two were in their 60s and the other was in his 50s. All of three patients have undergone laparoscopic-assisted low anterior resection and diverting ileostomy due to advanced rectal cancer for two patients and rectal GIST for the other. Each surgery has been completed successfully and curative. One of them complained about difficulty in defecating after ileostomy closure surgery and two were found the stricture before ileostomy closure by preoperative X-ray contrast enema. RIC was performed for each patient in mannered style. Each procedure was successful to obtain adequate dilatation by only one session. Each patient was discharged 3 days after RIC

Abstract number: P1697

	Normal defecation (n = 66)	Dyssynergic (n = 34)	p-value
Age	53.7 (49.8-57.6)	53.2 (47.9-58.4)	0.844
Sex (F)	53 (80.3%)	24 (70.6%)	0.274
BMI	26.1 (24.6-27.6)	27.3 (25.7-28.9)	0.415
Bristol scale 1-2 3-4 5-7	32.3% 40.9% 25.7%	38.3% 44.1% 27.6%	0.827
Incontinence (n = 39) Constipation (n = 47) Anal pain (n = 14)	26 (66.7%) 33 (70.2%) 7 (50%)	13 (33.3%) 14 (29.8%) 7 (50%)	0.318
Mean resting pressure (atmospheric) Maximum resting pressure (atmospheric)	87.3 (80.1- 94.5) 99.9 (91.8- 108.1)	94.2 (84.5-103.9) 105.3 (93.4- 117.1)	0.283 0.438
Maximum squeeze pressure (atmospheric)	169.5 (152.8-186.1)	167 (140.7-193.3)	0.741
% Increase during squeeze	81.5 (67.1- 95.8)	73.3 (50.3- 96.2)	0.264
Squeeze duration	16.3 (14.8-17.7)	16.2 (13.9-18.4)	0.991
Anal canal length	3.1 (2.9-3.2)	3.1 (2.7- 3.3)	0.939
Rectal pressure bearing down	50.5 (42.9-58)	39.7 (30.3-49.2)	0.059
Anal residual pressure bearing down	70.8 (65.7-75.8)	94.5 (84.8-104.1)	<0.001
% relaxation	31.1 (28.6-36.6)	11.5 (8.2-14.8)	<0.001
Rectoanal gradient	-19.5 (-27.8, -11.2)	-54.7 (-67.8, -41.5)	<0.001
Defecation index	0.7 (0.6-0.8)	0.4 (0.3-0.5)	0.001
RAIR volume	27.8 (20.6-34.9)	35.3 (22.3-48.3)	0.162
Rectal sensation First sensation Urgency Max. Tolerable volume	20.1 (14.2-26.1) 103.1 (92.2-114.1) 133.9 (121.8-146)	25 (13.4-36.6) 107.5 (91.6-123.4) 138.4 (121.8-155)	0.553 0.5570.561
BET Positive Negative	66 (100%) 0 (0%)	28 (82.4%) 6 (17.6%)	<0.001

as scheduled without any complications. Although one patient showed restenosis after RIC, that occurred half a year later. He underwent second RIC which resulted in successful again and clinically observed for more than another half a year. The other patients were also course observed for 4 months and 18 months respectively without any complaints even after ileostomy closure surgery.

Conclusion: The RIC method can be the novel option for the refractory rectal anastomotic strictures. We have experienced only a few examples to date, and long-term follow-up results are not yet clear. Further case series were required for assessment.

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Disclosure of Interest: None declared

P1702 THE FREQUENCIES OF BOTH HARD AND SOFT STOOLS ARE MAJOR RISK FACTORS FOR FECAL INCONTINENCE

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Introduction: Both loose/watery stools and hard stools have been identified as population risk factors for fecal incontinence (*Gastro* 2009;137(2):512-7), but how the risk varies with frequency of such abnormal stools has not been well characterized.

Aims & Methods: We aimed to elucidate these associations by using data from our nationwide U.S. 2013 Rome Normative Gastrointestinal Symptoms Survey, which was uniquely suited for this as it included the Rome III question on FI ("In the last 3 months, how often have you accidentally leaked liquid or solid stool?") and the Rome III questions on frequency of hard and loose stools with 10% increment response scales from 0 to 100%. A community sample of 1,665 U.S. adults provided by the market research company Cint USA, Inc., completed a secure Qualtrics internet survey including the Rome III Diagnostic Questionnaire with the new validated response formats (Gastroenterology 2013;144 (5), Suppl.1:S-916) planned for Rome IV, as well as demographic and health history questions. Stratified sampling was used to ensure equal gender proportions and adequate race/ethnic minority representation. Responders providing inconsistent survey answers were excluded from analysis, leaving 1,277 response sets.

Results: The analysis sample consisted of 648 females and 629 males, from all 50 U.S. states plus D.C. and Puerto Rico; 701 were white, 218 black, 240 hispanic and 118 other or undeclared race/ethnicity. Mean age was 46.4 years (range 18-94) and 45.7% had a college degree. Of the total sample, 69.8% reported having hard and/or loose/watery stools, and 39.9% experienced both. Overall FI rate in the sample (accidental leakage of liquid or solid stool at least monthly in the past 3 months) was 8.8%, and did not differ between males and females (8.7% vs. 9.0%), age groups or race/ethnic groups. Binary logistic regression analysis confirmed that both hard stools and loose stools were independent risk factors for FI and had similar impact on FI probability (Exp(B): 1.30 and 1.52 respectively, $p < 0.0001$ for both). Collectively, hard and loose stools accounted for 30.3% of the total variance (Nagelkerke R Square) in FI status. Equivalent results were seen for predicting having FI at least once a week (Exp(B): 1.39 and 1.63 respectively, $p < .0001$ for both; 38.9% of the variance explained). As seen in the table, FI risk rose substantially and steadily in the sample as hard stools, loose stools or both became a larger proportion of total bowel movements.

Table: % of individuals in the sample who had FI, by frequency of their abnormal stools

	% of stools with this abnormality in past 3 months								
	0%	10%	20%	30%	40%	50%	60%	70%	80%±
FI incidence (%of people)									
Hard stools:	3.0	6.7	10.0	16.9	33.3	22.4	29.2	30.8	30.6
Loose/watery stools:	1.8	5.9	11.9	20.3	18.6	22.6	40.0	45.5	57.6

Conclusion: Individuals with no stool consistency abnormality have negligible FI risk, but the risk rises dramatically with increasing frequency of hard and/or loose stools. These findings have important FI management implications: Normalizing stool consistency (reducing both hard and loose stools) by means of diet adjustment, fiber supplements and/or medication is likely to offer potent protection against FI incidents, and should be a first-line approach to addressing this health problem [Supported by the Rome Foundation and grants R01DK31369, R21DK096545, and R01HS018695]

Disclosure of Interest: None declared

P1703 FECAL CONTINENCE REFINED: THE PUBORECTAL CONTINENCE REFLEX

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Introduction: Recently, the anal-external sphincter continence reflex was shown to be an important factor involved in fecal continence. Nevertheless, still not all of the clinical continence patterns can be explained.

Aims & Methods: To further evaluate the presence of additional mechanisms that control fecal continence.

Anorectal pressure, balloon retention and rectal infusion tests were performed in twenty healthy subjects in order to follow contractions of the pelvic floor muscles that are involved in fecal continence.

Results: During anorectal pressure measurement, voluntary squeeze pressure was observed at the level of the anal sphincter and at the level of the puborectal muscle. Both contractions were held for maximal 90 seconds.
During balloon retention and rectal infusion tests, the anorectal pressure increased for a longer period at the level of the anal sphincter, which was the anal-external sphincter continence reflex. Interestingly, during balloon retention test we observed an additional, gradual increase of pressure at the level of the puborectal muscle, which was significantly longer and stronger (between 3 and 9 minutes continuously) than the contraction observed during voluntary squeeze.
Conclusion: Our results indicate that there is a second continence mechanism, which we call the puborectal continence reflex, that controls fecal continence by gradually increasing contraction of the puborectal muscle. This reflex is activated to maintain the balloon, but not water, therefore controlling only solid fecal continence. This reflex seems to be initiated by traction on the puborectal muscle Presumably, this puborectal continence reflex protects many patients against full fecal incontinence.

Reference

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Disclosure of Interest: None declared

P1704 A STUDY TO INVESTIGATE THE CHARACTERISTICS AND RISK FACTORS FOR RE-BLEEDING AND IN-HOSPITAL MORTALITY OF ACUTE HEMORRHAGIC RECTAL ULCER

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Introduction:
Acute hemorrhagic rectal ulcer (AHRU) is frequently encountered, especially in patients with serious comorbidities. This study was conducted to clarify the clinical features of AHRUand to identify risk factors for re-bleeding and the in-hospital mortality on the basis of a 10-year single-center experience in Japan.
Aims & Methods: In this study, we enrolled 45 AHRU patients between April 2005 and April 2015. The background of patients, the bleeding recurrence rate- and the in-hospital mortality were assessed. And potential risk factors for them, such as patient attributes (Age, sex, underlying conditions, and medication) and endoscopic procedures were retrospectively investigated. Multivariate logistic regression analysis adjusted for significant factors was used to evaluate the risk factors.
Results: Among 45 patients, 24 (53%) were male and the median age was 72.8 ± 9.7 years.
All patients had some sorts of atherosclerosis-related comorbidities such as hypertension (69%), diabetes mellitus (33%), cerebro-vascular disease (33%), end-stage renal disease requiring hemodialysis (47%), and cardio-vascular disease (22%). Additionally, 17 patients (38%) suffered from infectious disease.
15 patients were classified as American Society of Anesthesiologists (ASA) Score 4.
Endoscopic study revealed rectal ulcer in all patients and hemostasis procedures were performed to 35 (78%) patients with the result of success in 34 (97%). Surgical treatment was needed in one patient.
20 (44%) patients experienced recurrent bleeding within 14 days. Re-bleeding were found 4.5 ± 3.8 days after the initial endoscopy on average. Fatal outcome occurred in 11 (24%) during the same hospitalization.
In the multivariate logistic regression model, re-bleeding was correlated with hypo-albuminaemia (serum albumin level < 2.8 g/dl)(odds ratio [OR], 7.79 per point; confidence interval [CI], 1.70-42.9; $P = 0.077$). The in-hospital mortality was correlated with ASA score 4([OR], 12.57 per point; [CI], 1.758-140.6; $P = 0.011$) and infectious comorbidity ([OR], 10.02 per point; [CI],1.242-125.2; $P = 0.030$).
Conclusion: In our study, all patients with AHRU had some sort of atherosclerosis-related comorbidities. Re-bleeding tend to occurred in patients with hypo-albuminaemia. ASA score 4 and infectious comorbidity were significant independent predictors for the in-hospital mortality.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 09:00–14:00
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS III – HALL 7

P1705 GASTRIC MICROBIOTA CHANGES AND METABOLIC FUNCTION DIFFERENTIAL ENRICHMENTS AFTER GASTRECTOMY IN GASTRIC CANCER PATIENTS

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Introduction: Subtotal gastrectomy is the standard therapy for early distal gastric cancer. Along with vagotomy and Billroth II reconstruction, gastric environment changed significantly after gastrectomy. However, the alterations in compositions and metabolic potentials of human gastric microbiota after gastrectomy remain unknown.
Aims & Methods: Bacterial DNA extracted from 6 gastric cancer patients' biopsies from tumor and non-tumor (before gastrectomy), gastric stump and high body (after gastrectomy) was sequenced. We analyzed gastric microbiota by utilizing next generation sequencing on the V1-V3 hypervariable regions of bacterial 16S ribosomal RNA (rRNA) genes. The metabolic potentials were predicted from the microbial composition.
Results: Within the same patient, we did not find significant difference in microbial composition between different anatomic sites before and post-gastrectomy. After gastrectomy, the bacterial communities had larger diversities. Before surgery, *Ralstonia* and *Helicobacter* were the two most abundant genera, whereas *Streptococcus* and *Prevotella* represented the top-two genera after surgery. Comparative analysis on metabolic potentials revealed abundant functional genes related to *N*-nitrosation reaction in cancerous stomachs, whereas bile salt hydrolase enriched in the gastric microbiota after gastrectomy.
Conclusion: The gastric microbiota changes in composition after gastrectomy, with differential enrichments in metabolic functions tightly associated with gastric environment.
Disclosure of Interest: None declared

P1706 CONTAMINATION-FREE SAMPLING OF THE DUODENAL MUCOSA-ASSOCIATED MICROBIOTA

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Introduction: The duodenum represents a unique niche within the digestive tract, characterised by relatively acidic pH, digestive enzymes, and bile. Due to the harsh conditions, the duodenum has long been considered sterile, with bacteria only present as overgrowth resulting from immune deficiencies or motility disorders. Emerging evidence from molecular and culture based studies now supports the presence of bacteria in this region in healthy individuals. However, these studies are constrained by the issue of contamination: either during sampling, particularly from the upper GI tract (oral cavity and stomach); and/or during the technical steps involved with molecular studies.
Aims & Methods: To accurately characterise the duodenal microbiota, we developed the Brisbane Aseptic Biopsy Device (BABD), which is comprised of biopsy forceps protected by a sheath. This device allows targeted, aseptic sampling of the duodenal mucosa. The background microbiome signature in common reagents was also investigated, to further differentiate between resident microbiota and possible contamination. Patients undergoing upper GI endoscopy for iron deficiency, after an overnight fast, were recruited with ethical approval. Matched duodenal biopsies were obtained using the BABD. Total genomic DNA was extracted from samples and amplicon libraries spanning the V6-V8 region of the bacterial 16S rRNA gene were constructed. Reaction mixtures with no added DNA were processed in parallel. All libraries were sequenced using the Illumina MiSeq platform, with taxonomic assignment and bacterial community analysis performed through the QIIME bioinformatics pipeline.
Results: Microbial DNA was recovered from all biopsies obtained using either standard forceps or the BABD. Concurrent sequencing of controls also confirmed the presence of microbial DNA in common laboratory reagents. These sequences showed limited overlap with the duodenal samples, and were excluded during bioinformatics analysis, thereby restricting our comparisons to duodenum derived sequences. Phylogenetic based UniFrac evaluation of beta-diversity revealed samples collected using the BABD clustered together, and showed low levels of inter-individual variability. The duodenal microbiomes from all patients were dominated by *Streptococcus*, representing up to 50% of the total bacterial load, with lower levels of *Prevotella*, *Veillonella*, *Neisseria*, *Porphyromonas* and *Lactobacillus*. Some Streptococcal sequences recovered showed similarity to oral or lower gastrointestinal tract isolates, as well as common food-production organisms such as *Streptococcus thermophilus*. However, two-thirds of the more than 150 different taxonomically assigned sequences identified as *Streptococcus* did not match closely to the 16S reference database, suggesting unexplored diversity within this genus in the duodenum.
Conclusion: The combined use of the BABD and the elimination of contaminating DNA sequences allowed the duodenal mucosa-associated microbiota to be accurately characterised, and confirmed the presence of microbes that are specific to the duodenal niche.
Disclosure of Interest: None declared

P1707 THE ASSOCIATION BETWEEN STREPTOCOCCUS BOVIS BACTERCEMIA WITH GASTROINTESTINAL TRACT DISEASE

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Introduction: *Streptococcus bovis/gallolyticus* (*S. bovis*) bacteria are reported to associate with colorectal cancer and adenoma. 25 to 80% of patients with S. bovis bacteremia have concomitant colorectal tumors. But few studies reported the relation between *Streptococcus bovis* infection with other gastrointestinal disease.
Aims & Methods: To clarify the incidence of gastrointestinal tract disease in patients with *Strep. Bovis*. bactercemia. From Jan. 2004 to Jan. 2014, total 107 patients infected with *Strep. Bovis* bacteremia were retrospectively chart reviewed

from Kaohsiung Chang Gung Memorial Hospital and basic data including age, gender, gastrointestinal diseases (liver disease, gallbladder stones, cholecystitis, pancreatitis, esophageal varices, peptic ulcer disease, colorectal polyp); abdomen echo, panendoscopy and colonoscopy findings were recorded. We analyzed the association between patients with gastrointestinal disease and *Strep. Bovis* bacteremia.
Results: 107 patients (60% male; 66 ± 14 years) were analyzed. Only 49 patients received colonoscopy and 27 (55.1%) patients had colorectal neoplasm (tubular adenoma: 12 (24.5%); tubulovillous adenoma: 5 (10.2%); villous adenoma: 1 (2.0%); adenocarcinoma: 9 (18.4%). 69 (64.5%) patients had liver disease (parenchymal liver disease: 31 (30.0%); 28 (26.2%) with Liver cirrhosis). 10 (9.3%) patients had gallbladder stone. 11 (10.2%) had acute cholecystitis. 2 (1.9%) had acute pancreatitis. 16 (15.0%) had esophageal varices. 24 (22.4%) had peptic ulcer disease.
Conclusion: In current study, 55.1% of patients with *S. bovis* bacteremia had concomitant colorectal tumors and 26.1% patients had liver cirrhosis. Colon study should be done in patients with *S. bovis* bacteremia. High incidence correlation with liver cirrhosis in patients infected with S. bovis could be due to their immunocompromised condition.
Disclosure of Interest: None declared

P1708 A RETROSPECTIVE STUDY FOR IDENTIFYING RISK FACTORS OF DELAYED HEMORRHAGE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC TUMOR

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Introduction: Delayed bleeding is one of the serious complications of endoscopic submucosal dissection (ESD). In association with growing aged population, the number of elderly patients with gastric tumors has increased in Japan. Since the elderly have a several risk factors for hemorrhage, such as frequent use of antithrombotic drugs, there is concern about increase in delayed bleeding after ESD.
Aims & Methods: The purpose of this study was to clarify risk factors of delayed bleeding after ESD for gastric tumor. The study subjects were consecutive 103 patients (75 males and 28 females, mean age; 73.0 ± 8.3 years) who underwent ESD for single gastric lesion at Teikyo University Hospital (Tokyo, Japan) between 2010 and 2013. Cases in which two or more lesions were resected at the same procedure were excluded. Delayed bleeding was defined if patients presented hematemesis or hematochezia and blood or coagulants was found in the stomach by endoscopy. The following clinical factors were investigated by the chart review; gender, age, location of the lesion, operation time, tumor size, specimen size, use of oral antithrombotic drugs and heparinization.
Results: Of the study subjects, 19 patients occurred delayed bleeding. As for the clinical factors, specimen size was the significant risk factor for delayed bleeding (Bleed: 46.9 ± 18.7 mm, Nonbleed: 36.5 ± 12.9 mm, p-value: 0.005 by Student's t-test). Additionally, heparinization showed significant risk for bleeding on multivariate analysis (OR 2.278, 95%CI 1.254-11.951, p = 0.019), while oral antithrombotic drugs did not.
Conclusion: The specimen size and heparinization were significant risk factors for delayed hemorrhage after gastric ESD.
Disclosure of Interest: None declared

P1709 A STUDY TO INVESTIGATE THE CHARACTERISTICS AND RISK FACTORS FOR ASPIRATION PNEUMONIA AFTER ENDOSCOPIC HEMOSTASIS

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Introduction: Aspiration pneumonia is a well-known complication of emergent endoscopy for upper gastro-intestinal bleeding, however, little is known of the characteristics and risk factors for this complication. Endotracheal intubation may be effective for airway protection in this setting. But, in Japan, endoscopic procedure is usually performed without prophylactic endotracheal intubation for aspiration.
Aims & Methods: The aim of this study is to assess aspiration pneumonia after endoscopic hemostasis on the basis of single-center experience in Japan. Consecutive 504 patients who underwent endoscopic hemostasis for upper gastro-intestinal bleeding between January 2004 and January 2015 were enrolled. All procedures were performed under conscious sedation. The incidence rate, clinical course and potential risk factors for aspiration pneumonia, such as patient attributes (Age, sex, underlying conditions, and medication), and endoscopic hemostasis procedures were retrospectively analyzed. Multivariate logistic regression analysis adjusted for significant factors in univariate analysis was used to evaluate the risk factors for aspiration pneumonia.
Results: There were 381 male patients (76%)and the mean age was 65.2 ± 13.3 years. Five-hundred-four patients consisted of 361 non-variceal (72%) and 143 variceal (28%) bleeding. Thirty-one patients (6.2%) were diagnosed with aspiration pneumonia after endoscopic hemostasis. Fatal outcome occurred in 7 patients (1.4%). 8 patients (1.6%) were stepped up to intensive care unit and endotracheal intubations were performed in 3 patients (0.6%). The mean duration of antibiotic treatment was 8.6 ± 5.9 days. Multivariate analysis identified that age over 75 years (OddsRatio [OR] 5.35; 95% confidence interval [CI] 2.19-13.75, P = 0.0003), procedure time over 30 minutes (OR5.63;CI2.2-15.37, P = 0.0004), serum albuminlevel less than3.5mg/dl (OR5.16;CI1.36-34.25, P = 0.0365), and hemodialysis (OR3.43;CI1.16-10.28, P = 0.0258) were the independent risk factors which affected on aspiration pneumonia.
Conclusion: 6.2% patients developed aspiration pneumonia after endoscopic hemostasis. Age, longer procedure time, lower serum albumin level, and hemodialysis are the independent risk factors of aspiration pneumonia. Careful attention should be taken when managing patients with these attributes.
Disclosure of Interest: None declared

P1710 THE RISK OF PEPTIC ULCER BLEEDING IS HIGHEST IN *H. PYLORI* POSITIVE PATIENTS ON COMBINED ANTIPLATELET THERAPY

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Introduction: The role of *Helicobacter pylori* infection in nonsteroidal anti-inflammatory drug (NSAID) and low-dose aspirin (LDA) induced peptic ulcer bleeding (PUB) is still controversial. Whether *H. pylori* infection increases the risk of PUB in patients on non-LDA antiplatelet agents (APA), anticoagulants, SSRI and steroids is not known.
Aims & Methods: This was a case-control study. Patients with PUD diagnosed by endoscopy from 01/2004 to 12/2014 were identified (N ± 1722, 60% males, mean age 65.7 ± 14.7). 978 (56.7%) had PUB (cases), 744 (43.3%) had uncomplicated PUD (controls). Demographics, intake of NSAIDs, LDA, APA, anticoagulants, SSRI and steroids were documented. *H. pylori* status was determined by ^{13}C urea breath test, histology, rapid urease test or serology.
Results: *H. pylori* infection (OR 1.25, 95% CI 1.01-1.54), aspirin (OR 1.73, 95% CI 1.37-2.18) and NSAID intake (OR 1.79, 95% CI 1.36-2.36) increased the risk for PUB. *H. pylori* infection increased the risk for NSAID- and LDA-induced PUB (OR 3.99, 95% CI 2.36-6.75 and OR, 3.83 95% CI 2.47-5.94, respectively). *H. pylori* increased the risk of PUB in patients on APA (OR 6.09, 95% CI 1.79-20.67) and anticoagulants (OR 1.69, 95% CI 1.06-2.71) but not in patients on SSRI and corticosteroids. Medication with APA dramatically increased the risk of LDA-induced PUB in *H. pylori*-positive PUD patients (OR 16.15, 95% CI 2.11-123.24).
Conclusion: *H. pylori* infection increases the risk for PUB in PUD patients on NSAIDs, LDA, APA and anticoagulants. *H. pylori* positive patients on combined antiplatelet therapy carry the highest risk for PUB.
Disclosure of Interest: None declared

P1711 ENDOSCOPIC LIGATION OF BLEEDING ESOPHAGEAL VARICES A "GOLD-STANDARD" TO IMPROVE

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Introduction: Endoscopic variceal ligation (EVL) is widely accepted as the optimum endoscopic treatment for oesophageal variceal haemorrhage.
Aims & Methods: The aim of the study was to evaluate the effectiveness and safety of endoscopic variceal ligation in the management of oesophageal variceal bleeding, to define risk factors for early variceal re-bleeding and to identify the best method to reach the variceal eradication.
We retrospectively evaluated all the endoscopic procedures performed in the last 23 years, form 1991 to 2014, in 370 cirrhotic patients with endoscopically proven esophageal hemorrhage treated by endoscopic variceal ligation. 241 patients (65%) with complete clinical-endoscopic data, were included in the study. The early re-bleeding after EVL was confirmed by clinical signs or endoscopy. All clinical features, endoscopic data and technical details of endoscopic treatment were entered in a stepwise multivariate logistic regression analysis to identify time and rate of variceal eradication and risk factors for rate early re-bleeding and mortality.
Results: The mean patient follow-up was 56 months (range: 6-150 months). In the 241 patients the average number of EVL was 2.7 (range: 2-5) performed in a period of 3 months. Primary hemostasis was obtained in 239 patients (99.1%), while early re-bleeding after EVL occurred in 16 patients (4.4%). The stepwise multivariate logistic regression analysis showed that: a) the worst the endoscopic classification of varices the higher the number of rubber bands placed on the first ($p < 0.001$) and following sessions ($p < 0.001$); b) the number of bands placed on the first session influences the necessity of further treatment (< 6 vs. > 6 bands; $p < 0.05$) and c) the chance of varices eradication decreases with the increase of the extension of the varices in the oesophagus (LI: 81% vs. LIM: 72% vs. LIMS 50%; $p < 0.05$).
Conclusion: A more intensive approach in EVL, especially in the first session, is rewarded by a lower incidence of early re-bleeding and a longer free interval before bleeding recurrence. We recommended to place the higher possible number of bands during the first treatment, waiting few minutes before ending the session to fully evaluate variceal recanalization from the upper perforating veins.
Disclosure of Interest: None declared

P1712 PROGNOSTIC FACTORS FOR SECOND THERAPY FAILURE IN NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

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Introduction: A second endoscopic therapy is generally advocated for patients with non-variceal upper gastrointestinal (GI) haemorrhage in the setting of re-bleeding[1]. Risk factors for endoscopic hemostasis failure have been described and involve both patient's and endoscopic features.

Aims & Methods: Study objective was to identify specific risk factors for failure of the second endoscopic therapy in order to improve selection of high-risk patients for rescue surgery. A retrospective cohort study considering all admissions to a tertiary center gastrointestinal intensive care unit from 2003 to 2014 was conducted. Patients with upper GI bleeding who were submitted to two endoscopic therapies were included. Patient's demographics, comorbidities and endoscopic findings were reviewed from medical records. Endpoints were re-bleeding/failure of hemostasis and 28-days mortality.

Results: A total of 64 patients (n = 64) were included. Mean age (72.4 ± 13.5); male:female ratio (2.7:1). Hemostatic failure occurred in 20.3% (n = 13) and 28-day mortality was 3.1% (n = 2). Lesions were mainly located in the stomach (45.3%) and bulb (39.1%) and most were ulcers (82%). Mean lesion size: 14.92 ± 11.8 mm; mean number of blood units transfused (5.88 ± 3.5 units). Univariate analysis unveiled female sex (p = 0.03) RR: 3.21 (CI 95% 1.26-8.24); absence of chronic liver disease/alcoholism (p = 0.027) RR:1.37 (CI:1.15-1.63); posterior duodenal wall lesions (p = 0.023 RR:3.37 (CI95% 1.38-8.22); ulcer size (p = 0.017); units of blood transfused (p = 0.001) and lower baseline hemoglobin (p = 0.03) correlated with endoscopic failure. Ulcer size showed positive correlation with mortality (p = 0.05). In a stepwise multivariate binary logistic regression analysis, ulcer size (p = 0.036) and number of units of blood transfused (p = 0.033) were the only factors positively correlated with therapy failure. Ulcer size (p = 0.036) also correlated with 28-day mortality.

Conclusion: In the setting of upper gastrointestinal non-variceal re-bleeding, patients with higher blood transfusion requirements and large ulcers are at greater risk of hemostasis failure on second endoscopic therapy. Early surgical consultation and ICU admission should probably be considered for these patients.

Reference

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Disclosure of Interest: None declared

P1713 EFFICIENCY OF TERAPEUTIC ENDOSCOPY DONE BY FELLOW GASTROENTEROLOGISTS FOR BLEEDING ULCER

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Introduction: This is a descriptive study conducted in the Departement of Gastroenterology of Clinical Emergency Hospital Bucharest.

Upper gastrointestinal bleeding (UGIB) represents a substantial economic and clinical burden, with an incidence ranging from 48 to 160 cases per 100,000 adults per year. Historically, mortality has ranged from 10% to 14% and only recently has there been a suggestion of a possible decrease.

The training of young gastroenterologist in endoscopic management of the non-variceal bleeding has been a challenge.

Aims & Methods: To determine the outcome of patients with upper gastrointestinal non-variceal bleeding that received endoscopic treatment done by an gastroenterologist fellow on close supervision of an expert.

The study included 260 patients with bleeding ulcers admitted in Clinical Emergency Hospital Bucharest between January 2014 and December 2014. Very early endoscopy (< 6h) was performed on all pacients upon admission.

Results: 260 pacients (68.5% Male) with bleeding ulcer (49.6% duodenal ulcer, 49.2 gastric ulcer and 1.2% esophageal ulcer) were admitted between 0 and 20 days (mean admision duration 5,7 days +/- 7,6). 138 pacients (49.2% by an gastroenterologist fellow unde supervision by an expert) received terapeutic endoscopic treatment with Adrenaline, Alchool, Bipolar probe or hemoclip in different combinations.

Conclusion: Endoscopic treatment of bleeding ulcer done by an gastroenterologist fellow under close supervision by an expert is safe and with the same outcome for the pacient.

Reference

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Disclosure of Interest: None declared

P1714 CLINICAL FEATURES OF DELAYED BLEEDING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION ASSOCIATED WITH HEPARIN BRIDGE THERAPY

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Introduction: Heparin is administered to patients undergoing endoscopic treatment at high risk for thromboembolism. Anticoagulants have been known as a cause of delayed bleeding associated with endoscopic treatment, including endoscopic submucosal dissection (ESD). Little is known, however, about how heparin bridge therapy (HB) affects clinical outcome after gastric ESD.

Aims & Methods: The present study aimed to identify the clinical features of HB-associated delayed bleeding after gastric ESD. Data of consecutive inpatients who underwent ESD for gastric neoplasms in Osaka University Hospital between June 2004 and September 2014 were retrospectively investigated. Patients were categorized into a HB group or non-HB group, and the incidence of complication (delayed bleeding, perforation, and thromboembolism) was compared in two groups. The characteristics of HB-associated delayed bleeding were also investigated. The predictor of delayed bleeding after gastric ESD was analyzed using a multivariate analysis by logistic regression.

Results: A total of 605 patients with gastric neoplasm were identified. One hundred twenty-two cases have taken oral antiplatelet agents or anticoagulants, and of them, twenty-six patients were treated by gastric ESD under HB. Characteristics of patients were similar in two groups except for patient age. Four patients experienced delayed bleeding in the HB group (replaced from warfarin 3, novel oral anticoagulants 1), and the incidence of delayed bleeding was significantly higher in the HB group than the non-HB group (15.4% vs. 3.1%, respectively, p = 0.01). Bleeding onset was later in the HB group than the non-HB group [median postoperative day (range): 3.5 (1-5) vs. 1.0 (1-7), respectively], and hemorrhage volume tended to be more in the HB group [Average Hemoglobin reduction (g/dl): 4.6 ± 1.7 vs. 3.1 ± 1.3, p = 0.08]. Although two patients in the HB group required blood transfusion due to massive delayed bleeding, all bleedings were endoscopically controlled. One patient experienced transitional ischemic attack in the HB group. Procedure time, en bloc resection rate, and incidence of perforation were similar in two groups. Hospitalization was significantly longer in the HB group than the non-HB group. The univariate and multivariate analysis showed that HB was the predictor of delayed bleeding after gastric ESD [Odds ratio (95% Confidence Interval): 6.33 (1.67-19.83), p = 0.009].

Conclusion: HB was a predictor of delayed bleeding after gastric ESD, and HB-associated delayed bleeding is characterized by high incidence, late onset, and massive bleeding, resulting in prolonged hospitalization.

Disclosure of Interest: None declared

P1715 ROCKALL, GLASGOW-BLATCHFORD OR AIMS65: WHICH IS THE BEST SCORE FOR EACH OUTCOME?

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Introduction: Despite different scores have been suggested to predict several outcomes in the setting of upper gastrointestinal bleeding (UGIB), few comparative studies have been published. Our aim was to evaluate the accuracy of 5 different scores in predicting different outcomes, namely clinical intervention, rebleeding, and mortality.

Aims & Methods: Between January/2011 and December/2014, 433 UGIB episodes were selected. Pre- (PreRS) and post-endoscopic Rockall scores (PostRS), Glasgow-Blatchford score (GBS) and its simplified version (sGBS) as well as AIMS65 score were calculated for each patient. Areas under the receiver operating characteristics curve (AUROC) were used to evaluate the performance of each score to predict clinical intervention (blood transfusion, endoscopic therapy, surgery, or admission to intermediate care unit), as well as 30-day rebleeding or mortality.

Results: From the analysed patients, 281 (64.9%) were men and the median age was 67.8 years. The most common endoscopic findings were gastric ulcers (16.9%), esophageal varices (15.2%), and duodenal ulcers (14.8%). PreRS, PostRS, GBS and sGBS were calculated for all patients, but AIMS65 calculation was only possible for 315 patients. Any of the 5 scores was good in predicting need for endoscopic therapy or admission to intermediate care unit. GBS and sGBS were good in predicting blood transfusion (AUROC = 0.853, 95% CI, 0.812-0.893; AUROC = 0.854, 95% CI, 0.814-0.894, respectively) and reasonable in predicting surgery (AUROC = 0.734, 95% CI, 0.610-0.859; AUROC = 0.766, 95% CI, 0.640-0.893, respectively). Any of the scores was useful in predicting rebleeding. Only PreRS and PostRS were able to fairly predict 30-day mortality (AUROC = 0.711, 95% CI, 0.618-0.805; AUROC = 0.731, 95% CI, 0.640-0.823, respectively).

Conclusion: Owing the identified limitations, any of the 5 studied scores can be singly used to predict all the clinically relevant outcomes in the setting of UGIB. The simplified version of Glasgow-Blatchford score is as precise as its original version in predicting blood transfusion and surgery. Pre- and post-endoscopic Rockall Scores are the only scores that can predict 30-day mortality. Any of the 5

scores is sufficiently accurate in predicting endoscopic therapy or rebleeding. When globally applied to patients with UGIB, AIMS65 score seems to be useless.

Disclosure of Interest: None declared

P1716 HISTORY OF GASTRO-DUODENAL ULCER IS AN INDEPENDENT PREDICTOR FOR REQUIREMENT OF ENDOSCOPIC HEMOSTASIS FOR NON-VARICERAL UPPER GASTROINTESTINAL BLEEDING

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Introduction: Non-variceral gastrointestinal bleeding (NVUGIB) is still a life-threatening disease. It has been known that early endoscopic hemostasis (EH) improves outcomes in patients with NVUGIB. However, it's sometimes difficult to decide whether to perform urgent endoscopy in clinical practice. Some scoring systems are used for determination of need for HE of NVUGIB such as Glasgow-Blatchford score (GBS) and clinical Rockall score. They can securely exclude patients who don't need EH because of its high sensitivity, whereas the specificity remains less than 10%. Therefore, if other predictors for EH are clarified, we would be able to narrow down indication criteria of urgent endoscopy more efficiently.

Aims & Methods: This study was aimed to assess predictors for requirement of EH.

This was a retrospective cross-sectional study from a tertiary hospital. A total of 317 consecutive patients who underwent urgent endoscopy suspected of NVUGIB from April 2010 to March 2014 were included. Requirement of EH was defined as high-risk stigmata for bleeding based on Forrest classification (Ia, Ib, or IIa) by reviewing the recorded endoscopic images. We analyzed the association between high-risk stigmata and clinical factors (age, gender, antiplatelet/anticoagulant therapy, history of gastro-duodenal ulcer (GDU), systolic blood pressure (SBP), heart rate (HR), hemoglobin (Hb), mean corpuscular volume (MCV), PT-INR, blood urea nitrogen-creatinine ratio (BUN-Cr ratio), GBS) using multivariate logistic regression model. Factors were selected by stepwise method.

Results: One hundred thirty three (43.2%) patients underwent EH. History of GDU [OR 3.07, 95% C.I. 1.81-5.27], SBP [OR 1.17 (every 10), 95% C.I. 1.07-1.28], Hb [OR 1.10, 95% C.I. 1.02-1.19], BUN-Cr ratio [OR 1.21 (every 5), 95% C.I. 1.13-1.30], and GBS [OR 1.19, 95% C.I. 1.12-1.28] was significantly associated with high-risk stigmata for EH. In multivariate analysis, Age, HR, history of GDU, BUN-Cr ratio and GBS were selected as factors according to stepwise method. Of these, history of GDU was an independent risk factor for high-risk stigmata [OR 3.21, 95% C.I. 1.82-5.75] as well as HR [OR 1.14 (every 10), 95% C.I. 1.00-1.31], BUN-Cr ratio [OR 1.15 (every 5), 95% C.I. 1.07-1.25] and GBS [OR 1.17, 95% C.I. 1.08-1.27].

Conclusion: Previous history of GDU is an independent predictor for EH for NVUGIB. A careful medical interview in clinical practice would help us to decide whether to perform urgent endoscopy.

Disclosure of Interest: None declared

P1717 RESULTS OF PER-ORAL ENDOSCOPIC MYOTOMY (POEM) FOR RECURRENT ACHALASIA

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Introduction: Recurrence of achalasia cardia after laparoscopic Heller's cardiomyotomy (LHM) or endoscopic balloon dilatation (EBD) is not uncommon. Reported incidence is up to 30%. Per-oral endoscopic myotomy (POEM) is an emerging treatment modality for achalasia cardia. This study reports results of POEM in patients suffering from recurrent achalasia cardia.

Aims & Methods: Consecutive patients with achalasia cardia confirmed on endoscopy (EGD), high-resolution manometry (HRM) and barium swallow and undergoing POEM at three centers were included. Previous treatments for achalasia were recorded. Eckhardt dysphagia score was recorded before and after the procedure. Procedure time, technical success and complications were noted. Follow up was by EGD, HRM at 4 weeks and subsequently monthly by telephone.

Results: Out of 61 patients undergoing POEM over a 22-month period, 20 (32.78%) patients had history of previous treatment for achalasia cardia whereas 41 were naïve patients. Mean age 51.8 years, females – 5. Achalasia Type: I – 8, II – 12, III – nil. Previous therapies included – Heller's myotomy (4), balloon dilatation (14) botulinum injection (1), and POEM (1). Median symptom duration: 66 months. Mean pre-procedure Eckhardt score – 7.14 (range 6 – 9); mean LES pressure 34.94mmHg (17 – 68mmHg). Technical success was 100%. Technical difficulties were encountered during 9 procedures (45%); sub- mucosal fibrosis leading to difficult tunneling in 5, difficult entry due to thickened mucosa in 3 and thickened circular muscle causing difficult myotomy in 1. Mean procedure duration was 107.1 minutes (30 – 270). In comparison, mean procedure duration for the naïve group was 91.7 minutes (45 – 330). ($p > 0.05$, non significant). Clinical success (100%) and no major complications were encountered in both groups. Relief of dysphagia was seen in all 61 patients (100%). At 4-weeks follow up, mean Eckhardt score was 1.41 (range 1 – 2) and mean LES pressure was 10.4 (range 7 – 19). At mean 9-month (range 3 – 22) follow up, mean Eckhardt score remained at 1.48. Occasional heartburn was seen in 5/20 (25%) patients.

Conclusion: POEM is safe and effective treatment for both naïve and recurrent achalasia cardia. Although technical difficulties were encountered in nearly 50% patients in the recurrent group, there was no significant difference in the mean procedure time or complications in both naïve and recurrent groups.

Disclosure of Interest: None declared

P1718 HIGH-RESOLUTION MANOMETRY AND CLINICAL CHARACTERISTICS OF PATIENTS WITH OUTFLOW OBSTRUCTION: IS THIS A TRULY RELEVANT NOVEL MANOMETRIC DIAGNOSIS?

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Introduction: The introduction of high resolution manometry (HRM) in clinical practice implied the use of a new classification for motility abnormalities, the Chicago classification (CC). The CC introduced a novel diagnosis to define a manometric picture characterized by impaired relaxation of the lower esophageal sphincter and normal peristalsis: the outflow obstruction (OO). However, limited HRM and clinical data are available on the characteristics of patients presenting this manometric feature.

Aims & Methods: This study aimed to evaluate and compare the characteristics of consecutive patients with a manometric diagnosis of OO with those of a group of patients with GERD. Secondary aim was to evaluate their reserve of esophageal peristalsis by means of multiple rapid swallow (MRS).

Among 112 consecutive HRM, we included 21 patients with an HRM diagnosis of OO, characterized by impaired EGJ relaxation (Integrated Relaxation Pressure; IRP > 15 mmHg) but preserved peristalsis and 21 consecutive patients with GERD, as control patients group (CG). All patients underwent HRM after suspending proton pump inhibitors or prokinetics. We evaluated EGJ basal and maximal pressure, prevalence of compartimentalized waves (pressurization of > 30mmHg extending from front contractile to the EGJ) and intrabolus pressure (IBP) in both groups. All patients underwent a provocative MRS (4ml x 5 times consecutively). IRP and distal contractile integral (DCI) during MRS was evaluated in both groups. Ratio DCI MRS/wet swallow was also calculated and considered normal when higher than 1.

Results: Mean age (58 ± 14.4 vs 56.6 ± 17.4), female (15 vs 12) and BMI (24.2 ± 3.2 vs 22.7 ± 2.7) were similar in both group (p = ns). Dysphagia (100%) and regurgitation (59%) were prevalent symptoms in OO. Heartburn (100%) was the prevalent symptom in CG, whereas dysphagia was absent and regurgitation (28.6%) was less frequent. EGJ basal (32.6 ± 11.6 vs 19.5 ± 11.6) and maximal pressure (48.4 ± 13.7 vs 30.4 ± 13.3) were higher in OO ($p < 0.001$). Compartimentalized waves were found in 71.4% of OO patients. As shown in Table 1, IBP was higher in OO ($p < 0.005$). DCI-MRS was two time higher in CG group than in OO. IRP during MRS decreased under 15mmHg in 9/22 (40.9%) of patients with OO. DCI MRS/wet swallow ratio was > 1 in 20/21 patients from CG but only in 3/21 in OO.

Table 1: Main HRM finding between patients with OO and those with CG

	OO	CG	P value
IRP mean (sd)	21.3 (5.3)	9.7 (3.9)	< 0.0001
DCI mean (sd)	1864.4 (1085.7)	1352.1 (911.2)	0.106
DL mean (sd)	6.9 (1.3)	6.7 (1)	0.770
Intra bolus pressure, mean (sd)	20.6 (13.5)	11.2 (5.5)	0.005
MRS mean (sd)	949.9 (620.4)	1884.6 (1493)	0.011
MRS-IRP (sd)	16.7 (9.2)	6 (3.4)	0.001
DCI MRS/wet swallow ratio (sd)	0.6 (0.4)	1.4 (0.8)	< 0.0001

Conclusion: In our cohort, the diagnosis of OO was always associated with the presence of obstructive symptoms (dysphagia ± regurgitation) as major complaint supporting the relevance of this manometric diagnosis which can be achieved by HRM. Moreover, the reserve of esophageal function evaluated with MRS and DCI MRS/wet swallow ratio showed a reduction in OO group. These parameters should be considered in outcome studies evaluating endoscopic treatment in patients with OO.

Disclosure of Interest: None declared

P1719 CAN PER-ORAL ENDOSCOPIC MYOTOMY BECOME AN ELECTIVE TREATMENT FOR ACHALASIA ALSO IN CHILDREN?

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Introduction: Achalasia is very rare in pediatric patients. The usual therapy of achalasia in children is Heller myotomy. Peroral Endoscopic Myotomy (POEM) is a fascinating technique for the treatment of achalasia in adults. Few small series reported on this technique in a pediatric population. We report on a consecutive, prospective, series of children with achalasia who underwent POEM.

Aims & Methods: Between May 2011 and April 2015, 252 patients underwent POEM in a single tertiary referral endoscopy center. Patients who were younger than eighteen were included in this study. Patients were treated with a standard technique. After treatment, patients underwent a close follow-up including physical examination, EGD, high-resolution manometry, barium swallow and pH-monitoring study. The clinical history, procedural data and follow-up information were prospectively collected and analyzed.

Results: Eighteen patients (10 male, mean age 11.9, range 6-17 years) underwent POEM during the study period. In 16 patients achalasia was sporadic; 1 patient had Down's Syndrome, 1 patient was diagnosed with Allgrove's Syndrome. Patients have been presenting symptoms for a mean of 12 months (3-60 months) before the treatment. Growth retardation was a common sign. Preoperative mean Eckardt score was 7.6. Eight patients (50%) especially complained with respiratory symptoms (chronic cough and/or pneumonia). According to the Chicago Classification, 5 patients had type I achalasia, 9 patients type II and 1 type III. Three patients had a diagnosis of classic-type achalasia at standard manometry. One patient (5.6%) underwent one pneumatic dilation before POEM. Length of the myotomy was on average 11cm, but it was usually customized according to the length of the esophagus (range 8-14cm). Mean operative time was 59 minutes (range 37–82 minutes).

No significant adverse events or complications occurred during or after POEM. Median postoperative hospitalization was 3 days. POEM was clinically successful (Eckardt score < 4) in all the patients, during a mean follow-up of 11 months (1-36 months). All the patients gained weight and had a regular growth. Mean Eckardt score after POEM was 0.2. Mean postoperative 4sIRP was 11mmHg. Postoperative EGD revealed reflux esophagitis in 19% (2 out of 11) of the patients who underwent EGD during follow-up. Esophagitis healed completely after therapy with proton pump inhibitors. Only these two patients complained with heartburn. No patients required additional treatments after POEM.

Conclusion: Preliminary results show that POEM is safe and effective for the treatment of achalasia also in pediatric patients. However, because of the lack of long-term evaluations, and the potential risk of the consequences of a iatrogenic GERD, POEM should be still considered an investigational procedure in pediatric patients.

Disclosure of Interest: None declared

P1720 HETEROGENEITY IN HIGH-RESOLUTION MANOMETRY AROUND THE WORLD

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Introduction: Advances in High-Resolution Manometry (HRM) and the development of the Chicago Classification for esophageal motor disorders have enhanced our understanding of esophageal (dys)function; however much of what is observed remains subjective and open to interpretation. Before considering the developmant of standards in operating procedures, a better understanding of what actually takes place in labs around the world is required.

Aims & Methods: To assess current practice among clinicians and scientists performing manometry around the world.

An on-line survey was distributed through international NGM societies to esophageal laboratories using the internet-based Qualtrics platform. Questions explored infrastructure, staffing, technology, analysis and reporting in HRM. Responses from all labs were then compared.

Results: 90 labs from around the world responded (thus far); 45 were from the Europe (Figure 1). Overall 42 labs receive more than 500 referrals per year (22 in Europe). Of the 14 labs that see more than 1000 referrals per year, 7 are in Europe. High volume (HV; >500/year) and Low volume (LV; <500/year) centers employ a median of 7 and 6 members of staff ($p = 0.03$) and 4 and 3 non-clinicians respectively ($p = 0.09$). Europe employs a median of 8 members of staff overall, 5 of whom are non-clinicians.

74/90 (82%) centers internationally and 33/45 (73%) in Europe use at least a 26 sensor HRM system. Furthermore 52/90 (58%) in total, 20/45 (44%) in Europe and 14/14 (100%) centers in the USA also have HRM-Impedance systems. Water-perfused catheters are less common in the West (15/45 in Europe, 1/8 in South America (SA), 0/14 in USA) as opposed to 8/12 centers in Australia/New Zealand (NZ) and 7/11 centers in Africa/Asia/Fareast. 33% HV and 38% LV centers use water-perfused systems. Some form of anesthetic is used in the nares in 34/42 (81%) HV and 37/48 (77%) LV centers ($p = 0.15$).

Overall HRM studies in the Upright-seated position are included in 38/90 (42%) centers. Some form of adjunctive test is incorporated in 90% of all centers (Figure 1). Although Multiple swallows of water is the most common (70%), 56/90 (62%) centers use more than one adjunctive test (including single solids and/or meals). 64/90 centers use the Chicago Classification routinely, 21 sometimes, 1 rarely and 4 never.

When determining the lower esophageal sphincter margins, there is wide variation in whether to include/exclude a hiatus hernia of less or greater than 3 and 5cm ($p = NS$). There is general uniformity in the content of the final HRM report apart from inclusion of 'therapeutic recommendations' which is more likely in HV (23/42; 54%) than LV (18/48; 38%) centers ($p = 0.05$).

	Adjunctive tests (routinely/ as required)	Single solid/ Viscous swallows	Multiple swallows of water/ Free drinking	Meal	Upright-seated
Europe (n = 45)	40 (89%)	31 (69%)	37 (82%)	10 (22%)	18 (40%)
USA (n = 14)	10 (71%)	6 (43%)	7 (50%)	3 (21%)	6 (43%)
South America (n = 8)	8 (100%)	4 (50%)	7 (88%)	0 (0%)	5 (63%)
Australia/NZ (n = 12)	11 (92%)	3 (25%)	8 (67%)	2 (17%)	6 (50%)
Asia/Africa/ Fareast (n = 11)	11 (100%)	5 (45%)	4 (36%)	1 (9%)	3 (27%)
Total (n = 90)	80 (89%)	49 (54%)	63 (70%)	16 (18%)	38 (42%)

Conclusion: There is marked heterogeneity in the methodology, interpretation and presentation of HRM studies in esophageal laboratories around the world. Mechanisms to improve quality and uniformity in testing and reporting are required. This survey sets the background upon which standards can be developed.

Disclosure of Interest: R. Sweis Lecture fee(s): Given Imaging, M. Fox Lecture fee(s): Given Imaging/Reckitt Benckiser

P1721 THE ROLE OF INTEGRATED RELAXATION PRESSURE IN ACHALASIA AND ITS MODIFICATION AFTER HELLER MYOTOMY

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Introduction: A new classification for the diagnosis of primary esophageal motility abnormalities by means of High Resolution Manometry (HRM) has been recently proposed and a new parameter, the Integrated Relaxation Pressure (IRP), has been included for the assessment of esophagogastric junction (EGJ) relaxation. Indeed, the diagnosis of achalasia is established by HRM on the basis of an IRP $>$ 15mmHg and absence of normal peristalsis in the esophageal body.

Aims & Methods: The aims of this study were: a) to investigate the correlation of IRP values with the diagnosis of achalasia, the demographics and clinical findings in a group of consecutive well-defined achalasia patients, b) to assess the effect of Heller myotomy on IRP. We evaluated all consecutive patients who underwent laparoscopic Heller myotomy as first treatment from 2009-14 and had a HRM evaluation before surgery. Patients who had already been treated for achalasia (with Heller myotomy, endoscopic treatment) were excluded. The diagnosis of achalasia was established by manometry on the basis of accepted esophageal motility characteristics. Symptoms were collected and scored using a detailed questionnaire for dysphagia, food-regurgitation, and chest pain; barium swallow, endoscopy, HRM were performed, before and 6 months after surgical treatment.

Results: 139 consecutive achalasia patients (M:F = 72:67) represented the study population. All the patients had 100% simultaneous waves but 11 had a IRP $<$ 15 mmHg. According to the HRM classification, patients were classified as having: 60 (43.2%) type I, 63 (45.3%) type II and 16 (11.5%) type III.

At univariate analysis IRP was correlated with the gender, the basal and residuak lower esophageal sphincter (LES) pressure, and the dysphagia score (Table). All the patients had absence of normal peristalsis, but 11(10.9%) had an IRP $<$ 15 mmHg. All these patients had a barium swallow showing a grade I disease. At a median follow-up of 28 months, the symptom score was significantly lower after surgery (median preoperative score 18 [IQR 11-20] vs median postoperative score 0 [IQR 0-3]; $p < 0.0001$). The resting LES pressure (median preoperatively 27 [IQR 19-36] vs median postoperatively 11 [IQR 8-14]; $p < 0.001$) and IRP (median preoperatively 27.4 [IQR 20.4-35] vs median postoperatively 7.1 [IQR: 4.4-9.8]; $p < 0.001$). The failures of surgical treatment were 7 (5%).

	IRP	p-value
Sex:MF	25.1 (17.3-31.1) 29.0 (22.8-37.9)	**0.01**
Age*	–0.12	0.25
Manometric pattern		0.24
I	25.9 (18.7-31.3)	
II	29.9 (22.3-35.5)	
III	24.7 (17.2-44.3)	
Esophageal diameter *	–0.03	0.79
LES basal pressure *	0.56	**$<$0.001**
LES total length	0.17	0.08
LES abdominal length	0.15	0.14
LES residual pressure *	0.86	**$<$0.001**
Dysphagia score *	0.21	**0.002**
Symptoms score *	0.14	0.17

Conclusion: This is the first study evaluating the role of IRP in achalasia and its modifications after myotomy. An increased preoperative IRP directly correlate with severity of dysphagia in achalasia patients. IRP is reduced to normal values by Heller myotomy. Moreover, the occurrence of an IRP $<$ 15mmHg in more

than 10% of patients despite a clinical/radiological/endoscopic diagnosis of achalasia, requires caution in considering this parameter as a discriminating condition in the manometric diagnosis of the disease.
Disclosure of Interest: None declared

P1722 IMPAIRED RELAXATION OF THE LOWER ESOPHAGUS SPHINCTER – IS IT ALWAYS PRIMARY ACHALASIA? A CASE SERIES OF 31 PATIENTS WITH ACHALASIA

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Introduction: We report 31 cases of chronic dysphagia with an impaired function of LES treated in two centers between 2005 and 2014. Patients' notes were retrospectively analyzed.
Aims & Methods: Patients' notes were retrospectively analyzed.
Results: Mean age of patients was 14.2 years (7.1-17.6). Half of the patients were female. In 30 cases primary esophageal achalasia was diagnosed. Main symptoms were dysphagia, weight loss, regurgitation, vomiting and heartburn. Half of the patients had respiratory complications.
In one quarter of our patients recurring respiratory complications were misdiagnosed as asthma. Additionally, in 8 patients esophageal candidiasis was detected years before diagnosis of achalasia and could have led to early considering of esophageal motility disorder. In another 7% of patients dysphagia and dystrophy was misdiagnosed as eating disorders.
Bridging therapy with nifedipine showed good results but had to be discontinued in all patients due to side effects. Injection of botulinum toxin into LES had a primary success rate of 83%. Symptom-free interval was only 3 months and repeated interventions were necessary leading to surgery as definite therapy. Repeated pneumatic dilatation (PD) was performed in 63% of the patients and led to a short relief of symptoms for 3 months. Prevention of surgery by PD was not achieved in our cohort. All patients with primary achalasia underwent surgery consisting of Heller's myotomy and an anti-reflux procedure. Minor complications occurred in 10% but did not need extended surgical therapy going beyond intraoperative ligation of small esophageal perforations and did not extend length of hospital stay nor increased postoperative morbidity. At 1-year follow-up 64% were symptom-free. Symptomatic patients complained about heartburn but not dysphagia. After surgery good thriving could be achieved as BMI at follow-up increased by 19 percentiles above BMI at initial presentation.
Interestingly, one patient presented with chronic dysphagia and diagnostics were consistent with achalasia. Additional MRI showed leiomyoma of the esophagus leading to secondary achalasia.
Conclusion: Early and correct detection of achalasia is often impaired by heterogeneous clinical manifestations and low sensitivity of diagnostic tools. Misdiagnoses and inadequate or delayed therapy is common. Oral nifedipine, intraesophageal injection of botulinum toxin and/or pneumatic dilatation can provide a short relief of symptoms. Heller's myotomy combined with a reflux procedure as definite therapy showed good clinical and diagnostic results at follow-up. Additionally, endosonography or MRI of the esophagus might be useful to detect secondary achalasia due to extraesophageal tumors.
Disclosure of Interest: None declared

P1723 AN INSERTION OF 8 AMINO ACIDS IN THE CYTOPLASMIC TAIL OF HLA-DQB1 IS A STRONG RISK FACTOR FOR ACHALASIA IN SWEDEN

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Introduction: Idiopathic achalasia represents a motility disorder of the esophagus and is characterized by a failure of the lower esophageal sphincter to relax due to a loss of neurons in the myenteric plexus. Most recently, an insertion of 8 amino acids in the cytoplasmic tail of HLA-DQβ1 has been identified as being independently disease-associated.[1]
Aims & Methods: The goal of the present study was to assess whether this variant also confers risk in a Swedish population. Moreover we aimed to compare the frequency found in Sweden with those found in other European conutries. We genotyped the marker rs28688207 in 171 achalasia patients from Sweden. To obtain the information of the insertion in a control cohort, we used a genome-wide genotyped dataset of 732 controls and applied SNP2HLA to imput the insertion. In addition, we analyzed samples from 5 other EU countries (Belgium, Germany, The Netherlands, Spain and Italy; (n = 1480)) that were part of our previous study, but which have not been evaluated separately up to now.[1]
Results: The insertion showed a strong association in the cohort of 171 patients ($P = 7.44 \times 10\text{-}05$; RR = 2.93) with a frequency of 6.1% in patients and only 2.2% in controls. Of note, the frequency of the insertion exhibited a geospatial north-south gradient and was nearly four times more common in southern compared to northern Europeans and showed a stronger attributable risk (AR) in southern Europeans.
Conclusion: The variant rs28688207, which leads to an alternative splicing of the HLA-DQB1 exon 5, is a strong genetic risk factor for achalasia in Swedish patients with achalasia. In addition, the prevalence of achalasia appears to differ geo-epidemiologically.

Reference

1. Gockel et al. *Nat Genet* 2014; 46: 901-4.

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P1724 OUTCOMES OF PNEUMATIC DILATIONS ACCORDING TO ACHALASIA SUBTYPES

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Introduction: The treatment of achalasia is not consensual. Some studies have suggested that the response to endoscopic treatment may be influenced by achalasia subtypes as defined by the Chicago classification. The aim of this single-center study was to assess the efficacy of pneumatic dilations according to the different achalasia subtypes.
Aims & Methods: From January 2010 to September 2013, 49 treatment-naive patients were included in our study (20 men, mean age 64.8 +/- 17.3 years). Achalasia subtypes were diagnosed with high resolution manometry (Given Imaging), and classified as type I (no contraction and no esophageal pressurization), type II (esophageal pressurization > 20% of cases) and type III (esophageal premature contractions > 20% of cases). Pneumatic dilations were performed with balloons ranging from 30 to 40 mm until clinical remission (Eckardt score $\leq$3 with each item $<$2) and during follow-up in cases of symptomatic recurrence. Predictive factors of remission were determined by univariate and multivariate analysis using a logistic regression model.
Results: Initially, pneumatic dilation achieved clinical remission in 85% of patients. After a median follow-up of 27 months (5 to 48 months), overall remission rate was 71%, significantly higher for type II (76.6%) and type I (63.6%) than for type III (25%) ($p = 0.024$). In comparison with type II, type III was associated with treatment failure (OR 9.8; 95% CI: 1.6-60.2). Seven patients had surgery, including 25% of type III patients. The overall evolution of the Eckardt score was less favourable for type III compared to type II or I ($p = 0.0006$). In univariate analysis, in addition to achalasia subtypes, female gender ($p = 0.016$) and number of dilations ($p = 0.0002$) were associated with treatment failure. In multivariate analysis, only achalasia subtypes ($p = 0.039$) and female gender ($p = 0.018$) were associated with treatment failure. At the end of follow-up, 35 patients (71%) were in remission after treatment with pneumatic dilations of all types. There was no dilation-related esophageal perforation in this series.
Conclusion: This single-center study further confirms that type III achalasia has less favourable outcome after pneumatic dilation. Whether this subtype should be preferably treated by endoscopic or surgical myotomy needs to be determined by adequate studies.
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P1725 THE EFFICACY AND SAFETY OF NEW PROKINETKC AGENT BENACHIO Q SOLN.® IN PATIENTS WITH POSTPRANDIAL DISTRESS SYNDROME SUBTYPE IN FUNCTIONAL DYSPEPSIA: A SINGLE-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PILOT STUDY

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Introduction: Functional dyspepsia (FD) is gastrointestinal disorder in which the patient suffers from chronic abdominal symptoms despite the absence of organic disease. The cause of functional dyspepsia is unclear and treatment is not efficacious. Benachio Q soln.® is a new prokinetic herbal medicine fomulated with Licorice, Corydalis tuber, Fennel, Citrus unshiu, Ginger, Cinnamon bark, Atractylodes rhizome. Several studies showed that Corydalis tuber, Citrus unshiu, Ginger, Cinnamon bark, Atractylodes rhizome promoted gastric motor function and Licorice, Fennel improved dyspepsia symptoms.
Aims & Methods: The aim of the present study is to determine the efficacy and safety of Benachio Q soln.® in patients with postprandial distress syndrome (PDS), subtype in FD. A single-center, randomized, double-blind, placebo-controlled pilot study was performed in 20 patients with PDS. Patients were assigned to receive either Benachio Q soln.® or placebo t.i.d. After 4 weeks of treatment, the data of response rates, symptoms severity of PDS and gastric emptying time were analyzed for its efficacy. Adverse events, laboratory tests and vital sign were analyzed for its safety.
Results: Nine and 10 patients were assigned to the Benachio group and placebo group. The response rate after 4 weeks were 44.4% and 20.0% in Benachio and placebo group, respectively ($p = 0.350$). The response rates during first week of Benachio group were better compared with placebo group but without statistical significance (33.3% vs 0.0%, $p = 0.087$). Changes of severity score in early satiety on second and third week were -1.8 ± 0.6, -1.9 ± 0.4 and -1.3 ± 0.5, -1.4 ± 0.6 in Benachio and placebo group, respectively ($p = 0.059$ vs $p = 0.033$). No adverse event, significant change of laboratory tests and vital sign were observed.

Conclusion: A new herbal drug, Benachio Q soln.® improved the symptoms of PDS subtype in FD and can be used safely.
Disclosure of Interest: None declared

P1726 PATIENTS WITH HYPERMOBILITY TYPE EHLERS-DANLOS SYNDROME AND FUNCTIONAL GASTROINTESTINAL SYMPTOMS DISPLAY ACCELERATED GASTRIC EMPTYING BUT DECREASED GASTRIC MOTILITY COMPARED TO MATCHED CONTROLS

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Introduction: Patients with hypermobility type Ehlers-Danlos syndrome frequently present with debilitating functional upper gastrointestinal (GI) symptoms including early satiety, bloating, epigastric pain and postprandial distress. EDS-HT is characterized by abnormalities in collagen synthesis potentially resulting in altered mechanical characteristics of the gastric wall serving as a theoretical background for explaining upper GI symptoms. In this study we investigate gastric emptying and motility using Magnetic Resonance Imaging in a group of EDS-HT patients and matched healthy controls.
Aims & Methods: Six patients (mean age 34, range 26 to 50, all female) with a diagnosis of hypermobility-type Ehlers-Danlos (EDS-HT) and referred with upper GI symptoms to a tertiary referral centre were prospectively recruited. An additional six age, sex and body mass index matched healthy subjects were recruited as controls. EDS-HT patients discontinued all motility influencing medication approximately four days before their MRI scan. All subjects' lay prone in a Philips Achieva 3T MRI scan and underwent baseline anatomical (3T BTFE BH) and motility (2D BTFE FB) imaging through the stomach before consuming 300ml of water. The anatomical and motility scans were repeated immediately following the water drink and repeated at 10 minute intervals for a total of 60 minutes. An experienced gastroenterologist manually segmented the total stomach volume for each subject from the anatomical images to provide:
1) Gastric emptying time defined as the time taken for 50% of the water bolus to clear the stomach adjusted for baseline gastric content.
2) Gastric accommodation examined by segmenting the gastric volume above the incisure before and after water challenge presented as a percentage change in volume.
3) Gastric motility was measured by plotting the diameter of the gastric lumen at the incisure and counting the number of contractions that occluded $>10\%$ of the mean gastric diameter at that location, standardised as contractions per minute.
Gastric emptying, accommodation and motility was compared between EDS-HT patients and controls using the paired t test.
Results: 1) The mean gastric emptying time for the EDS-HT patients was 16 minutes (range 8 to 26) and for the healthy controls was 25 minutes (range 8 to 30), $P=0.04$.
2) Gastric accommodation in EDS-HT showed an increase in volume of 244% (range 82 to 468%) and in controls was 317% (range 170 to 567%) with a mean difference of 73%, $P=0.3$.
3) The mean number of contractions for the EDS patients was significantly lower than that of healthy controls (1.1cpm (range 0 to 2.7) vs 2.9cpm (range 2.3 to 3.6), respectively, $p=0.006$.
Conclusion: Gastric empting appears accelerated in EDS-HT patients compared to controls despite a decreased number of contractions. This may reflect disturbances in gastric motor activity and/or altered mechanoelastic properties of the stomach. The protocol was well tolerated by all subjects further supporting MRI's value as a non-invasive, safe and quantitative method to interrogate gastric physiology.
Disclosure of Interest: None declared

P1727 ARE GENERIC PPIS LESS EFFECTIVE ANTISECRETORY DRUGS THAN BRANDED FORMULATIONS? A STUDY IN DYSPETIC PATIENTS WITH THE USE OF NON INVASIVE MARKERS OF GASTRIC FUNCTION

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Introduction: Proton pump inhibitors (PPIs) are the most effective antisecretory compounds used in the treatment of acid-related diseases and represent today the most widely prescribed class of drugs. Some studies have shown that generic PPIs are less effective than the corresponding branded formulations. However, available data are scarse and sparse.
Aims & Methods: The purpose of this study was to evaluate the effect of these drugs on serum levels of amidated gastrin-17 (G-17) and pepsinogens (PGI & PGII) in dyspeptic patients and to compare the antisecretory efficacy of branded and generic PPIs.
740 dyspeptic patients ($M=268$, $F=472$, mean age $=45.6\pm14.7$ years, range = 18-86 years) under PPI therapy for at least 1-3 months and without any alarm symptom (i.e. dysphagia, anemia, weight loss and vomiting) were selected from their General Practitioners for fasting blood collection and assay of G-17 and pepsinogens (Biohit Oyj, Finland). To each of them a standard questionnaire (including upper gastrointestinal symptoms, thyroiditis history, family history of stomach cancer and PPI regimen) was administered. Patients with *H. pylori*-related gastritis, chronic atrophic gastritis, half-dose PPI or no compliance were excluded from the study.
Results: 354 patients ($M=138$, $F=216$, mean age $=46.3\pm14.4$, range = 18-83 years) under standard dose PPI were recruited: 154 patients taking a branded PPI and 200 a generic one PPI. The PPIs prescribed were: omeprazole ($n=37$), lansoprazole ($n=72$), pantoprazole ($n=131$), rabeprazole ($n=31$) and esomeprazole ($n=83$). The serum G-17 (15.1 ± 19.4 *versus* 7.7 ± 9.9, $p=0.0001$), pepsinogen I (171.2 ± 92.7 *versus* 144.4 ± 79.4, $p=0.004$) and pepsinogen II (13.7 ± 10.8 *versus* 11.4 ± 9.6, $p=0.031$) concentrations were - in patients taking branded PPIs - significantly higher than those found in patients using generic formulations.
Conclusion: Since, under antisecretory therapy, the G-17 and pepsinogen levels depend on intragastric pH (the higher intragastric pH, the higher the gastric markers), these findings show – *indirectly* – that, in dyspeptic patients, generic formulations of PPIs are less effective than the corresponding branded products.
Disclosure of Interest: None declared

P1728 PATIENTS WITH TENASCIN-X DEFICIENT EHLERS-DANLOS SYNDROME EXPERIENCE GASTROINTESTINAL SYMPTOMS AND MEET THE CRITERIA FOR FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Tenascin X (TNX) is an extracellular matrix glycoprotein, deficiency of which causes a recessive form of Ehlers Danlos Syndrome (EDS), a hereditary disorder of connective tissue. It is now known that gastrointestinal (GI) and somatic symptoms, and functional GI disorders are associated with EDS Hypermobility-Type (1,2), however these symptoms have not been systematically characterized in TNX-deficient EDS patients.
Aims & Methods: To determine the GI and somatic symptom profile in a group of TNX-deficient adult EDS patients presenting primarily to neurology clinics, validated questionnaires were completed. Scores on the GI symptom rating scale (GSRS) were compared to those in a Scandinavian control population ($n=2162$, 51% male, age: 19-84) (3) and somatic symptom scores (PHQ15) were compared to those in a primary and secondary care control population ($n=3000$ each) (4). The prevalence of functional dyspepsia and irritable bowel syndrome were determined using ROME III criteria.
Results: 11 patients (3 male, age range: 24-66 years) with TNX mutations and/or absence of TNX serum levels participated. GI scores for indigestion, reflux, abdominal pain and diarrhoea domains were significantly higher than quoted population scores (Table 1). 33% of patients had high somatic sensitivity, which was significantly higher than in a primary care (10%, $p=0.02$) and secondary care control population (9%, $p=0.01$). 3 patients (27%) had irritable bowel syndrome (IBS) (1 IBS-M, 2 IBS-D). 7 (64%) patients had functional dyspepsia (3 postprandial distress syndrome (PDS), 2 epigastric pain syndrome, 2 unspecified). 2 (66%) patients with IBS had overlapping functional dyspepsia (PDS).
Table 1: Mean scores and confidence intervals for each GSRS domain

GSRS Domain	TNX-deficient patients	Swedish control population	p
Reflux	2.68 (1.62-3.75)	1.39 (1.36-1.43)	0.02
Abdominal pain	2.58 (1.69-3.47)	1.56 (1.53-1.59)	0.01
Constipation	2.03 (1.09-2.97)	1.55 (1.51-1.58)	0.2
Indigestion	3.25 (2.53-3.97)	1.78 (1.75-1.82)	0.006
Diarrhoea	2.33 (1.26-3.40)	1.38 (1.35-1.41)	0.02
Total GSRS score	2.61 (1.97-3.26)	1.53 (1.5-1.55)	<0.001

Conclusion: TNX-deficient EDS patients have a high prevalence of functional dyspepsia, an abundance of reflux, indigestion, diarrhoea and abdominal pain symptoms, and high somatic sensitivity, which is similar to EDS-HT patients but greater than in control populations. These findings suggest that abnormalities in extracellular matrix proteins may impact on GI function. Further work is necessary to elucidate possible mechanisms.

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P1729 IS PROTON PUMP INHIBITOR THERAPY ALWAYS NEEDED IN THE ELDERLY?

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Introduction: Proton pump inhibitors (PPIs) represent a widely prescribed class of drugs, often used long-term, especially in the elderly.
The appropriate indications of PPI therapy are the so-called acid-related diseases, including peptic ulcer, GERD and gastro-duodenal protection during NSAID treatment.
Gastric function, however, is not usually assessed before starting PPI therapy. It is therefore not always known whether an antisecretory effect is really needed.
Aims & Methods
Aim: To evaluate gastric function by means of GastroPanel®, i.e. the measurement of serum pepsinogens I and II (PGI and PGII), gastrin-17 (G-17) as well as anti-*Helicobacter pylori* antibodies (IgG against *H.p.*), in a large population of elderly patients.
The use of these gastric biomarkers allows a non-invasive diagnosis of chronic, atrophic gastritis (CAG) as well as of (present and past) *H.p.* infection.
Subjects and Methods: 328 elderly patients (M = 111, F = 217, mean age = 81 ± 9.3, range = 65-103), hospitalized from March to December 2014, were included in the study.
Medical history, existing morbidities and current drug therapies were collected. PGI, PGII and G-17 concentrations as well as anti-*H. pylori* antibodies were all determined *via* a specific ELISA test (Biohit Oyj, Helsinki, Finland) in fasting serum samples.
Results: 192 (M = 60, F = 132) out of 328 patients (58.5%) were on PPI therapy. GastroPanel® analysis showed that 62 patients (18.9%, M = 19, F = 43, mean age = 81.5 ± 9.0) had CAG, later confirmed by gastric biopsy and histology, while 82 patients (25%, M = 32, F = 50, mean age 81.2 ± 9.0) had *H.p.* infection. More than half (i.e. 32 out of 62, i.e. 51.6%) of the patients with CAG, in whom acid secretion is low or absent, were on PPI therapy.
Conclusion: GastroPanel® is able to identify elderly patients, characterized by low rates of acid secretion, in whom PPI administration is not needed and, therefore, inappropriate, exposing them merely to the long-term risks of this kind of therapy.
This non-invasive approach might decrease drug-induced morbidity and reduce healthcare costs.
Disclosure of Interest: None declared

P1730 THE OVERLAP OF FUNCTIONAL GASTROINTESTINAL DISORDERS AND THEIR ASSOCIATION WITH PERCEIVED JOB STRESS AND PSYCHOSOCIAL FACTORS

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Introduction: The pathophysiologic mechanisms of overlaps of functional gastrointestinal disorders (FGIDs) are not well understood, but it has been hypothesized that they share a common pathogenesis such as psychosocial factors.
Aims & Methods: The purpose of this study was to determine the effect of job stress and other psychosocial factors on the overlap syndrome. Within a cross-sectional survey, 1140 firefighters completed validated questionnaires regarding FGIDs by at least once a week of typical reflux symptoms and Rome III criteria. Self-reported questionnaires for perceived job stress (KOSS-26), anxiety (GAD-7), depression (PHQ-9), coping styles (WCC), social support and quality of life (WHOQOL-BREF) was also completed.
Results: The overlap syndrome was observed in 134 subjects (11.8%) and each two-way combination of the overlap syndrome was present in overlaps between GERD and IBS were found in 86 subjects (7.6%), GERD and FD in 81 subjects (7.1%), GERD and FC in 49 subjects (4.3%), FD and IBS in 48 subjects (4.2%), FD and FC in 19 subjects (1.7%). The overlap syndrome highly associated with perceived job stress compared to the subjects without overlap syndrome (OR = 10.6, 95% CI: 2.3-49.3, p = .002). Subjects reporting anxiety had a 6.3-fold increased risk of the overlap syndrome (95% CI: 4.2-9.3, $p < 0.001$), and with depression had a 9.3-fold increased risk of the overlap syndrome (95% CI: 5.9-14.6, $p < 0.001$) compared to the subjects without overlap syndrome. We also observed a weak inverse association between informative support and the overlap syndrome (OR = 0.1, 95% CI: 0.0-0.9, p = .043). Impaired quality of life was found in the subjects with overlap syndrome.
Conclusion: Perceived job stress is strongly associated with the overlap syndrome in firefighters. Anxiety and depression was also related to the overlap syndrome and weak inverse association with informative support. Recognition and management of these psychosocial factors may aid in the management of the overlap syndrome.
Disclosure of Interest: None declared

P1731 VISCERAL ABDOMINAL OBESITY MEASURED BY CT SCAN IS ASSOCIATED WITH AN INCREASED RISK OF FUNCTIONAL DYSPEPSIA

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Introduction: Functional dyspepsia (FD) is very common, but its negative influences significantly affect the quality of life. The prevalence of obesity has been increasing worldwide and has been shown to increased risk of various gastrointestinal symptoms. But the relationship between visceral abdominal obesity and incidence of FD is not studied yet.
Aims & Methods: The purpose of this study was to evaluate the association between abdominal adipose tissue area and the risk of FD.
This is a case-control study that compared the abdominal adipose tissue area between subjects with FD and controls without FD, who underwent abdomen computerized tomography (CT) images for routine health checkups in a health promotion center. Retrospectively, telephone survey was conducted to diagnose FD by Rome III criteria. We measured body mass index (BMI), waist circumference, visceral adipose tissue (VAT) area, subcutaneous adipose tissue (SAT) and VAT/SAT ratio to evaluate the association between FD and abdominal obesity.
Results: A total of 363 subjects were included. FD was diagnosed in 90 subjects (24.8%). Among them, postprandial distress syndrome (PDS) was diagnosed in 42 subjects (46.7%), epigastric pain syndrome (EPS) in 33 subjects (36.7%) and mixed type (overlapping PDS and EPS) in 15 subjects (16.7%). In the univariate analysis, waist circumference, VAT area, TAT area, VAT/SAT ratio and erosive esophagitis subjects were significantly higher in the FD group than in the non-FD group. In the multivariate analysis, a higher VAT area (odds ratio (OR), 3.76; 95% confidence interval (CI), 1.24–11.40; highest quartile vs. lowest quartile, $p = 0.019$) and VAT/SAT ratio (OR, 2.35; 95% CI, 1.27–4.32; highest quartile vs. lowest quartile, $p = 0.006$) were independently associated with a risk of FD.
Conclusion: Visceral abdominal obesity measured by VAT area and VAT/SAT ratio is associated with an increased risk of FD.

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P1732 FUNCTIONAL DYSPEPSIA IS ASSOCIATED WITH DUODENAL EOSINOPHILIA IN AN AUSTRALIAN PAEDIATRIC COHORT

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Introduction: Functional dyspepsia (FD) is a highly prevalent functional gastrointestinal disorder with unknown aetiology. Duodenal eosinophilia has been implicated in the pathophysiology of functional diseases in adults[1] and in a few paediatric studies[2].
Aims & Methods: We aimed to assess the association between dyspeptic symptoms and duodenal eosinophilia in children referred for upper endoscopy. All children who had normal endoscopic and pathologic findings on initial reports were included in this retrospective single centre cohort study (2010-2014). Cases were children with FD, defined as epigastric pain or discomfort for more than 2 months with no response to acid suppressants. Controls were those with non-erosive reflux disease, dysphagia or adolescent rumination syndrome. Duodenal biopsies were reevaluated by pathologists blinded to clinical diagnosis. Intramucosal eosinophils were counted per mm^2 on haematoxylin and eosin stained digital imaged sections using Aperio eSlide Manager. Demographics, clinical variables, family history and histologic findings were compared between cases and controls.
Results: In total, 36 FD cases and 36 controls were identified of which 56% and 53% were female, respectively (p = 0.81). Mean (± SD) age was higher in cases compared to controls (13.6 (± 3.1) vs. 10.5 (± 4.0) years; p = .001). Dyspeptic symptoms (epigastric pain in 81% and upper abdominal discomfort in 33%) were food-related in 69% and nocturnal in 31% of cases. Self-reported nausea (64% vs. 17%; p < .0001), lethargy (19% vs. 0%; p = .005) and family history of functional gastrointestinal disorders (28% vs. 3%; p = .003) were more common in cases than controls. There was a higher rate of atopic history (39% vs. 25%; p = .21) and psychological co-morbidity (53% vs. 39%; p = .24) in cases than controls, but this did not reach statistical significance.

Duodenal intraepithelial lymphocyte counts per 100 enterocytes were similar in cases and controls (median (IQR) 10 (8-13) vs. 12 (8-18); p = 0.12). Duodenal eosinophil counts per mm^2 were significantly increased in cases compared to controls (151 (118-207) vs. 76 (60-106); p < 0.001).

Conclusion: FD is associated with duodenal eosinophilia in children. The high rate of atopic and psychological co-morbidity suggests multifactorial mechanisms in FD, and may explain why current therapeutic options aimed at symptom control (acid suppression and prokinetics) are largely unsatisfactory. This study confirms recent reports of duodenal eosinophilia in adults with FD, and underlines the potential role of eosinophils in symptom generation as well as being a potential therapeutic target.

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P1733 HIGH PREVALENCE OF POSTPRANDIAL DISTRESS SYNDROME-LIKE DYSPEPSIA IN PATIENTS WITH AUTOIMMUNE ATROPHIC GASTRITIS

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Introduction: Autoimmune gastritis (AG) is a chronic disease characterized by loss of oxyntic glands, leading to hypochlorhydria and intrinsic factor deficiency, and, in a later stage, pernicious anemia. AG is considered a silent disease, often occurring with unspecific symptoms and to date, few data on its clinical features are available.

Aims & Methods: Aim of this study was to assess the presence of gastrointestinal (GI) symptoms in AG patients. A cohort of 379 AG patients diagnosed from 1995 to 2013 in a tertiary referral center, was retrospectively analyzed. Gastroscopy was performed in 62.9% of patients for anemia, in 29.8% for GI symptoms and in 7.3% for extra GI or other symptoms. GI symptoms were detected at the time of the first visit and classified following Rome III Criteria. Symptoms were analyzed either separately or altogether to classify patients in dyspepsia, subdivided in epigastric pain (EPS) and post-prandial distress (PDS) syndromes or gastro-esophageal reflux disease (GERD). Since the study dealt with patients affected by AG, PDS and EPS dyspepsia will be indicated as PDS- and EPS-like throughout the abstract. Data were expressed as median (range), and differences between symptomatic and asymptomatic patients were analyzed using Fisher's exact test or Mann-Whitney test; *P* values <0.05 were considered statistically significant.

Results: 56.7% of AG patients had one or more GI symptoms. The table shows the comparison of clinical features between symptomatic and asymptomatic patients.

(*p < 0.05)	All patients n = 379	Symptomatics n = 215	Asymptomatics n = 164
Female gender	266 (70.2%)	162 (75.3%)	104 (63.4%)*
Age median (range)	55 (17-83)	53(22-80)	57 (17-83)*
Smoking	72 (19%)	33 (15.3%)	39 (23.8%)*
Pernicious anemia	203 (53.6%)	101 (47%)	102 (62.2%)*
Parietal cell autoantibodies (PCAs)	255 (67.3%)	144(67%)	111 (67.7%)
Active *H. pylori* (histology)	95 (25.1%)	54 (25.1%)	41 (25%)
Autoimmune disorders	158 (41.7%)	90 (41.9%)	68 (41.4%)

Females were more prevalent in the symptomatic patients. Symptomatic patients were significantly younger and more often no smokers in comparison to asymptomatic. Pernicious anemia was significantly more frequent in the asymptomatic group. No differences were found between symptomatic and asymptomatic patients concerning the presence of PCAs, prevalence of *H. pylori* infection and the concomitant presence of autoimmune disorder. Among symptomatic patients, 69.8% had only upper symptoms, 15.8% lower symptoms and 14.4% upper and lower combined. Analyzing patients with upper GI symptoms, 60.2% reported PDS-like dyspepsia, 3.8% EPS-like dyspepsia, 7.2% overlap PDS and EPS-like dyspepsia, 7.2% GERD, 17.7% GERD and dyspepsia, and 3.8% nausea and/or vomiting.

Conclusion: AG is not a paucisymptomatic condition since more than half of patients have one or more GI symptoms. The most frequently reported symptom is PDS-like dyspepsia. The presence of GERD, even if unfrequently present, does not exclude the diagnosis of AG. This study suggests that in the diagnostic work-up of functional upper GI disorders AG should be considered, especially in PDS-like dyspepsia.

Disclosure of Interest: None declared

P1734 CHILDHOOD RECURRENT ABDOMINAL PAIN IS ASSOCIATED WITH DUODENAL EOSINOPHILIA REGARDLESS OF *H. PYLORI* INFECTION IN A CHILEAN COHORT

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Introduction: Childhood recurrent abdominal pain (RAP) is a common functional gastrointestinal disorder (FGID) with poorly understood pathophysiology.

Aims & Methods: We aimed to investigate histologic features of children with RAP undergoing upper gastrointestinal endoscopy, after exclusion of common organic disease. Children referred for endoscopy were prospectively enrolled at a single tertiary centre between 2008 and 2010, after obtaining informed consent. Cases were defined as children with a clinical diagnosis of RAP, as opposed to controls with proven or suspicious organic disease. Gastric and duodenal biopsies were analysed by pathologists blinded to clinical indication. Demographic and clinical variables, *H. pylori* infection, biochemical, endoscopic and pathologic results were compared between cases and controls.

Results: A total of 101 children were included after exclusion of villous enteropathy (n = 6) and parasitic, rotavirus or salmonella enteritis (n = 14), resulting in 72 cases and 29 controls. There were no significant differences in demographics, clinical symptoms, *H. pylori* infection and endoscopic findings between cases and controls. Duodenal eosinophil counts/5 HPF were significantly increased in cases vs. controls (median (IQR) 86 (62-114) vs. 49 (31-88); p < 0.001) and did not differ regarding age, gender and *H. pylori*. Intraepithelial lymphocytes/100 enterocytes were similar in cases vs. controls (19 (15-25) vs. 18 (14-23); p = 0.89) with ≥ 25 in 25% of cases. Duodenal eosinophilia was equally observed in *H. pylori* negative cases (n = 50) vs. controls (n = 19) (87 (61-119) vs. 53 (36-95); p = 0.01), as well as positive cases (n = 21) vs. controls (n = 10) (85 (55-105) vs. 42 (18-65); p = 0.03). Logistic regression yielded an adjusted odds ratio of 1.23 (95% CI 1.08-1.40) for duodenal eosinophilia in RAP.

Conclusion: Children with RAP have marked duodenal eosinophilia, independent of *H. pylori* infection, suggesting the role of unknown infectious or inflammatory triggers. These findings implicate eosinophils in the pathogenesis of FGIDs in childhood. Further research is needed on the diagnostic and therapeutic benefits of targeting duodenal eosinophilia. Funded by EU CONTENT Project (INCO-CT-2006-032136), CONICYT/BM (RUE #29) and Fondecyt #1100654 and 1130387 (Chile).

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P1735 ENDOSCOPIC MYOTOMY FOR ACHALASIA USING THE HOOK KNIFE FOR A PRECISE CIRCULAR MUSCLE CUT: EVALUATION OF THE SAFETY AND THE EFFECTIVENESS OF THE 54 FIRST CASES

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Introduction: The peroral endoscopic myotomy (POEM) is a promising method for the treatment of the esophageal achalasia. But the precise technique can be refined and the hook knife can be used to precise the myotomy and we evaluated its results in the 54 first patients of our institution.

Aims & Methods: All the consecutive cases refferred for POEM were included and the database was completed prospectively. The patients presented with a complete or incomplete achalasia regarless of the previous treatments were assessed in terms of procedure information and surveillance results.

Results: 54 patients (29 men, average age 59 years) were included. Typical achalasia represented 48 cases (type I: 6, II: 30, III: 12), Jackhammer in 1 case and manometry failure in 6 cases due to the incapacity to pass the probe through the cardia. 36 patients were naives of previous treatments, 10 received previous dilations, 5 Heller's myotomy, 2 botulic toxin and dilation and 1 only botulic toxin. Among the 54 patients, 2 were recused at the beginning of the endoscopy for 1 diverticulum on the tunnel way and 1 largely open cardia. 49 procedures were complete (94.2%), 3 were interrupted (2 sub-mucosal fibrosis preventing the realization of the tunnel and 1 mucosal injury of the tunnel in the cardia). 2 other mucosal injuries occurred but did not prevent to continue the procedure after mucosal closure by clips. Dual Knife ® (n = 41) or the water jet Nestis Enki 2 ® (n = 11) were used for the tunnel. No mucosal injuries were observed with the water-jet system. Hook Knife ® was used for all the myotomies and allowed a precise circular myotomy. The average time of procedure was 96.2 min with a clear learning curve (135-41 min). A pneumoperitoneum was exsufflated with a needle during the procedure in 31 cases (63.2%) without any visible perforation. The 18 first patients were explored by systematic CT scan at day 1 with a pneumomediastinum (n = 14/18), a pneumoperitoneum (n = 14/18) and/or a peumothorax (n = 3/18). 3 patients presented unusual bleedings and one of them presented an hematoma of the tunnel at day 1 without overt bleeding. No sepsis was observed. Feeding was always possible with liquids at day 1. All patients noted a clinical improvement. At 3 months surveillance(available in 42 cases), the mean eckardt score was 1 (0-4) verus 6.5 (3-11) before. The basal

pressure of the SIO was measured in 25 cases and decreased for all patients (8 mmHg (0-15) against 23 mmHg (7-48) initially, $p < 0.01$) as well as the PRI (8 mmHg (0-16) against 23 mmHg (9-28), $p < 0.01$).
Conclusion: Water-jet injection allows rapid and safe tunneling of the submucosa and myotomy with hook knife is very precise. Safety and effectiveness of mytomy is reinforced using these technical refinements.
Disclosure of Interest: None declared

P1736 EFFICACY OF PSYCHOTROPIC DRUGS IN FUNCTIONAL DYSPEPSIA: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Functional dyspepsia (FD) is a chronic gastroduodenal disorder. Individuals with FD demonstrate visceral hypersensitivity, abnormal central pain processing, and low mood. However, it is unclear whether psychotropic drugs are an effective treatment for the condition as, surprisingly, there has been no definitive systematic review and meta-analysis undertaken to date.
Aims & Methods: We performed a systematic review and meta-analysis of randomised controlled trials (RCTs). MEDLINE, EMBASE, EMBASE Classic, PsychINFO, and the Cochrane Controlled Trials Register were searched (up to March 2015) to identify RCTs recruiting adults with FD, which compared psychotropic drugs with placebo. We contacted authors directly to obtain extra data in order to maximise trial eligibility and minimise risk of bias of included RCTs. Dichotomous symptom data were pooled to obtain a relative risk (RR) of remaining symptomatic after therapy, with a 95% confidence interval (CI). Adverse events data were also summarized with RRs. The number needed to treat (NNT) and the number needed to harm (NNH), with 95% CIs, were calculated.
Results: The search strategy identified 2572 citations. Nine RCTs were eligible for inclusion, containing 1099 patients. Six trials were at low risk of bias. Overall, 340 (56.5%) of 602 patients assigned to psychotropic drugs reported persistent or unimproved FD symptoms following therapy, compared with 350 (70.4%) of 497 allocated to placebo. The RR of FD symptoms persisting or not improving after treatment with psychotropic drugs versus placebo was 0.77 (95% CI 0.64 to 0.91) (NNT = 6; 95% CI 4 to 16). The efficacy of individual drug classes is provided in the table. The incidence of adverse events was not significantly higher among those taking psychotropic drugs (RR = 1.17; 95% CI 0.85 to 1.62) but, overall, there were more adverse events leading to withdrawal with psychotropic drugs (RR = 1.96; 95% CI 1.17 to 3.27, NNH = 20; 95% CI 8 to 109).

Drug class	Number of trials	Number of patients	RR of persistent symptoms (95% CI)	Number needed to treat (95% CI)
Antipsychotics	4	197	0.48 (0.36-0.63)	3 (2-4)
Tricyclic antidepressants	2	153	0.75 (0.60-0.94)	7 (4-29)
Selective serotonin re-uptake inhibitors	2	388	1.01 (0.89-1.15)	Not estimable
Serotonin norepinephrine re-uptake inhibitors	1	160	1.02 (0.80-1.30)	Not estimable
5-hydroxytryptamine-$_{1A}$ receptor agonists	1	150	0.79 (0.66-0.94)	5 (3-19)

Conclusion: Psychotropic drugs may be an effective treatment for FD, but the effect appears to be limited to antipsychotics, tricyclic antidepressants, and 5-hydroxytryptamine-$_{1A}$ receptor agonists. Intolerable adverse events may be an issue. More data from large, high quality RCTs are required to support the use of psychotropic drugs in the treatment of FD.
Disclosure of Interest: None declared

P1737 AUTOFLUORESCENCE IMAGING ENDOSCOPY IN DIFFERENTIATING NON-EROSIVE REFLUX DISEASE FROM FUNCTIONAL HEARTBURN: A NEW COMPLEMENTARY METHOD

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Introduction: It is difficult to make a distinction between functional heartburn (FH) and non-erosive reflux disease (NERD) endoscopically. Recently, indistinct mucosal lesions invisible on conventional endoscopy could be revealed [1] with the help of tri-modal endoscope which combines white light imaging (WLI) with autofluorescence imaging (AFI) and narrow band imaging. Also, it was found that AFI could reveal indistinct acid reflux-related mucosal changes [2]. NERD is characterized of the etiology of acid reflux, while FH isn't. Whether AFI endoscopy can be used to differentiate NERD from FH hasn't been investigated.
Aims & Methods: This study aimed to explore the diagnostic ability of AFI endoscopy in distinguishing NERD from FH in patients with classic reflux symptoms but no esophageal mucosal breaks at WLI. In our prospective observational trial, 127 consecutive patients with heartburn or acid regurgitation for more than 6 months were screened in a tertiary referral center. All the participants underwent endoscopy during which WLI was followed by AFI with special focus on the esophagus. Finally, 84 patients with negative esophageal findings at WLI were enrolled. Ambulatory 24-h pH/impedance monitoring was performed and a positive finding was defined as a DeMeester score no less than 14.72 or a positive correlation between symptoms and acid reflux. Accordingly, the subjects were divided into two groups including NERD and presumed FH. On AFI endoscopy, the appearance of one or more longitudinal purple lines longer than 1 cm was defined as indicative of NERD [2]. The diagnostic ability of AFI endoscopy to distinguish NERD from FH was assessed by comparison with the pH/impedance test.
Results: The results of the pH/impedance test and AFI endoscopy in 84 endoscopy-negative patients was listed in Table 1. Comparing with the pH/impedance test, the sensitivity and accuracy of AFI in detecting NERD were 71.7% and 64.3%, respectively. Meanwhile, the specificity of AFI was 55.3%. McNemar test showed no significant difference between AFI and the pH/impedance test ($P = 0.584$).
Table 1: Results of the pH/impedance test and AFI endoscopy

the pH/impedance test positive	AFI endoscopy negative		Total
positive(NERD)	33	13	46
negative(presumed FH)	17	21	38
Total	50	34	84

Conclusion: These findings suggest that AFI may serve as a complementary method when evaluating NERD and FH, although the specificity of this method is needed to be improved.

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P1738 PERORAL ENDOSCOPIC MYOTOMY FOR ACHALASIA - LONG MYOTOMY VERSUS MODIFIED-LENGTH MYOTOMY-A PILOT STUDY

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Introduction: Peroral endoscopic myotomy (POEM) is a minimally invasive endoscopic treatment for achalasia.1 Our objective was to evaluate the relationships between length of myotomy, symptoms, and manometry.
Aims & Methods: Long myotomy (LM) and modified-length myotomy (MM) were defined as ≧ 10cm and ≦5cm length esophageal myotomies, respectively. Nineteen patients with achalasia (n = 19) undergoing POEM underwent LM (n = 8, [Chicago classification type I: 5, type II: 2, type III: 1]) or MM (n = 11, [type I: 8, type II: 3]).2 Written informed consent was obtained from all subjects. All patients had follow up at two months. Procedural success was defined as a post-POEM Eckardt score of less than 2.3
Results: POEM was successfully performed in all patients and no adverse events were observed (0.0%). The overall procedural success rate (Eckardt score less than 2) was 100% in both groups. MM significantly improved achalasia-related symptoms (median Eckardt score; 6 to 1) and reduced lower esophageal sphincter (LES) pressure (37.8 to 7.9 mmHg) with results comparable to LM (Eckardt score; 7.5 to 1, and LES pressure; 30.3 to 7.5 mmHg). Gastroesophageal reflux symptoms were seen in one patient (performed LM for type I achalasia) not receiving a proton-pump inhibitor. There was no recovery of esophageal peristalsis in patients with type I achalasia after POEM in both the LM and MM group. In three patients with type II achalasia who underwent MM (n = 3), two (pre-POEM manometry; single pan-pressurization or week plural pan-pressurization per swallow) had partial recovery of peristalsis, and the other (pre-POEM manometry; strong plural pan-pressurization) had hypercontraction in the esophageal body and developed an esophageal diverticulum. LM for type II&III achalasia (n = 3) completely suppressed esophageal body contractions.
Conclusion: MM and LM are considered equally effective for the treatment of type I achalasia. With type II&III achalasia, preoperative manometry is essential, and LM might be needed in patients with strong plural pan-pressurization (potential for hypercontraction) to prevent the formation of post-POEM esophageal diverticulum.

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P1739 SYMPTOM-BASED DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE: LOW DIAGNOSTIC ACCURACY FOR TYPICAL GERD AS WELL AS SUSPECTED EXTRAESOPHAGEAL DISEASE RESULTS FROM A PROSPECTIVE, MULTICENTRIC SURVEY USING WIRELESS CAPSULE PH METRY

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Introduction: Diagnosis of gastroesophageal reflux disease (GERD) is recommended as a clinical diagnosis based on symptoms. For proper diagnosis of GERD pH metry remains the GOLD standard and is recommended especially for refractory and/or suspected extraesophageal reflux disease (EER).

Aims & Methods: In a multicentric, open label survey in 6 different tertiary centers in Germany, 184 patients (male 111, female mean age 55.9 +/-9.8 years, 2011-2014) were prospectively investigated by wireless capsule pH metry (BRAVO capsule).

Clinical indications for referral were categorized in a) ''typical GERD symptoms'' (n = 60), b) ''suspected EER'' (n = 20) and c) ''exclusion of GERD'' for patients unlikely to have GERD (n = 39).

Furthermore, patients were systematically asked for the exact description of symptoms and for a self-report about the occurrence of heartburn and regurgitation as well as cough and hoarseness. Diagnosis of GERD was confirmed by wireless pH metry (acid exposure time $<$ pH1 (AET) $>$ 4.5% and/or DeMeester $>$ 14.72). The parameters of pH metry were further compared between the three clinical groups.

Results: 139 patients were included in the final analysis. Reasons for exclusion were previous anti-reflux surgery (n = 6), ongoing PPI therapy (n = 38) and drop-off the capsule (n = 1).

Diagnosis of ''typical, symptomatic GERD'' was proven in 61.6%; suspected EER pH metry was confirmed in only 40%. In group (c) (to exclude GERD), 75% of the patients actually had abnormal acid exposure.

Regarding symptom-based diagnosis, heartburn as predominant was described by 63 patients with very poor diagnostic values; regurgitation by 15 patients, only; cough and hoarseness by 28 and 25 patients, respectively. All self-reported symptoms had comparable low diagnostic test values (table 1). Analyzing all patients with abnormal AET, patients with EER showed less intense acid exposure to the distal esophagus than patients with ''typical GERD'' and patients ''to exclude GERD'' (AET %: 9.95 ± 1.85 vs. 5.44 ± 0.89, p = 0.06; DeMeester score: 32.77 ± 5.81 vs. 20.30 ± 3.77, p = 0.07).

	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (PPV, 95% CI)	Negative predictive value (NPV, 95% CI)
Heartburn	48% (0.37-0.59)	59% (0.44-0.72)	67% (0.54-0.78)	40% (0.29-0.52)
Regurgitation	10% (0.05-0.19)	88% (0.77-0.96)	60% (0.33-0.84)	37% (0.28-0.46)
Cough	20% (0.12-0.29)	79% (0.65-0.89)	61% (0.40-0.79)	37% (0.28-0.47)
Hoarsness	17% (0.10- 0.27)	81% (0.67-0.90)	60% (0.39-0.79)	37% (0.28-0.46)

Conclusion: Accuracy of symptom-based diagnosis for GERD was poor in this study cohort, even by GI specialists. Description of symptoms and self-reports are most likely influenced by linguistic differences, therefore early referral to reflux testing should be considered in the clinical management.

Disclosure of Interest: None declared

P1740 GASTRIN 17 AS NON INVASIVE MARKER OF REFLUX DISEASE

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Introduction: Gastrin-17 (G-17) could be related to the pathophysiology of GERD through its motor and secretory activities on the upper GI Tract. The peptide indeed decreases lower esophageal sphincter pressure (LESP) and increases the number of transient lower esophageal sphincter relaxations (TLESR), features that are associated with the disease. Gastrin also stimulates gastric acid secretion, thus increasing the aggressive power of the gastric contents that will reflux into the esophagus. Thanks to a feed-back mechanism, plasma G-17 can be considered a mirror of acid secretion: the lower G-17 values, the higher gastric acid secretion. G-17 low levels could therefore be a marker of acid-related conditions, like GERD.

Aims & Methods

Aim: To evaluate the role of G-17 in the diagnosis of GERD in a cohort of GERD or dyspeptic patients.

Material and Methods: 639 patients with typical GERD or dyspeptic symptoms were enrolled in the study. Every patient underwent upper GI endoscopy and had a Gastropanel® by means of immunoassay. 126 out of patients had Los Angeles A esophagitis, 28 patients had Los Angeles B esophagitis, 214 had negative endoscopy (NERD), 114 had chronic atrophic gastritis and 127 were *H.p.* negative dyspeptic subjects.

Statistical analysis was performed by means of logistic regression.

Results: Patients with A esophagitis A and B esophagitis as well as those NERD patients showed a basal G-17 value, which was significantly lower ($p = 0.0001$) than that seen in patients with dyspepsia or CAG (used as control groups).

Conclusion: These results confirm that – by taking a cut-off $<$ 1.9 ng/dL - G17 basal values are useful in the diagnosis of reflux disease. Moreover, being a non-invasive test, able to identify patients with GERD or NERD, G-17 measurement should allow to limit unnecessary endoscopy and histology.

Additional studies are needed to confirm these results.

Disclosure of Interest: None declared

P1741 A NEW DEVICE FOR DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE: ESOPHAGEAL MUCOSAL IMPEDANCE (MI)

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Introduction: Despite the high prevalence of gastroesophageal reflux disease (GERD) and its impact on quality of life and economic burden, the current GERD diagnostics are suboptimal due to limited sensitivity and specificity, and they are constrained by measurement of esophageal reflux during *a single time point* at *a specified location*. They measure the presence of reflux but do not measure the *long-term mucosal consequences of GERD*, a significant limitation of existing platforms. We developed a minimally invasive device to assess changes in esophageal mucosal impedance (MI), a marker of reflux.

Aims & Methods: The aims of this study were to test the accuracy and reliability of our new devoloped device and identify how measurements react to the used ring sizes and separations.

Methods: Six combinations of single channel Mucosal Impedance (MI) catheters with 360 degree rings were tested by varying ring length to 2 or 3 mm and ring separation to 2, 3 or 4 mm. Each catheter could be easily traversed through the working channel of an upper endoscope. We performed a prospective longitudinal study of patients with erosive esophagitis (n = 40), nonerosive but pH-positive GERD (n = 49), and those without GERD (n = 55). All patients underwent endoscopy and wireless 48-hour pH monitoring 10-days *off* PPI therapy. During index endoscopy, *MI* was measured from the esophagitis site as well as 2, 5 and 10-cm above squamocolumnar junction (SCJ). The optimal MI sensor ring size and separation were determined based on ROC analysis. Predictive value positive of MI measurements were then compared to pH monitoring in diagnosing GERD.

Results: When MI measurements were done on esophagitis site, we observed that MI tracked the grade of esophagitis, $F(3, 57) = 5.34$, $p < .0027$. Next, we evaluated whether MI values can predict esophagitis when the ring size and spacing was 3 and 2 mm, respectively. Our results indicated that MI measured with the 2 mm spacing predicted esophagitis, $\chi^2(1, 109) = 10.38$, $p < .0014$, showing that 3 mm ring size and 2 mm spacing is adequate for prediction of esophagitis. The Spearman's rank correlation between Bravo pH Monitoring values and MI measurements was significant when 2 mm spacing was used from the probes which were placed 2 or 5 cm above SCJ, rs = -.442 and -.430 for 2 cm and 5 cm probes, respectively.

Conclusion: Our results support the conclusion that when the ring size of 3 mm and 2 mm separation are used for MI measurements, we can track the grade of esophagitis. Further, with this configuration, the existence of esophagitis could be predicted. Sensitivity and specificities in this configuration were found to be comparable to Bravo pH Monitoring. Last but not least, we observed significant correlations between our MI values from this configuration and Bravo pH Monitoring. All in all, we conclude that the ability of this configuration to diagnose GERD simply, efficiently and reliability by through the endoscope application during index endoscopy is an innovative step forward in reflux monitoring.

Disclosure of Interest: None declared

P1742 QUESTIONNAIRES MAY BE INSUFFICIENT TO DIAGNOSE GASTROESOPHAGEAL REFLUX DISEASE (GERD) IN MORBIDLY OBESE PATIENTS WITH TYPE 2 DIABETES

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Introduction: GERD is highly prevalent in morbidly obese subjects. Bariatric surgery with gastric sleeve may worsen existing GERD, but few studies have assessed how GERD should be diagnosed in a population referred for bariatric surgery.
Aims & Methods: Our aim was to assess and compare the prevalence of GERD as evaluated by endoscopic examinations and validated questionnaires, respectively, in a population of morbidly obese subjects with type 2 diabetes. Consecutive patients with type 2 diabetes and BMI ≥ 35 kg/m^2 eligible for bariatric surgery, recruited from a tertiary care obesity centre in Southern Norway were included. The validated questionnaires GERD Q and GSRS (Gastrointestinal Symptom Rating Scale) were used for diagnosis of GERD. Upper endoscopy was used for diagnosis and grading of esophagitis, according to the Los Angeles (LA) classification.
Results: A total of 51 patients were included, mean age 47 years (range 32-61) and BMI 43 kg/m^2 (range 35-58). Four out of 51 patients reported dyspepsia according to the GERD Q or GSRS questionnaires. Upper endoscopy showed no erosive reflux in 18 out of 51 patients (35%), reflux LA grade A in 20 out of 51 patients (39%) and reflux LA grade B in 13 out of 51 patients (26%). No patients had reflux LA grade C or D. Twenty-nine out of 33 patients (88%) with reflux A or B were asymptomatic according to the applied questionnaires. No patients used proton pump inhibitors.
Conclusion: Few patients had symptomatic reflux disease as compared with previous studies, although upper endoscopy revealed pathological findings in 65% of the participants. There was no association between symptomatic disease and endoscopic finding. Our findings indicate that the GERD Q and GSRS questionnaires have a too low sensitivity to diagnose reflux disease in this patient group.
Disclosure of Interest: None declared

P1743 ARE BASELINE IMPEDANCE LEVELS ASSESSED DURING ESOPHAGEAL IMPEDANCE MANOMETRY HELPFUL IN DISCRIMINATING PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE FROM THOSE WITHOUT? A PILOT STUDY

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Introduction: Previous studies by means of 24h impedance-pH monitoring highlighted the correlation between baseline impedance levels and integrity of the esophageal mucosa and, more important, the possibility to use this parameter to discriminate between different subtypes of GERD. However, no previous studies investigated the possibility to achieve similar results by using impedance-manometry, a test requiring shorter time and providing further data about esophageal motility.
Aims & Methods: Aim of our study was to measure baseline impedance levels during manometric assessment and to correlate them with those obtained at 24h impedance-pH monitoring. Consecutive patients with typical reflux symptoms underwent upper endoscopy and multiple biopsies were taken at Z-line and 2 cm above it, in order to assess the presence and severity of microscopic esophagitis. Within 3 days from endoscopy, patients underwent esophageal impedance-manometry and impedance-pH testing off-therapy. We evaluated BI values for at least 30 seconds during impedance manometry, expressed as mean value over 3 intervals of 10 seconds each. Moreover, BI at 3 and 5cm above the LES, was assessed on MII-pH recording during the overnight rest, for at least 30 minutes. Twenty healthy volunteers (HVs) who underwent the same procedures were also used as controls.
Results: We included 38 patients (M/F 17/11; BMI 27; age 46) with classified according to endoscopy and impedance-pH as: 8 grade A erosive esophagitis (EE), 10 non-erosive reflux disease (NERD), 10 hypersensitive esophagus (HE) and 10 with functional heartburn [(FH) M/F 2/8; BMI 25; age 40]. Moreover, 20 HVs [11F/9M; BMI 24; mean age 44] were included. BI values during impedance-manometry were lower in patients with GERD (2290; 95%CI:1518-3476) than in those without (FH/HVs; 3677, 95%CI: 2648-5074) ($p < 0.05$). Moreover, BI values were lower in patients with ME compared to those without (mean 2178 vs 3328; $p < 0.05$). Although BI levels progressively decreased with the increasing severity of mucosal damage (EE < NERD < HE < FH), a statistical significance was not reached. Finally, BI values assessed during manometry showed a positive correlation with BI levels assessed during impedance-pH monitoring ($r = 0.37$; $p = 0.06$).
Conclusion: Baseline impedance levels measured during esophageal impedance-manometry havebeen associated to the diagnosis of GERD in patients with typical reflux symptoms. In patients with limited compliance this may represent an alternative method in order to investigate GERD. However, due to the complexity of this disorder, the miscellaneous manifestations and inconstant benefit of treatment, MII-pH study remains crucial in the management of patients referred to tertiary centers.
Disclosure of Interest: None declared

P1744 PEPSIN DETERMINATION IN SALIVA AND OROPHARYNGEAL PH - MONITORING FOR THE DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH PRIMARY EXTRA-ESOPHAGEAL SYMPTOMS

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Introduction:
The common standard methods do not enable a sufficient and accurate diagnosis, if extraesophageal symptoms are related to gastroesophageal reflux disease (GERD). The aim of this study was to evaluate the role of pepsin in saliva and oropharyngeal pH - monitoring for the diagnosis of extraesophageal reflux disease.
Aims & Methods: Twenty consecutive patients with primary extra-esophageal GERD symptoms underwent gastroscopy, high-resolution esophageal manometry, 24-hour esophageal impedance pH monitoring (MII-pH) and a barium esophagography. In addition, an ENT examination was performed, including the Belafsky Reflux Finding Score (RFS) as assessment tool. Quality of life was evaluated by means of the Gastrointestinal Quality of Life Index (GIQLI). Evaluation of extra-esophageal symptoms was carried out, using the standardized Belafsky Reflux Symtom Index (RSI) questionnaire. Three times during the 24-h-MII-pH monitoring, a pepsin - determination in saliva (Peptest, RDBiomed ^{TM}) was accomplished, one sample with a pepsin concentration > 210ng/ml was regarded as positive test. Simultaneous to the 24-h-MII-pH monitoring and collection of saliva samples, a detection of laryngopharyngeal reflux events by using the Restech Dx-pH Measurement System ^{TM} (Dx-pH) was performed. Correlation analyses were performed, and statistical significance was defined as a p-value of <0.05.
Results: Of the 20 patients, 12 (60%) patients were male and 8 (40%) were female, the mean age was 49.58 ($\pm$ 11.47) years. There was a significant correlation ($p < 0.038$) between the mean values of RFS score and GIQLI score, as well as between the mean values of RSI score and GIQLI score ($p < 0.029$). A positive Peptest showed a correlation with a pathological DeMeester score ($p < 0.039$), RSI score ($p < 0.002$), pathological results in Dx-pH monitoring ($p < 0.002$) and layringitis gastrica ($p < 0.0001$). Furthermore, elevated Dx-pH results showed a significant correlation with a pathological DeMeester score ($p < 0.002$), RSI score ($p < 0.002$) and laryngitis gastrica ($p < 0.002$).
Conclusion: Pepsin seems to play a major role in the pathophysiology of extra-esophageal symptoms of GERD. Patients refractory to medical treatment, but with positive pepsin testing in saliva and pathological findings in oropharyngeal pH-metry could profit from antireflux surgery. To substantiate this conclusion, further studies will have to be conducted in the future.
Disclosure of Interest: None declared

P1745 USAGE OF NEW NORMAL DATA FOR PH-IMPEDANCE MONITORING IN THE DIAGNOSIS OF PATIENTS WITH REFRACTORY REFLUX SYMPTOMS SIGNIFICANTLY DECREASES FUNCTIONAL HEARTBURN IN FAVOR OF REFLUX

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Introduction: Multichannel intraluminal impedance (MCII) and pH monitorization while receiving drug therapy have an importance place in differential diagnosis of patients presenting with the symptoms of refractory gastro-esophageal reflux disease (GERD) as well as in the evaluation of the efficiency of treatment (1). In the evaluation of the efficacy of therapy with proton pump inhibitors (PPIs), it would be a more appropriate approach to take normal data from healthy volunteers who are already on therapy with PPIs as the reference rather than obtaining reference values from healthy volunteers (2,3).
Aims & Methods: The aim of the present study was to evaluate the impact of the normal ranges on the diagnosis that were obtained from the healthy volunteers on PPI therapy in a recent study by Zerbib et al and which shows efficacy of the anti-reflux therapy with PPIs in healthy volunteers. In the present study, MCII and pH monitorization data of patients with refractory GERD were compared to the reference values obtained from healthy volunteers receiving or those not receiving PPI therapy in the study by Zerbib et al (3).
Results: The present study included 41 patients with refractory reflux who underwent MCII and pH monitorization while receiving therapy with PPIs. Considering normal data from healthy volunteers who were not receiving PPI therapy, 29% were diagnosed with persistent GERD, 54% were diagnosed with functional heartburn, and 17% were diagnosed with hypersensitive esophagus. Of healthy volunteer's normal data who were receiving PPI therapy, 80% were diagnosed with persistent GERD, 13% were diagnosed with functional heartburn, and 7% were diagnosed with hypersensitive esophagus. We found a significant difference between healthy volunteers receiving and those not receiving therapy with PPIs in terms of the diagnosed conditions in each group ($p = 0.0001$).
Conclusion: Our study showed that changes in the reference values also resulted in a change in the diagnosis of refractory reflux. Setting reference values based

on the data of healthy volunteers who are receiving PPI therapy may significantly decrease the rates of functional heartburn and hypersensitive esophagus, while evaluating patients with refractory GERD who are on PPI therapy, using MCII and pH monitorization, and this may substantially affect the diagnosis and the treatment thereafter.

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Disclosure of Interest: None declared

P1746 BASELINE IMPEDANCE VALUES CAN REPRESENT A MARKER OF GASTROESOPHAGEAL REFLUX DISEASE AND ARE STRONGLY RELATED WITH THE DURATION OF THE DISEASE

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Introduction: Baseline impedance values (BI) has been recently proposed as an up and coming parameter to diagnose gastroesophageal reflux disease (GERD) in patients with typical reflux symptoms. Moreover, it has been described a strong correlation between BI values and the symptom relief during proton pump inhibitor treatment (PPI). However, a partial overlap between BI levels in responders and non-responders has been observed.

Aims & Methods: The aim of the study was to evaluate BI levels in consecutive patients with heartburn responder and non-responder to acid suppressive therapy and to detect the relationship between BI values and number of months of GERD-related symptoms in the same population.

NERD patients with heartburn were enrolled and asked to indicate the level of severity of their symptoms and from how long they experienced heartburn (i.e. disease durantion in months). Thereafter, this patients underwent 24-h impedance-pH testing off-PPI therapy and we selected those with normal acid exposure (AET) and number of reflux events. Thus, 120 patients undertook an 8-week course of PPIs. Sixty of them with $>50\%$ symptom improvement were classified as PPI-responders: 30 patients with pathophysiological characteristics of functional heartburn (negative symptom-reflux correlation; FH + PPI) and 30 with hypersensitive esophagus (positive symptom-reflux correlation; HE). The remaining 30 patients with a $<50\%$ improvement to treatment and with pathophysiological characteristics of functional heartburn were classified as PPI non-responders (negative reflux symptom correlation; FH-PPI). All impedance-pH tracks were manually reviewed and BI value were calculated at the impedance channel placed 5cm above LES for 30 minutes during overnight rest.

Results: The mean duration of symptoms (in months) was not different between FH + PPI (34.1 ± 15.4), HE (35.7 ± 17.8) and FH-PPI (36.5 ± 15.5); p = ns. Patients with FH + PPI showed a higher mean AET (1.9%±1 *vs* 0.6%±0.6, $p < 0.05$), mean reflux number (30.4 ± 9.3 *vs* 23.5 ± 7.9, $p < 0.05$) and acid reflux number (17.1 ± 8 *vs* 10 ± 6.9, $p < 0.05$) compared to FH-PPI. Patients with HE showed mean AET (2.3%±1.8) and total reflux number (34.6 ± 10.4) similar to those recorded in FH + PPI (p = ns). Baseline impedance levels were lower in FH + PPI (1949.6 ± 548.8) and in patients with HE (1839.7 ± 467.6) than in FH-PPI (3812.8 ± 810.2) ($p < 0.001$). The overall correlation between BI and disease duration in months was poor (r = -0.343; p = 0.065) but when we evaluated the patients who responded to PPI (HE and FH + PPI) we found a very strong correlation between baseline value and duration of the disease (r = -0.920; p = 0.0001).

Conclusion: Our results showed a very strong correlation between lower BI and response to PPI treatment. BI could represent a marker for reflux-induced changes of the esophageal mucosa and could help to identify patients affected by HE, especially when reflux-symptom association analysis fails to do it. We also found a strong negative correlation between BI values and disease duration in PPI-responder patients, thus corroborating the relevance of this objective marker in evaluating the esophageal mucosal impairment.

Disclosure of Interest: None declared

P1747 THE DISTAL CONTRACTILE INTEGRAL DURING MULTIPLE RAPID SWALLOWS IS INVERSELY CORRELATED WITH ACID EXPOSURE TIME

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Introduction: Multiple rapid swallowing (MRS) during esophageal high-resolution manometry (HRM) is increasingly utilized as provocative maneuver to assess post deglutitive inhibition and rebound contraction (i.e., esophageal smooth muscle peristaltic reserve).

Aims & Methods: The aim of this study was to evaluate the correlation between amplitude of MRS and ratio DCI MRS/wet swallow with esophageal acid exposure time (AET) and baseline impedance values (BI) in patients with heartburn. We enrolled 48 consecutive patients with heartburn and negative endoscopy who underwent HRM and 24-h impedance and pH study to detect GERD. All patients were divided into two different groups: abnormal AET (NERD); normal AET, normal number of reflux episodes and negative symptom-reflux association (functional heartburn, FH). HRM was performed with 10 wet swallows and one MRS (one swallow every 2–3s, each of 4 ml of water). Patients with major motor disorders were excluded. Mean distal contractile integral (DCI) and MRS-DCI were calculated and then correlated with AET.

Results: We analyzed 40 patients: 22 NERD patients (12 male, 10 female), and 26 FH patients (10 male, 16 female). Mean age was similar between the two groups. Eight patients were excluded (5 for major motor disorders, 3 for positive SI/SAP with normal AET/number of refluxes). As expected, mean AET and number of refluxes were higher in NERD compared to FH ($p < 0.05$). HRM was normal in all selected patients. Mean DCI was similar between NERD and FH (p = n.s.). Mean MRS-DCI was higher in FH than in NERD ($p < 0.005$). The ratio DCI MRS/wet swallow was higher in FH than in NERD (1.8 vs 0.9 respectively). The ratio DCI MRS/wet swallow was inversely correlated with AET (-0.828; $p < 0.001$) and directly correlated with BI (0.854; $p < 0.001$).

TABLE 1: epidemiologic, MII-pH and HRM findings in NERD and FH patients

	NERD (22)	FH (26)	p
Mean age (sd)	51.2 (14.9)	48.2 (14.5)	0.484
Mean BMI (sd)	24.8 (3.8)	23 (2.5)	0.265
Mean AET (%) (sd)	6.7 (3.3)	0.9 (0.8)	0.001
Number of refluxes (sd)	77.7 (31.8)	29 (10.1)	0.001
Patients with negative SI/SAP (%)	5 (22.7%)	26 (100%)	0.05
Mean DCI (mmHg*cm*s) (sd)	1342.4 (801.3)	1404.3 (972.6)	0.813
Mean MRS-DCI (sd)	1268.1 (833.2)	2264.8 (1411.9)	0.005
DCI MRS/wet swallow¶	0.9 (0.2)	1.8 (0.8)	0.0001

¶ = DCI MRS/wet swallow has been provided as suggested by Shaker A et al.

Conclusion: Following MRS, NERD patients showed suboptimal contraction response as compared with FH. Moreover, MRS response was inversely correlated with AET. Overall, this parameter is another potential tool to assess risk for increased acid exposure time.

Disclosure of Interest: None declared

P1748 THE MEASUREMENT OF BASELINE IMPEDANCE IS USEFUL FOR DIAGNOSIS OF PPI-RESISTANT NERD PATIENTS

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Introduction: The basal impedance level evaluated by 24-hour intraesophageal pH-multichannel intraluminal impedance (24pHMII) has been reported to be the index of inflammation of the esophageal mucosa caused by acid exposure. However, there has been no unified opinion regarding the 24pHMII procedure or evaluation system. Moreover, no report exists regarding the relationship between the condition of proton pump inhibitor (PPI)-refractory non-erosive gastro-esophageal reflux disease (NERD) patients and the basal impedance level.

Aims & Methods: We evaluated the usefulness of the measurement of impedance in PPI-refractory NERD patents, and the relationship between the impedance and reflux symptoms. Sixty-seven NERD patients without esophageal motility disorder underwent 24-pHMII while taking the PPI. The impedance was measured at three time points; 0:30 am, 10:00 am and 04:00 pm.

Results: The mean value of the impedance did not differ among the three time points in 67 PPI-refractory NERD patients (0:30 am, 3162.0 ± 2035.0 Ω; 10:00 am, 3140.6 ± 1986.5 Ω; 04:00 pm 3124.8 ± 1816.1 Ω). Therefore, we defined the mean value of the impedance at 10:00 am as the basal impedance value. Acid exposure time (AET) negatively correlated the acid present time (APT) among the three time points ($p < 0.01$). Sixty-seven NERD patients were divided into two groups; 49 patients with esophageal acid reflux events [endoscopy-negative reflux disease (ENRD) group] and 18 patients without esophageal acid reflux events [functional heartburn (FH) group]. ENRD group were subdivided into 20 patients with prolonged acid exposure time (pH-POS group) and 29 patients with normal acid exposure time [Hypersensitive esophagus (HE) group]. There

were no significant differences related with the patients' background, their quality of life and symptoms between ENRD group and FH group. There were also no significant differences related with the patients' background, their quality of life, gastroesophageal reflux (GER) episodes among pH-POS group and HE group. The average of basal impedance in the ENRD group was significantly lower than FH group (ENRD group, 2793 ± 2125.5 vs. FH group, 4085.9 ± 265.7, $p < 0.01$). AET and APT were significantly related with the basal impedance in the ENRD group (AET, r = -0.34, $p < 0.05$; APT, r = -0.43, $p < 0.05$). Median Bolus Clearance Time (MBCT) and the Longest Episode (LE) were significantly related with the basal impedance in the ENRD group (MBCT, r = -0.45, $p < 0.01$; LE, r = -0.48, $p < 0.01$). However, there was no significant difference between the basal impedance and the reflux in the FH group.

Conclusion: The measurement of basal impedance is simple method for evaluating the condition of PPI-resistant NERD patients. The measurement of basal impedance value was useful for distinguishing ENRD patients from FH patients in the PPI-resistant NERD patient.

Disclosure of Interest: None declared

P1750 INCREASING MICRO-RNAS EXPRESSION IN BARRETT'S ESOPHAGUS AFTER RADIOFREQUENCY ABLATION

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Introduction: Radiofrequency ablation (RFA) leads to replacement of Barrett's esophagus (BE) mucosa with a neosquamous epithelium, but sometimes the metaplastic mucosal regression is unsatisfactory after initial procedure. Thus the additional biomarkers that are associated with an increased risk of progression to adenocarcinoma are needed.

Recently, it has been shown that several microRNAs (miR-192, miR-194, miR-196a, and miR-196b) high expression is associated with the progression of BE to esophageal adenocarcinoma (EAC).

Aims & Methods: This study aim was to identify microRNAs levels before and after RFA procedure and to assess their prognostic role in RFA outcome.

We included 13 patients who underwent RFA for BE with low grade dysplasia. Esophageal mucosa of 4 patients with BE without dysplasia represented controls.

The expression of 4 miRNAs (hsa-miR-192, hsa-miR-194, hsa-miR-196a, hsa-miR-196b) in esophageal mucosa and blood samples before RFA procedure and in 6 months after first RFA procedure was determined using quantitative real-time RT-PCR technique (iQ5 Biorad, USA). MiRNA was extracted using MirVana miRNA Isolation Kit (Thermo Fisher Scientific, USA). cDNA expression levels was measured by using TaqMan MicroRNA RT kit and TaqMan MicroRNA Assay (Thermo Fisher Scientific, USA).

6 patients required only one RFA procedure to complete IM eradication, which was confirmed both in endoscopy and pathology. Another 6 patients needed more than 1 RFA procedure (2-4).

Results: Expression levels (mean Ct - threshold cycle) of miR-192, -194, -196a, -196b assessed before RFA were: 20, 23; 21,6; 24,47; 27,14, respectively. All 4 microRNAs expression levels were significantly lower compared to their expression levels after RFA (23,14; 25,71; 31,06; 32,63, respectively; $p < 0.01$; $p < 0.05$). Expression levels of miR-192, -194, -196b before RFA were also significantly lower compared to controls (20.23 vs 24.15; 21.6 vs 21.47; 27.14 vs 30.76, respectively). Expression levels of all miRNAs assessed after RFA were not different from controls (NS).

There were no differences in expression levels of miR-192, -194, -196a, -196b between those with satisfactory first RFA attempt compared to the remaining group (22.45 vs 23.62; 26.06 vs 24.66; 29.68 vs 31.3; 30.83 vs 33.69).

Differences in expression of microRNAs in blood samples did not reach statistical importance.

Conclusion: Regaining miRNA expression after RFA the normal levels which are seen in controls could be considered a sign of the recovery. Increased expression levels of miRNA after ablation could represent their temporary apoptotic affect, however the continuation of surveillance is essential. miRNA levels did not predict initial response to RFA, however studies on larger groups are needed.

Disclosure of Interest: None declared

P1751 MULTI LAYERED EPITHELIUM INDUCED BY BILE AT THE SQUAMO-COLUMNAR JUNCTION IN MICE ORIGINATES FROM SQUAMOUS AND COLUMNAR CELLS

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Introduction: Barrett's esophagus (BE), a premalignant condition of esophageal adenocarcinoma (EAC) is defined as the replacement of normal stratified squamous epithelium of the lower esophagus by metaplastic columnar epithelium [1]. The observation of multi-layered columnar epithelium (MLE) regularly observed at the squamo-columnar junction (SCJ) in BE patients suggests a transitional stage between these two types of epithelia. Studies, in both human and rats, have shown that especially the combination of acid and biles can induce MLE and metaplasia at the SCJ [2,3]. In this study we investigated if the diverse layers as observed in MLE is a transitional stage between epithelia originating from one progenitor cell, or is a mix of different types of epithelia with diverse progenitors.

Aims & Methods: 0.5% deoxycholic acid (DCA) was given to mice in drinking water for a maximum of 30 weeks. Animals were sacrificed and studied by immunohistochemistry (IHC) at different time points. Bile treatment induced gland formation at the SCJ starting from week 15. The MLE glands were positive in the outer layer for squamous markers K14, p63 and K5 and in the inner layer for columnar markers K19, TFF2 and Alcian Blue. In one of our previous studies we also observed Lgr5 positive cells (*RNA in situ*) in these multi-layered glands [4].

To investigate if MLE originates from a squamous or columnar stem cell, we performed lineage tracing experiments. A Cytokeratin 5 (K5)-cre (n = 20) mouse specific for tracing squamous progenitor lineages, and a Leucine-G-coupled receptor (Lgr5)-cre mouse (n = 20) were crossed with Rosa-lacZ mice. Lineage tracing was induced by tamoxifen injection prior to bile treatment at the age of 8 weeks. Mice were sacrificed 20 weeks after induction.

Results: K5-lacZ-positive cells were present in the outer layer of the gland demonstrating that the origin of these cells is from squamous progenitors, which is in concordance with the IHC results. Negative K5 lineage tracing in columnar cells within the MLE in mice excludes the transdifferentiation hypothesis in which squamous cells change into columnar cells, which has been a prevailing theory for many years. The negative lineage experiments for LGR5 suggests a columnar cell of origin, other than Lgr5 for the inner layer.

Conclusion: Continuous acid and bile reflux changes the environment at the SCJ in mice and disrupts the natural homeostatic environment of squamous and columnar cells. It appears that MLE is the result of competitive interactions between cell lineages driven by environmental changes.

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Disclosure of Interest: None declared

P1752 BARRETT'S ESOPHAGUS CELL OF ORIGIN DOES NOT DERIVE FROM CYTOKERATIN 5 EXPRESSING SQUAMOUS CELLS IN MICE

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Introduction: Barrett's esophagus (BE) is defined as replacement of the stratified squamous epithelium in the distal esophagus with a metaplastic, intestinal like columnar epithelium [1]. A major unanswered question is whether the BE cell of origin derives from transdifferentiation of the esophageal squamous epithelium [2], or originates rather from a progenitor cell in the esophagus [3], the esophageal submucosal glands [4], residual embryonic cells located at the squamocolumnar junction [5] or from the gastric cardia [6].
Since Lgr5 expressing cells have been observed in human BE, it has been suggested that the stem cells that give rise to BE may originate from the neighboring columnar epithelia harboring Lgr5+ stem cells [7]. Recently we showed by performing lineage tracing experiments that Lgr5+ progenitors are not at the basis of the columnar metaplasia that develops in the tubular esophagus in a surgical esophagitis-metaplasia mouse model [8].
Aims & Methods: To investigate if the metaplasia observed in the esophagus in a surgical mouse model originates from cytokeratin 5 (CK5) expressing esophageal cells, we performed lineage tracing by creating the esophago-jejunostomy in CK5-EGFP-ires-CreERT2/Tomato-GFP mice ($n=13$). The anastomosis was performed one week after administering Tamoxifen, and metaplasia was allowed to develop over six ($n=3$), twelve ($n=5$) and sixteen weeks ($n=5$).
Results: Development of metaplastic glands at the junction was observed in 2 of the animals. None of the glands in all the animals studied showed positive GFP staining although the normal esophagus lying adjacent to the site of the metaplasia showed entire green squamous tissue indicating successful lineage tracing in the esophagus. Our data suggests that CK5+ esophageal cells are not at the basis of the columnar metaplasia that develops in the tubular esophagus and at the neo-SCJ in our surgical model.
Conclusion: In conclusion, progenitors other than Lgr5 and CK5 positive stem cells might be candidates for the cell of origin in the metaplastic lesions as observed in a surgical Barrett mouse model.

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P1753 MICROSATELLITE INSTABILITY IN BARRETT ESOPHAGUS; FROM INTESTINAL METAPLASIA TO ESOPHAGEAL ADENOCARCINOMA

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Introduction: Barrett esophagus (BE) is one of the most common premalignant conditions and it is considered to be a primary risk factor for esophageal adenocarcinoma (EAC). BE-associated EAC develops through a multi-step process (intestinal metaplasia-dysplasia-adenocarcinoma) that involves different triggers of neoplastic progression such as chromosomal abnormalities, genetic and epigenetic events and environmental factors. Many biomarkers have been tested in BE but none of them have shown clinical significance in disease progression besides dysplasia.
Aims & Methods: The aim of this study was to evalute the role of mismatch repair system (MMR) in metaplasia-dysplasia-adenocarcinoma sequence of Barrett's esophagus (BE). Data from 70 patients with patohistological diagnosis of BE or esophageal adenocarcinoma (EAC) was retrospectively analysed. Patients were divided into three groups: BE with intestinal metaplasia without dysplasia (22 patients), BE with dysplasia (37 patients) and adenocarcinoma (11 patients). Immunohistochemical expression of MLH1, MSH2, PMS2 and MSH6 of DNA mismatch repairs (MMR) system in different groups was measured, statistically analysed and compared with p53 expression.
Results: MLH1 and PMS2 expression in different phases of BE was statistically significant. Loss of MLH1 and PMS2 expression was present in 81.8% patients with adenocarcinoma, 67.6% and 64.9% respectively in dysplasia group, 50% and 54.5% respectively in patients without dysplasia. Neither patients with adenocarcinoma or dysplasia had MSH2 or MSH6 loss of expression, and in group without dysplasia loss of expression was observed in 18.2% patients, which was all statistically significant. There is a strong positive correlation between MLH1 and PMS2 expression and also MSH2 and MSH6 in the whole sample and in different BE groups. Patients who had positive p53 expression did not have MLH1 or PMS2 expression but statisticaly significant correlation was only shown in dysplasia group.
Conclusion: MLH1 and PMS2 can be a promising biomarkers in surveillance and therapy making decisions of BE patient.
Disclosure of Interest: None declared

P1754 EFFECT OF DIET-INDUCED OBESITY ON PROGRESSION OF CHRONIC ESOPHAGITIS IN EXPERIMENTAL MODEL OF BARRETT'S OESOPHAGUS. BENEFICIAL EFFECT OF MELATONIN AND L-TRYPTOPHAN, A PRECURSOR OF MELATONIN

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Introduction: Gastro-oesophageal reflux disease (GERD) is a major health problem in Western countries and obesity is also a major risk factor for reflux-associated oesophageal lesions, such as erosive oesophagitis, Barrett's oesophagus, and oesophageal adenocarcinoma. The effects of diet-induced obesity (DIO) in development of chronic esophagitis and the therapeutic efficacy of melatonin precursor, L-tryptophan and melationin in mediating of the effects of body and abdominal obesity in experimental rodent model of Barrett's esophagus has not been extensively studied.
Aims & Methods: Using eighty rats surgically prepared with esophagogastroduodenal anastomosis (EGDA) resulting with esophageal mucosal damage we studied the hypothesis that 1) diet-induced obesity (DIO) augments the severity of chronic esophagitis, and 2) exogenous melatonin or that originated in the gut from its precursor, L-tryptophan, could attenuate the experimental Barrett's esophagus in DIO rats. Rats fed with high- or low-fat-diet were randomly divided into five groups and received for 12 weeks: 1) standard laboratory rodent diet (control, fat equivalent 30 kcal%); 2) high-fat diet (fat equivalent of 70 kcal%) and 3) low-fat diet (10 kcal %) with or without vehicle (saline), melatonin (40 mg/kg i.g.) or L-tryptophan (200 mg/kg i.g.). The effect of removal of major source of melatonin, the pineal gland (pinealectomy) without or with melatonin treatment, was studied in separate group of animals fed with DIO and low-fat diet. At 8 and 12 weeks esophageal damage was evaluated by macroscopic and histological lesion index (LI), esophageal blood flow (EBF) was determined by H_2-gas clearance technique, and malonyldialdehyde (MDA) contents were assessed in the esophageal mucosa. The mucosal expression of mRNA and protein for caudal-related homebox gene family Cdx1 and Cdx2, COX-2, and proinflammatory cytokines IL-1β and TNF-α were analyzed by RT-PCR and Western Blot.
Results: Chronic esophagitis developed in all EGDA animals fed with DIO as manifested by a significant decrease in EBF, an increase in body weight, MPO activity, oesophageal MDA content and an increase in Cdx2- and COX-2 mRNAs. In EGDA rats, extensive esophageal ulcerations, development of columnar epithelium, formation of mucus glands in squamous epithelium and intestinal metaplasia were observed. These effects were further significantly more pronounced in pinealectomized rats fed with DIO. Melatonin and its precursor L-tryptophan which raised significantly the plasma melatonin levels and EBF, significantly reduced the LI and attenuated expression of Cdx2 and COX-2 in both non-pinealectomized and pinealectomized animals fed with DIO compared with those fed normal or low fat diet. The expression of IL-1β and TNF-α was downregulated and plasma levels of these cytokines were significantly reduced in melatonin and L-tryptophan rats fed with DIO.
Conclusion: Melatonin and that derived endogenously from L-tryptophan may represent a novel therapeutic option against reflux esophagitis progressing to Barrett's esophagus due to an improvement of esophageal circulation, antiinflammatory activity resulting in attenuation of proinflammatory markers COX-2-, Cdx2, IL-1β- and TNF-α and inhibition of lipid peroxidation.
Disclosure of Interest: None declared

P1755 IMPACT OF ENDOSCOPIC SURVEILLANCE IN BARRETT 'S ESOPHAGUS WITHOUT DYSPLASIA - A RETROSPECTIVE STUDY

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Introduction: Barrett's esophagus (BE) is a potentially malignant entity, with an annual incidence of esophageal cancer of 0.5% per year and a risk of progression to adenocarcinoma varying from 0% to 2.9%. According to guidelines, endoscopic surveillance should be performed in patients with BE with predefined intervals related to the grade of dysplasia[1,2,3].
Aims & Methods: The aim of this study is to evaluate the impact of endoscopic evaluation of patients with BE without dysplasia and to assess incidence of low-grade dysplasia, high-grade dysplasia and adenocarcinoma. This is a retrospective analysis of a cohort of patients with Barrett's esophagus in surveillance program between 2008-2014. We evaluated the number of endoscopies per patient and the progression to dysplasia and ADC.
Results: We included 52 patients, of whom 69% were male, with an average age at diagnosis of 67 ± 12.81 years old. 73% of patients had symptoms of gastroesophageal reflux medically controlled. At diagnosis, 48 patients (92.3%) had no dysplasia and 4 (7.7%) had low-grade dysplasia. The average number of endoscopies was 4.8 ± 1.37 per patient. During the study period, 3 patients without dysplasia at diagnosis (6.2%) progressed to low-grade dysplasia and 2 patients (4.2%) progressed to adenocarcinoma. Both patients with adenocarcinoma were submitted to surgery.
Conclusion: The data obtained demonstrate the importance of endoscopic surveillance in patients with BE without dysplasia. The results of our study are different from the literature, in the incidence of adenocarcinoma. This can be related with the small sample size and to the fact that this was a retrospective study.

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P1756 STATIC IMAGES VERSUS DYNAMIC VIDEOS FOR ENDOSCOPIST TRAINING: THE ELEPHANT IS IN THE ROOM!

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Introduction: Training modules on lesion recognition and in-vivo diagnosis have traditionally utilised static images. In real-life, assessments are made on dynamic and moving organs. Therefore, assessment and training of endoscopists in lesion recognition and characterisation using video-clips would reflect real-world practice. There have been no studies thus far comparing assessments using still images versus videos in lesion recognition and characterisation.
Aims & Methods: We aimed to assess the difference in accuracy and confidence in Barrett's neoplasia recognition and characterisation when using still images versus videos. We also want to assess the impact of a training intervention using the same library of static and video files. 14 endoscopists, with varying degrees of experience in the use of acetic acid chromoendoscopy (AAC), were asked to identify neoplasia versus metaplasia in Barrett's oesophagus (40 static images and 20 videos each approximately 3 minutes long) using a web-based platform. Accuracy and confidence in diagnosis were measured. No feedback was given. Following this intial test, participants completed a structured online training programme on the concepts of in-vivo diagnosis of Barrett's neoplasia using AAC including both stills and videos. Upon completion of the training module, participants repeated the test.
Results
Three Experts when tested with this library showed an accuracy of 93% with static images and 93% with video based assessment. 14 endoscopists (6 regular users of AAC) participated in the training study. Diagnostic accuracy improved from 78% (pre-training) to 85% (post-training) when images were used as the assessment tool ($p < 0.05$). Additionally, confidence in diagnosis improved by(?% to? %) 7% ($p < 0.05$). In contrast, the training intervention showed an improvement in diagnostic accuracy (77% to 81%) and confidence (75% to 80%) on video-based assessments ($p = 0.19$).

	Pre-Online Module Test		Post-Online Module Test	
	Mean accuracy (%)	Confidence (%)	Mean score (%)	Confidence (%)
Images(n = 40)	31 (78)	31 (78)	34 (85)	34 (85)
Videos(n = 20)	15 (77)	15(75)	16 (81)	16 (80)

Conclusion: This is the first study comparing image and video-based assesments in Barrett's neoplasia recognition. Experts did not show any difference in accuracy between images and videos. Endoscopists with no or little experience with AAC in Barrett's oesophagus had a significantly lower accuracy rates then experts but it was equally low on images and videos. Training led to significant improvements in accuracy and confidence in image-based assessment but not on video-based assessment. This questions the validity of static image-based training and assessment as a surrogate marker of real life.
Disclosure of Interest: None declared

P1757 HIGH PREVALENCE OF BARRETT'S ESOPHAGUS AND HISTOLOGICAL ESOPHAGITIS AFTER ESOPHAGEAL ATRESIA REPAIR

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Introduction: Esophageal atresia (EA) is a rare congenital anomaly and requires surgical correction shortly after birth. In EA patients gastroesophageal reflux (GER) is frequently reported (25-58%). Due to the high prevalence of GER and increased survival in EA patients (>90%), concerns arise about an increased risk of developing Barrett's esophagus (BE) and esophageal carcinoma in this population.
Aims & Methods: Esophageal atresia (EA) is a rare congenital anomaly and requires surgical correction shortly after birth. In EA patients gastroesophageal reflux (GER) is frequently reported (25-58%). Due to the high prevalence of GER and increased survival in EA patients (>90%), concerns arise about an increased risk of developing Barrett's esophagus (BE) and esophageal carcinoma in this population.
Results: To date, 74 patients (60.8% male; median age (range) 21.9 years (16.8-55.9)) underwent a gastroscopy. History of GER before adulthood was present in 47 (63.5%) patients, 21 (28.4%) of whom underwent fundoplication surgery. At baseline, 19 (25.7%) patients had GER complaints and 7 (9.5%) patients used anti-reflux medication. Endoscopic findings were: extension of gastric epithelium above the GEJ in 20 (27%) patients, esophagitis in 4 (5.4%) patients and normal mucosa in 50 (67.6%) patients. In one patient biopsies were not taken. Histology revealed BE without dysplasia in 7 (9.6%) patients with a median age of 31.0 years (range 17.9-45.3 years; 86.7% male) and gastric metaplasia in 1 patient. Esophagitis was present in 21 (28.8%) patients. In 44 (60.3%) patients inflammatory changes were within normal limits. One male had developed squamous cell carcinoma of the distal esophagus at the age of 44 years. This was before endoscopic screening and surveillance of EA patients had started in our hospital.
Conclusion: EA patients have a six-fold increase in developing BE compared to the general population (9.6 vs 1.6%) and at a much younger age (31 vs 55 years). One third of the adult EA patients have histological esophagitis at the GEJ. These findings may signify important and relevant clinical implications including use of proton pump inhibitors and lifelong endoscopic follow-up by experts to facilitate early diagnosis of clinically relevant lesions.
Disclosure of Interest: None declared

P1758 THE POSITION WITHIN THE OESOPHAGEAL CIRCUMFERENCE PREDICTS LOW-GRADE DYSPLASIA IN SHORT SEGMENT BARRETT'S ESOPHAGUS: A 7-YEAR RETROSPECTIVE SERIES OF 341 LESIONS

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Introduction: Barrett's esophagus (BE) is a premalignant condition which may lead to oesophageal cancer. For this reason, a careful endoscopic surveillance is of paramount importance. So far, only few data on the preferred location of BE and high-risk lesions associated with BE are available.
Aims & Methods: The aim of this study is to identify the preferred circumferential location of BE and associated high-risk lesions. We retrospectively reviewed a prospectively maintained database of patients with noncircumferential, short-segment, histologically proven BE who underwent upper endoscopy between January 2008 and February 2015 at our Endoscopy Center. In the case of multiple BE lesions, each tongue was counted individually. The circumferential location of each lesion was identified as on a clock face. The position of dysplastic lesions was compared with that of simple BE tongues without dysplasia (S-BE). Chi-square test was used to compare the expected and observed distribution of lesions both in the left and right hemicircumferences and in the 4 quadrants.
Results: Over the study period, a total of 209 subjects were newly diagnosed of BE or had an endoscopic follow-up of BE. 24 patients with long-segment BE and/or circumferential lesions were excluded. Among the 185 remaining patients, multiple lesions were diagnosed in 110 of them, for a total amount of 341 areas of BE. 28 of them were associated with low-grade dysplasia (LGD-BE), and 1 with adenocarcinoma. No lesions with high-grade dysplasia were found. LGD-BE lesions were significantly more common in the posterior wall (5 to 7 o'clock) than within other areas of the esophageal circumference, accounting for 42% versus, respectively, 38% in the anterior wall (11 to 1 o'clock), 23% in the right wall (2 to 4 o'clock), 4% in the left wall (8 to 10 o'clock) ($P = 0.03$). S-BE lesions were more frequently observed in the posterior wall (38%), compared with right wall (29%), anterior wall (22%), left wall

(11%), in a significant manner ($P < 0.0001$). Both S-BE lesions and LGD-BE lesions were more commonly found in the right (1 to 6 o'clock) than in the left (7 to 12 o'clock) arc, respectively, with a significant (S-BE: 63% versus 37% – $P < 0.0001$) and non-significant difference (LGD-BE: 64% versus 36% – $P = 0.13$) between the two hemispheres.

Conclusion: Our results show a non-homogenous location of BE lesions with and without dysplasia in the circumference of the distal oesophagus, LGD-BE was more commonly observed in the posterior quadrant. Accurate evaluation of these areas is therefore advisable during the endoscopic follow-up of BE. Should our findings be confirmed by further, larger experiences, they should be taken into account for the development of future surveillance protocols of BE.

Disclosure of Interest: None declared

P1759 USEFULNESS OF INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3 IN BARRETT'S ESOPHAGUS AS A POTENTIAL BIOMARKER OF NEOPLASTIC PROGRESSION. PRELIMINARY RESULTS

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Introduction: Barrett's esophagus (BE) is an entity with a well known histological progression to malignancy.

Malignant transformation in patients with BE may arise from alterations of apoptotic regulatory proteins and the insulin-like growth factor (IGF) system is involved in the regulation of cell proliferation, diferentiation and apoptosis. Dys-regulation of IGF1 increases the risk of a number of malignancies. IGF binding protein-3 (IGFBP3) is over-expressed in BE, dysplastic and tumour tissue of patients with adenocarcinoma. The possibility of having a plasmatic biomarker of BE progression is very appealing. However, the role of IGFBP3 in cancer progression is not clear with controversial results regarding circulating levels of this protein.

Aims & Methods: The objective of this study is to evaluate circulating levels of IGFBP-3 in patients with BE at different histological stages.

We performed a prospective longitudinal study and determined baseline concentrations of IGFBP3 in all patients with BE who underwent an upper endoscopy from May 2012 to May 2015. Endoscopy was performed under conscious sedation and biopsies were obtained following the Seattle protocol. Ten mL of blood were taken and determination of IGFBP-3 was performed using the ELISA technique. We included patients without BE as a control group. The protocol was approved by the Ethics Committee and patients gave informed consent.

Results: A total of 61 patients with blood samples were included at the time of this preliminary analysis: 42 with BE (15 non-dysplastic, 13 with low-grade dysplasia and 14 with adenocarcinoma) and 19 controls. BE patients had a mean age of 60.4 ± 13.7 years and 39 (92.9%) were male with a mean BMI of 26.2 ± 3.3.

Mean levels of IGFBP3 were equal in BE and control group (2.1 ± 1 and 2.1 ± 1.1 ug/ml, respectively, p = NS), with 20 cases (including 5 controls) over the upper limit of reference (>2.3 ug/mL). No patient showed levels of IGFBP3 below the inferior limit of reference (<0.7 ug/mL).

There were no differences in IGFBP-3 serum levels between non-dysplastic BE (2.1 ± 0.7 ug/ml), low-grade dysplasia (2.2 ± 0.8 ug/mL), and adenocarcinoma (1.9 ± 0.6 ug/mL), p = NS.

Conclusion: In this preliminary analysis, IGFBP-3 circulating levels are similar in patients with BE (including BE associated neoplasia) and patients without BE. Serum levels of IGFBP-3 are not different in non-dysplastic BE compared to dysplastic and adenocarcinoma, bringing into question its potential role as a biomarker of neoplastic progession in BE.

Disclosure of Interest: None declared

P1760 SAFETY AND EFFICACY OF CIRCUMFERENTIAL RADIOFREQUENCY ABLATION OF BARRETT'S ESOPHAGUS USING THE BARRX™ 360 EXPRESS RFA BALLOON CATHETER: RESULTS OF A PILOT STUDY

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Introduction: Radiofrequency ablation (RFA) is an established endoscopic therapy for treatment of Barrett's esophagus (BE) with different grades of dysplasia. Generally, patients are initially treated with circumferential RFA using the balloon-based Barrx360 system. A standard procedure consists of sizing the esophageal inner diameter at multiple levels using a sizing catheter. Then an ablation balloon with the appropriate diameter is selected and introduced to ablate the BE using 2 applications of 12 J/cm^2 with cleaning of the ablation zone and catheter in between. A recent study comparing different regimens for circumferential RFA demonstrated that this standard circumferential RFA procedure using the Barrx360 balloon results in a BE surface regression of 83% at 3-month follow-up, with a median total procedure time of 39 minutes. By incorporating the sizing and ablation balloon into a single device, procedure time may be shortened and patient discomfort decreased, since less introductions of the endoscope and catheters are needed.

Aims & Methods: Aim of this pilot study was to assess efficacy and safety of the recently developed Barrx™ 360 Express RFA Balloon Catheter (360 Express). Patients with BE 2-10cm with low-grade dysplasia (LGD), high-grade dysplasia (HGD) or early cancer (EC), confirmed by an expert pathologist, were included. In case of visible lesions, endoscopic resection (ER) was performed prior to RFA. Circumferential RFA was performed using the 360 Express catheter, applying 2 applications of 12J/cm^2 with cleaning of the ablation zone and catheter in between. The first follow up endoscopy was performed 3 months after treatment. Primary outcome: percentage of endoscopically visual surface regression of BE at 3 months graded by two independent endoscopists. Secondary outcomes: procedure time and complications.

Results: Thirty patients (24 men, median age 66 yrs (IQR 62-73), median BE C4 (IQR 2-6) M6 (IQR 4-8)) were included. Four patients underwent ER prior to RFA (worst pathology: EC (n = 2), HGD (n = 1), LGD (n = 1)). Worst histological grade prior to RFA: HGD (n = 6), LGD (n = 22), no dysplasia (n = 2). Median BE surface regression at 3 months was 90% (IQR 77-95). Median procedure time was 31 min (IQR 28-38); median ablation time was 20 min (IQR 17-25). Complications occurred in 4 patients (13%): 1 superficial mucosal laceration that did not require intervention; 1 patient showed atrial fibrillation after the RFA procedure; 1 patient presented with vomiting and dysphagia, however, endoscopy did not show any signs of esophageal narrowing; 1 patient was admitted with dysregulated diabetes mellitus. In seven patients esophageal scarring was observed during the 3 months endoscopy, however, all patients were asymptomatic and no interventions were needed.

Conclusion: This pilot study shows that circumferential RFA using the Barrx™ 360 Express RFA Balloon Catheter may shorten procedure time, but maintains efficacy when compared to standard circumferential RFA using the Barrx360 balloon. No severe adverse events related to use of the device were observed.

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P1761 FEASIBILITY OF HIGH RESOLUTION IMPEDANCE MANOMETRY IN ASSESSING BARRETT'S ESOPHAGUS EXTENSION

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Introduction: Diagnosis and surveillance of Barrett's esophagus (BE) is commonly performed by means of upper endoscopy with biopsies, which is also important to assess the extension of Barrett's metaplasia. Several studies demonstrated the risk of dysplasia and adenocarcinoma development in BE is associated to its extension. However, endoscopic evaluation of esophago-gastric junction (EGJ) may be inaccurate, especially in patients with hiatal hernia, reflux esophagitis and abnomal z-line. Recent studies carried out with 24-h impedance-pH testing showed that Barrett mucosa is characterized by very low basal impedance values compared to the normal esophageal epithelium. High resolution impedance manometry (HRiM) is able to localize with more accuracy than upper endoscopy the EGJ and, also, has been recently applied for baseline impedance levels in patients with reflux disease.

Aims & Methods: We aimed to assess Barrett extension by means of baseline impedance levels (BIL) assessed by HRiM using upper endoscopy as reference standard. In contrast, HRiM was considered reference for EGJ evaluation. Consecutive patients with proven Barrett's esophagus and a group of healthy volunteers (HVs) were enrolled. Patients underwent endoscopy and HRiM before imp-pHmetry off-PPI therapy was performed.BE extention was endoscopically assessed according to Prague classification. During HRiM, EGJ has been identified by assessing the position of lower esophageal sphincter (i.e. proximal and distal borders) and crural diaphragm. BIL was recorded every cm above the EGJ. After measuring BIL at Barrett mucosa level and normal esophageal epithelium in each patient we decided that a stable increase $\geq 100\Omega$ was a good cut-off to discriminate BE length. Maximal length (M) at endoscopy was used for comparison.

Results: Ten HVs (4M/6F; mean age 35, BMI 23) and 20 consecutive BE patients (11M/9F; mean age 46, BMI 25.9) were enrolled. Among BE, hiatal hernia (HH) was found in 15 pts (75%) during endoscopy and 12 (60%) with HRiM. Endoscopy overestimated HH of at least $\geq$1cm in 9 cases. Mean HH was 1.7 vs0.9cm, respectively (mean error 0.75 cm, median SD:0.25; r:0.78). HVs had no HH. During HRiM BE mucosa showed lower BIL compared to the normal epithelium in each BE patients ($p < 0.01$; median BIL 430Ω vs 650Ω 1 to 3 cm above BE, vs 1077Ω 4 to 7cm) and Hvs (shown in Table). Median BE length was 1.7cm (1.5-2.3) at endoscopy, whereas was 2cm (1.0-3.5) at HRiM (median SD error:1cm; r:0.32).

	Barrett (Ω) median (IC95%)	HVs (Ω) median (IC95%)
Z-line	412 (295-562)	1690 (1286-2181)
1 cm	473 (378-584)	1678 (1516-2308)
2 cm	544 (425-683)	1859 (1644-2344)
3 cm	573 (441-732)	2176 (1775-2416)
4 cm	738 (478-856)	2267 (1943-2303)
5 cm	899 (550-1121)	2278 (2159-2523)
7 cm	1191 (953-1248)	2495 (2380-2604)
9 cm	1241 (1029-1633)	2718 (2612-3134)
13 cm	1334 (1128-1691)	2835 (2623-3476)

Conclusion: Our data showed that HRiM was able to discriminate Barrett mucosa from normal esophageal epithelium. Considering that HRiM is the reference standard to assess EGJ position and borders, this technique might become a useful tool combined with endoscopic examination to assess more precisely BE length.
Disclosure of Interest: None declared

P1762 INVESTIGATION OF THE INFLUENTIAL FACTORS PROVIDING TECHNICAL DIFFICULTY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY CANCER LOCATED IN ESOPHAGO-GASTRIC JUNCTION

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Introduction: Endoscopic submucosal dissection (ESD) is accepted as a curative treatment for early gastrointestinal cancer, although only skillful endoscopists can perform ESD. Especially, esophago-gastric junction (EGJ) is known as difficult area to work with endoscope due to narrow space, and reflux. However, the influential factors providing technical difficulty of ESD in EGJ region are uncertain.
Aims & Methods: The aim of this study is to reveal the short-term outcomes after ESD and the influential factors for technical difficulty of ESD in EGJ.
We enrolled consecutive patients who were treated with ESD for EGJ cancer in our institution from January 2006 to December 2014 and met the following criteria: 1) histologically confirmed adenocarcinoma (Adeno) or squamous cell carcinoma (SCC), 2) the depth of tumor invasion limited within T1 (submucosal layer). We adopted the Japanese criteria of EGJ (area within 2cm above and below the EGJ). For ESD procedure, a electric device (Dual Knife, IT knife, Olympus) was used through a single-channel endoscope (GIF-Q260J or -H260Z, Olympus). We defined the case requiring more than 120 minutes for the procedure as difficult case. Curative resection was defined if the pathological assessment of the resected specimen fulfilled following criteria: 1) The depth of invasion was limited within muscularis mucosa in SCC, and within 500μm of submucosa in Adeno, 2) No lymphovascular invasion, 3) No cancer cells at horizontal and vertical margin in the resected specimen. Comparative investigations were conducted regarding: short-term outcomes, complete en bloc resection rate, procedure time of ESD, complication, curative resection rate and assessed the influential factors for long procedure time.
Results: A total of 70 lesions in 70 patients with a median age of 70 years (range, 42-86) and a male/female ratio of 57:13 were enrolled in this study. The median tumor size was 21.5mm in diameter (range, 6-49 mm), and there were 14 lesions (20%) spreading more than half of circumference of the lumen. Histologically, 44 lesions (including 21 lesions deriving from short-segment Barrett's esophagus) were Adeno, besides the remaining 26 lesions were SCC. The en bloc resection rate by ESD was 94% (66 of 70 lesions), and the remaining 4 cases forced to be piecemeal resection were SCC. Severe complications were seen in 2 cases; one case with bleeding required blood transfusion; another with perforation during ESD. 32 lesions (46%) were assessed as non-curative resection due to following reasons: submucosal invasion in 18, presence of cancer cells at horizontal margin in 5 and vertical margin in 2, and lymphovascular invasion in 7 lesions. Median procedure time was 90 minutes (range 20-260). Furthermore, 21 cases (30%) were assessed as difficult cases. In multivariate logistic regression analysis, ''more than half of circumference of the lumen'' was the most influential factor for technical difficulty in ESD ($p = 0.035$, 95%CI: 1.198-129.379, Odds ratio: 12.451). Second influential factor was SCC in histology ($p = 0.043$, 95%CI = 1.055-23.962, Odds ratio: 5.027).
Conclusion: We should pay attention for the difficulty of ESD for early EGJ cancer, in case of the lesion spreading more than half of circumference of the lumen, or if the lesion is revealed as SCC histologically.
Disclosure of Interest: None declared

P1763 THE ROLE OF SURVEILLANCE ENDOSCOPIC ULTRASOUND AFTER ENDOSCOPIC TREATMENT OF INTRAMUCOSAL CANCER IN THE SETTING OF BARRETT'S ESOPHAGUS

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Introduction: Endoscopic treatment, including endoscopic mucosal resection (EMR) of visible lesions and radiofrequency ablation (RFA) of the remainder of Barrett's Esophagus (BE) epithelium, has become standard of care in the management of Intramucosal cancer (IMC) in patients with BE (1). The risk of lymph node metastases (LNM) among patients with IMC is estimated to be less than 2% (2) and Endoscopic Ultrasound (EUS) may be performed at evaluation to exclude LNM. After endoscopic therapy, regular endoscopic follow up is required to detect potential recurrence. There is a lack of consensus of whether follow up of patients with IMC should include EUS for detection of LNM.
Aims & Methods: The aim of this study is to evaluate the value of EUS added to endoscopy in the setting of follow up after endoscopic treatment for IMC in patients with BE. For that purpose a retrospective chart review was conducted on a prospectively collected database to select cases. Cases were identified as patients referred for BE associated neoplasia and were diagnosed with IMC, either by endoscopic biopsy or EMR from August 2003, through May 2013. All patients underwent endoscopic therapy either with complete endoscopic resection of the BE or with hybrid therapy (EMR for visible lesions and RFA/Cryoablation of the remainder epithelium). Patients lost to follow up were excluded. Patients in which an EUS was performed in follow up at least one year after initial diagnosis were selected for analysis.
Results: Out of 59 patients with IMC who completed endoscopic therapy, 50 patients fulfilled inclusion criteria. (39 Male, median age 70) with BE (mean length, 4.7cm) Ten were diagnosed with IMC by initial biopsy and 40 were diagnosed by EMR specimen. Median follow up time from diagnosis was 46.5 months (range 12-124). During this follow up period, a total of 165 EUS (mean 3.3) were performed. Confirmed lymph node metastasis (LNM) was found in two patients on EUS during follow up. One patient (2%) presented a positive lymph node for metastatic esophageal adenocarcinoma at 1 year after endoscopic treatment associated with buried neoplasia. Another patient had LNM found by EUS from a non-gastrointestinal malignancy without any evidence of recurrence of BE associated neoplasia. In 5/50 patients (10%) enlarged lymph nodes were found on EUS during follow up without evidence for malignancy after FNA sampling and/or by subsequent exams. One patient had an incidental newly diagnosed malignancy (dendritic cell tumor) and 5/50 patients had other benign findings, including choledocolithiasis and gallbladder stones.
Conclusion: The rate of LNM from esophageal neoplasia in patients who were endoscopically treated for IMC is very low. Although EUS has the potential to demonstrate significant incidental pathology, its role in serial examinations during follow up after treatment of IMC is limited.

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Disclosure of Interest: None declared

P1764 COLUMNAR-LINED OESOPHAGUS AND ASSOCIATED NEOPLASIA IN THE MALTESE ISLANDS

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Introduction: Malta is a southern European island-state with a relatively homogenous and stable population of 400,000 served by a centralised national health service. Oesophageal adenocarcinoma (OAC) is not considered to be a common pathology but accurate data are lacking. This study is a preliminary assessment of the prevalence of columnar-lined oesophagus (CLO) and associated neoplasia.
Aims & Methods: Since the inception of a specialist oesophago-gastric endosurgical practice all patients with endoscopically identified CLO equal to or longer than 1cm, were enrolled into a prospective longitudinal cohort study. Endoscopic assessment of the oesophageal mucosa was carried out using i-scan (Pentax), narrow band imaging (NBI, Olympus) and acetic acid spray as necessary. Subjects were assigned a Prague CM classification noting Kudo pit patterns. Biopsies were taken following the Seattle protocol with additional biopsies taken from visible lesions. Nodular lesions, especially if confirmed histologically as dysplastic or in keeping with T1a lesions were excised by EMR, employing argon plasma coagulation (APC) to complete ablation. The data collected were analysed with SPSS v. 23 (IBM SPSS Statistics).
Results: In the period January 2012 to April 2015, a total of 98 subjects were enrolled, 60 males and 36 females, with a mean age 58 years (range 19-94, SD 16.4). The mean circumferential CLO segment length (C) was 2.2cm with the mean mucosal (M) length being 3.4cm. Sixty eight subjects (70%) had short segments. Nine subjects were of Northern European extraction and longer segments were significantly higher in this subgroup ($p = 001$). Prevalent low

grade dysplasia was identified in 2 subjects, high grade dysplasia in 2, T1a OAC in 5 and invasive OAC in 17. Specialised intestinal metaplasia (SIM) was identified in 73 subjects and its presence was positively associated with longer segment lengths ($p = 0.014$), benign stricturing ($p = 0.010$) and neoplasia ($p = 0.004$).
Conclusion: This is the first study addressing CLO and OAC in this country. SIM was identified in 75% of subjects with CLO. Short segments appear to constitute the predominant indigenous phenotype, whereas immigrant Northern Europeans are more likely to have long segments. At present prevalent invasive cancer is commoner than early cancer three-fold. A comprehensive surveillance programme has been implemented to follow these CLO patients up in order to identify disease at an early and curable stage.
Disclosure of Interest: None declared

P1765 RADIOFREQUENCY ABLATION FOR PATIENT'S WITH LOW GRADE DYSPLSIA: RESULTS FROM A MULTICENTRE UNITED KINGDOM PATIENT REGISTRY

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Introduction: Combined RFA and EMR are now established as first-line intervention for patients with mucosal HGD and IMC arising in BE. Patients with LGD have previously been managed with vigilant surveillance but more recently guidelines have changed to allow treatment to be offered to these patients. Accurate histological diagnosis of LGD remains problematic with inter-observer variability even amongst expert pathologists. However with confirmed LGD, rates of progression to cancer can be as high as 20% justifying early endoscopic treatment.
Aims & Methods: A multi-center patient registry of patients in the UK to assess the efficacy of RFA in the treatment of patients with LGD arising in BE. Patients for this study were included from 12 of the sites within the registry.
All patients required at least two successive procedures where LGD was identified. All LGD pathology was confirmed by two expert pathologists prior to treatment. Before RFA, any superficial lesions were removed by EMR. Patients then underwent RFA every 3 months until all visible BE was ablated there was disease progression (endpoints). Biopsies were taken at 12 months or when endpoints reached.
Primary outcomes for clearance of all dysplasia (CR-D) & BE (CR-BE) at 12 months were assessed.
Results: Forty patients, mean age 62 years (range 42-68), mean BE length 5.7cm (range 1-14) have undergone treatment. Six patients (15%) had EMR for visible lesions prior to RFA therapy. Once RFA was started no patients needed rescue EMR for new lesions. Patients needed a median of 2 RFA treatments (range 1-5) before reaching the end of protocol. Reversal of dysplasia (CR-D) was seen in all patients (100%) at 12 months. CR-IM was observed in 88% of patients after treatment. Three patients (8%) had symptomatic strictures that required endoscopic dilatation. With a median follow up of 6 months after completion of therapy, there has so far been no progression to HGD or cancer observed although long-term follow-up data are yet to surface.
Conclusion: In patients with confirmed LGD by expert pathologists, RFA is highly effective in the short term at eradicating neoplasia and BE following sequential treatments.
Disclosure of Interest: None declared

P1766 HYBRID ARGON PLASMA COAGULATION (HYBRID APC) FOR ENDOSCOPIC ABLATION OF BARRETT'S ESOPHAGUS (BE): THE FIRST EXPERIENCE IN TERTIARY REFERRAL CENTRE

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Introduction: Argon-plasma coagulation (APC) is a widely used, contact-free, operator-dependent endoscopic ablation technique for the eradication of BE with the relevant risk of stricture formation and buried metaplastic glands under a layer of neosquamous epithelium. Novel hybrid ablation method based on combination of APC and submucosal saline injection (Hybrid APC) has been recently developed to overcome these disadvantages [1].
Aims & Methods: The aim of the present trial was to evaluate efficacy and safety of Hybrid APC in ablation of BE. From July 2014 to March 2015 12 patients (mean age 54, range 40-68) with BE (median length C 1 M2) and low-grade dysplasia confirmed by two expert pathologists were selected for Hybrid APC. After raising the Barrett's mucosa with 0.9% saline solution injected by the high-pressure water jet system (ERBEJET 2, Erbe Elektromedizin, Tuebingen, Germany), the mucosa was ablated with the aid of the Hybrid APC probe (PULSED APC, Effect 2, 60 Watt). The ablation zone was mechanically cleaned with a transparent cap on the tip of the endoscope for further detailed inspection. Detected remnant areas of Barrett's mucosa were re-treated with a second APC application with the lower power (PULSED APC, Effect 2, 40–50 Watt). High dose PPI regimen (esomeprazole 80 mg/day) was used after procedures for strong acid suppression that provided an environment for development squamous mucosa on the site of ablation [2]. 1 and 3 months after completion of Barrett's ablation, upper GI endoscopy was carried out for evaluation of treatment-related strictures and for taking 4-quadrant biopsies from the whole area of the former BE segment including the Neo-Z-line.
Results: In a total of 12 patients complete macroscopic BE ablation was achieved after a mean of 3.4 (range 1-4) treatment sessions and the rate of histologically complete Barrett's ablation was 100%. A mean duration of one treatment session was 14.1 ± 3.2 min. No perforations or uncontrollable bleeding occurred during and after the procedures. In none of the patients stricture formation was observed after Hybrid APC. Mean follow-up after APC was 4.5 months. Buried metaplasia was not found in biopsy specimens contained sufficient subepithelial lamina propria.
Conclusion: Hybrid APC is a new operator dependent treatment modality for BE with LGD that has been shown to be effective and safe, especially in cases of short-segment BE. Short-term follow up didn't reveal any recurrence of BE mucosa or any major complications. Future evaluation of Hybrid APC in a multicenter study an interesting next step in this field.

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P1767 ESGE SURVEY: PRACTICE PATTERNS AMONGST EUROPEAN GASTROENTEROLOGISTS REGARDING THE ENDOSCOPIC MANAGEMENT OF BARRETT'S OESOPHAGUS

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Introduction: Barrett's Oesophagus is a common condition that is widely encountered in clinical practice. This European Society of Gastrointestinal Endoscopy (ESGE) survey asked clinicians attending United European Gastroenterology Week (UEGW) 2014 in Vienna to answer questions about their practice in the diagnosis and management of Barrett's Oesophagus.
Aims & Methods: A ten-question survey was programmed on to two iPads and delegates attending the ESGE learning area were asked to complete it. The information gathered was demographics, practice settings and management strategies for Barrett's Oesophagus. This survey was based on a similar survey done in the USA in 2013[1], and was carried out as an ESGE initiative on behalf of the ESGE research committee. Permission was obtained from the original author of the American survey to reproduce it in a European setting.
Results: 163 responses were obtained. Over half of respondents (61%) were based in university hospitals, the majority (78%) were aged 30-50 and half had more than ten years' experience in gastroenterology. 66% routinely attended courses on Barrett's Oesophagus and more than half (60%) used the Prague C&M classification. Advanced imaging was used by 73% of clinicians and 72% of respondents stated that their group practiced ablation therapy. Most (76%) practiced surveillance for non-dysplastic Barrett's, 6% offered ablation therapy in some situations and 18% offered no intervention. For low grade dysplasia 56% practiced surveillance, 19% ablated some cases and 15% ablated all cases. 32% of clinicians referred high grade dysplasia to expert centres, 20% referred directly for surgery and 46% used ablation therapy in certain cases. Endoscopic mucosal resection was the most commonly used ablation technique (44%).
Conclusion: There has been good uptake of the Prague C&M classification for describing Barrett's Oesophagus and ablation is widely practiced. However practice patterns in the endoscopic diagnosis and management of Barrett's Oesophagus vary widely between clinicians. Clear guidance and quality standards are therefore required.

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P1768 ENDOSCOPIC THERAPY VERSUS SURVEILLANCE FOR PATIENTS WITH BARRETT ESOPHAGUS AND LOW-GRADE DYSPLASIA: PROSPECTIVE MULTICENTER TRIAL

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Introduction: Barrett esophagus with low-grade dysplasia is associated with an increased risk of developing esophageal adenocarcinoma
Aims & Methods: Prospective multicenter trial that enrolled 86 patients with a confirmed diagnosis of Barrett esophagus containing low-grade dysplasia at four Czech endoscopic sites since January 2012. Patient follow-up will end in December 2015. Eligible patients were assigned to either endoscopic treatment or endoscopic surveillance. Radiofrequency ablation was performed with the balloon device for circumferential ablation of the esophagus (Barrx^{TM}360 RFA Balloon Catheter), or the focal device for targeted ablation (Barrx^{TM} 90 and 60 RFA Focal Catheter). In case of visible lesion, endoscopic resection was performed with suck-and-cut technique. The primary outcome was comple teeradication of dysplasia during an 12 months follow-up with surveillance endoscopy in 6th and 12th month. Secondary outcomes were neoplastic progression to high-grade dysplasia or adenocarcinoma, complete eradication of intestinal metaplasia and adverse events.
Results: Since January 2012 until March 2015, 49 individuals (43 men, mean age 54 years) received endoscopic therapy and 37 persons (22 men, mean age 61 years) received control. All patients used proton pump inhibitor (esomperazol 40mg daily) during the follow-up. The results at 6th month of follow-up are being presented. Among 25 patients in the therapy group who underwent surveillance endoscopy, complete eradication occurred in 100% for dysplasia and 60% for intestinal metaplasia. Among 27 patients in the control group, complete eradication occurred in 19% for dysplasia and 0% for intestinal metaplasia. One progression to high-grade dysplasia was recorded in the control group. Treatment-related adverse events occurred in 5 patients (10%) receiving endoscopic therapy (esophageal stricture, chest pain after procedure, overwedging of the ablation catheter and one perforation after dilatation of esophageal stricture)
Conclusion: In this multicenter trial, endoscopic therapy of Barrett esophagus with low-grade dysplasia has appeared to have a high effectivity in eradication of dysplasia. Low incidence of neoplastic progression in control group can be explained by the short period of follow-up.
Disclosure of Interest: None declared

P1769 A COMPARISON OF HIGH DEFINITION WHITE LIGHT ENDOSCOPY (HD-WLE) VERSUS HIGH DEFINITION MICROSCOPY IN PATIENTS DIAGNOSED WITH BARRETT'S ESOPHAGUS: A RETROSPECTIVE REVIEW

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Introduction: Probe-based confocal laser endomicroscopy (pCLE) is a new technique allowing in vivo detection of neoplastic tissue using a standard endoscope.
Our aim was to compare the dysplasia detection rate of biopsies obtained by high-definition white light endoscopy (HD-WLE) or by pCLE in a cohort of patients with Barrett's esophagus (BE) referred for definitive therapy with ablation at a tertiary referral center between 2012-2014. Data was analyzed with SAS Software (version 9.4, SAS Institute, Cary, NC). Categorical variables were analyzed using the Pearson's chi-square test. Continuous variables were assessed for normality via the Shapiro Wilk statistic, and then the T-test or Wilcoxon rank sum test was applied where appropriate. Multivariate logistic regression was used to determine the impact of group assignment when considering other factors related to dysplasia. P values < 0.05 are considered statistically significant.
Aims & Methods: Data for 218 BE patients was reviewed. 105 of these patients underwent pCLE in addition to HD-WLE. Seattle protocol biopsies were obtained in WLE only group while targeted biopsies were taken in pCLE group. Diagnosis of dysplasia/neoplasia was made by a blinded gastrointestinal pathologist. pCLE images were reviewed by 2 experienced reviewers.
Results: There were more males ($p = 0.016$) and Caucasians ($p = 0.004$) in the non-pCLE group, and this group was slightly older ($p = 0.0081$). Histological diagnosis of dysplasia was significantly higher in the pCLE group ($p = 0.0052$), where 22.86% of patients were diagnosed with dysplasia in the group with pCLE and 9.09% of patients diagnosed in the group without pCLE. Logistic regression analysis indicates that age ($p = 0.006$) and use of pCLE ($p = 0.0019$) are significantly related to positive histological dysplasia diagnosis. There was a significantly higher quantity of biopsies in the pCLE group ($p = 0.0041$), specifically high-grade dysplasia biopsies ($p = 0.0019$). This difference was not seen in low-grade dysplasia biopsies ($p = 0.2433$).
Conclusion: 1. Incident dysplasia can be more frequently detected by pCLE than by HD-WLE in BE. The higher dysplasia detection rate provided by pCLE could improve the efficacy of BE surveillance programs and lead to early detection and ablative therapy.
2. pCLE targeted biopsies have higher yield of dysplasia detection than standard Seattle protocol biopsies.
Disclosure of Interest: None declared

P1770 ADENOCARCINOMA RISK IN PATIENTS REGISTERED WITH POLISH BARRETT ESOPHAGUS REGISTRY (POBER)

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Introduction: Barrett Esophagus (BE) is a complication of chronic gastroesophageal reflux disease and is a major risk factor for esophageal adenocarcinoma. BE registries are regarded useful tools in expanding the knowledge and natural progression of this disease.
Aims & Methods: Polish Barrett Esophagus Registry (POBER) was established in 1999 after a dedicated training of endoscopists and histopathologists. The aim of the POBER was to characterize patients with BE and estimate the risk of BE malignant progression. Physicians registered newly diagnosed BE patients (with confirmed intestinal metaplasia) using a dedicated registry form. After excluding patients known to have endoscopic ablative therapies, follow-up < 1 year and adenocarcinoma found at index endoscopy we have linked patients personal identification numbers with the National Cancer Registry to identify those with a diagnosis of esophageal or gastric cardia adenocarcinoma.
Results: In total 843 patients were registered [609 men (72.2%), male to female ratio 2.6:1] with median age at diagnosis of 56 years (IQR:47-67). Long segment BE was found at index endoscopy in 294 patients (39.4%) whereas low grade dysplasia in 147 (17.4%). 112 (13.3%) patients fulfilled the exclusion criteria and the remaining 731 were followed for a median of 9.8 years (IQR: 9.3 – 10.0). After 6,779 patient–years 6 adenocarcinomas were diagnosed yielding an incidence rate of 0.89 per 1000 patients–years (95% confidence interval [CI 0.40-1.97]). Patients with low-grade dysplasia had malignancy incidence rate of 3.70 per 1000 patient–years (95% CI 1.39-9.85).
Conclusion: In BE patients the risk of malignant progression was lower than previously reported, however it was notably higher in those with low-grade dysplasia at index endoscopy.
Disclosure of Interest: None declared

P1771 HIGH PREVALENCE OF RISK FACTOR FOR GI ADVERSE EFFECTS OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN RHEUMATIC PATIENTS AND LOW ADHERENCE TO THE ADMINISTRATION OF GASTROPROTECTIVE AGENTS IN LATIN AMERICA: RESULTS OF AN OBSERVATIONAL STUDY

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Introduction: Non-steroidal anti-inflammatory drugs (NSAIDs) are a long established first-line treatment for the management of pain associated with rheumatic diseases but carry a risk of gastrointestinal (GI) disturbance. Evidence-based guidelines recommend concomitant use of gastroprotective agents (GPAs) in NSAID users with one or more risk factors. Current data from developed countries (USA and Europe) suggests that a significant proportion of these patients are at risk for GI events; however they do not receive properly a GPAs strategy. The prevalence of GI risk factors (RF) and recommendations for an appropriate therapeutic strategy in Latin America countries remain unknown.
Aims & Methods
Objectives: To describe the prevalence of GI risk factors and the adherence to the use of GPAs in patients with rheumatic diseases in Latin America.
Methods: An observational, multicenter and cross-sectional study (RATIONAL) was conducted in patients with rheumatoid arthritis (RA), osteoarthritis (OA) and ankylosing spondylitis (AS) receiving at least one dose of NSAIDs in the 15 days before enrolment. The single study visit was part of standard practice and was conducted by rheumatologists in four countries from Latin America. Information collected included the presence of well-established GI risk factors, NSAID treatment over the year preceding the study visit and GPA use.
Results: The distribution of rheumatic disorders in the 2469 consecutive patients from Latin America (Argentina, Colombia, Mexico and Venezuela) was OA 1200 (48.6%), RA 1050 (42.5%), AS 145 (5.9%), and a combination of them 74 (3.0%). The prevalence of individual RF and treatment with GPAs is shown in the Table. A great proportion (85.6%) of the study population had one or more GI risk factors and 32.0% of patients had two or more RF. The most commonly occurring RF was age ≥ 60 years' (48.0%). Treatment with GPAs was received by 55.9%of the study patients. Of the well established RF, only patients with histories of GI complications or GI ulcer had appropriate and high prescription rates of GPA agents (90.0% and 95.0%,

respectively), whereas patients with other RFs such age, or concomitantly using antiplatelets or anticoagulants had much lower rates of GP.

Risk factor	Risk factor present		Receiving a GPA	
	n	%	n	%
Any risk factor	4711	87.70	3112	57.9
Age ≥60 years	2627	48.89	1534	58.4
Concomitant ASA	564	10.64	360	63.8
Concomitant corticosteroids	1202	22.37	850	70.7
Concomitant anticoagulants	87	1.64	53	60.9
History of complicated ulcer	45	2.08	42	93.3
History of GI complications	405	7.50	28	96.6
History of dyspepsia	569	26.34	501	88.0
High dose NSAID	1206	22.45	773	64.1
More than one NSAID	21	0.39	15	71.4

Conclusion: Most patients with rheumatic diseases requiring NSAIDs from Latin America showed a high prevalence of GI risk factors. However, only less than 60% received any form of GPA. While age was not perceived as a significant RF, history of ulcer was clearly considered for GPAs. A poor physician adherence with published safe NSAID prescribing guidelines are common in these Latin American countries.

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P1772 CHARACTERISTICS OF ANTICOAGULANTS ASSOCIATED UPPER GASTROINTESTINAL MUCOSAL INJURY - COMPARISON BETWEEN WARFARIN AND NOAC -

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Introduction: Since non-vitamin K antagonist oral anticoagulants (NOAC) was released in 2011, the therapeutic strategy for the prevention and treatment of thrombosis has been changed greatly in Japan. NOAC have similar efficacy as vitamin K antagonists (VKA), however, recent studies have reported some kinds of NOAC increase risk for gastrointestinal bleeding compared with VKA (1, 2). Previous reports were investigated the relationship between NOAC and gastrointestinal bleeding or bleeding risk, however there is no reports which were investigated the relationship between NOAC and gastrointestinal mucosal injury. As it is known individual NOAC have different bioavailability (2), each NOAC might have a different effect in upper gastrointestinal tract.

Aims & Methods: To reveal the clinical features of NOAC-associated upper gastrointestinal mucosal injury, we evaluate mucosal injury endoscopically in patients taking VKA or NOAC. Data were extracted from the records of subjects who underwent upper gastrointestinal endoscopy in our department between March 2011 and March 2015. Of the 41,040 subjects analyzed, 564 subjects who took VKA (Warfarin) or NOAC (Rivaroxaban, Apixaban, Edoxaban, Dabigatran). Esophageal mucosal injury are based on the definition of Los Angeles classification and gastroduodenal mucosal injury are based on the definition of ulcer classification which was defined by Murakami et al (3). Statistical analyses were performed by Fisher's exact test.

Results: The results are shown in the figure below. There was no significant difference in prevalence of upper gastrointestinal mucosal injury in individual organs between Warfarin users and each NOAC users. However, NOAC users tend to have less mucosal injury than Warfarin users except for the case of esophageal mucosal injury in Dabigatran users.

	Number of subjects	Concomitant use of PPI	Esophageal mucosal injury	Gastric mucosal injury	Duodenal mucosal injury
Warfarin	487	276(56.7%)	23(4.7%)	159(32.7%)	23(4.7%)
Rivaroxaban	22	13(59.1%)	0(0%)	6(27.3%)	1(4.6%)
Apixaban	8	5(62.5%)	0(0%)	2(25.0%)	0(0%)
Edoxaban	1	1(100%)	0(0%)	0(0%)	0(0%)
Dabigatran	46	30(65.2%)	4(8.7%)	11(24.4%)	2(4.4%)

Conclusion: These results suggested that taking NOAC is not a risk factor for upper gastrointestinal mucosal injury. Although further consideration will be needed to confirm these results, it's going to be possible that NOAC is more mucosal-friendly agent than Warfarin.

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P1773 INDOMETHACIN-INDUCED ENTEROPATHY IS ASSOCIATED WITH AN IMPAIRED AUTOPHAGY REGULATION IN THE ILEUM

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Introduction: Gastrointestinal damage is the major limitation to the use of NSAIDs. These drugs cause gastric damage by hampering the epithelial defence through cyclooxygenase inhibition. However, the pathogenesis of NSAID enteropathy is still not fully understood. Autophagy is a catabolic process that degrades superfluous and damaged organelles, cytosolic proteins and invasive microbes. In the gut, autophagy plays a role as part of the defensive mechanisms that protect the intestinal mucosa. It is important for the clearance of bacteria by immune cells and it controls the function of Paneth and goblet cells. Furthermore, defective autophagy has been related with inflammatory bowel disease.

Aims & Methods: Our aim is to study the effects of indomethacin on intestinal autophagy in a well-known in vivo model of intestinal damage by NSAIDs. BALB/C mice were treated with 10 mg/kg indomethacin (s.c.) for 24 hours. The presence of ulcers along the small intestine was assessed histologically in Swiss roll preparations. The effects of indomethacin on intestinal autophagy were studied in samples of stomach, duodenum, jejunum and ileum. The autophagic flux was analyzed by measuring the levels of an autophagosome component (LC3-II protein) and the accumulation of an autophagic substrate (p62 protein).

Results: The histological analysis revealed that intestinal ileal, but not duodenal and jejunal, mucosa of mice treated with indomethacin presented several ulcers with complete loss of the epithelium. Western blot analysis of gastric and intestinal samples showed that indomethacin treatment increased LC3-II protein levels and decreased p62 protein levels in stomach, duodenum and jejunum, indicating an activation of autophagy in these territories. In contrast, both LC3-II and p62 protein levels remained unaltered in ileal samples.

Conclusion: Our data show that indomethacin activates autophagy in the stomach, duodenum and jejunum, but not in the ileum, where it causes ulcerations, and suggest that this increased autophagy constitutes a defensive mechanism that preserves mucosal integrity in the proximal gut while its absence makes the ileum more susceptible to indomethacin-induced damage.

Disclosure of Interest: None declared

P1774 ASPIRIN-INDUCED GASTRIC DAMAGE IS ASSOCIATED WITH AN INHIBITION OF EPITHELIAL CELL AUTOPHAGY

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Introduction: Treatment with NSAIDs constitutes a challenge to gastric epithelium because, by suppressing gastric prostaglandin synthesis, it debilitates the gastric mucosal barrier. Autophagy is an intracellular process for elimination of

long-lived proteins and organelles in which a portion of the cytoplasm is sequestered by a double-membrane structure called autophagosome, which fuses with lysosomes in order to degrade its content. It is assumed that autophagy contributes to basal cellular homeostasis and acts as a survival mechanism under conditions of stress, maintaining cellular integrity by regenerating metabolic precursors and clearing subcellular debris.

Aims & Methods: We aim to analyze whether aspirin (ASA) affects the autophagic flux in gastric epithelial cells and, if so, the consequences of those effects on ASA-induced gastrotoxicity. The effects of aspirin on gastric epithelial cell autophagy were studied in a rat model of ASA-induced gastric damage and in human gastric epithelial AGS cells. The autophagic flux was analyzed by measuring LC3 protein levels and the accumulation of the autophagic substrates p62 and ubiquitinated proteins. We also analyzed the phosphorylation of mTOR and ULK1, which regulate the autophagy process. In parallel, macroscopic gastric damage and cell viability was evaluated after treatment with ASA in the presence of the autophagy inhibitor 3-methyladenine (3-MA).

Results: The gastric mucosa of rats treated with ASA (150 mg/kg, p.o., 3h) presented multiple haemorragic wounds, an increased presence of ubiquitinated proteins, a significant increase in LC3-I and LC3-II (total LC3) protein levels as well as a reduction in the LC3-II/LC3-I ratio (suggestive of a reduced autophagosome formation). The mucosa of ASA-treated rats also presented an increased level of mTOR-mediated ULK1 phosphorylation, which negatively regulates autophagy. Administration of the autophagy inhibitor 3-MA enhanced the macroscopic damage induced by ASA. In AGS cells, treatment with ASA (1-10 mM, 24h) significantly and dose-dependently reduced the autophagic flux, as demonstrated by a reduced LC3-II accumulation in the presence of lysosomal inhibitors and increased levels of p62. Treatment of cells with the autophagy inhibitor 3-MA (2 mM), reduced the concentration of ASA necessary to induce cell apoptosis and necrosis.

Conclusion: Our results demonstrate that aspirin inhibits autophagy in the gastric mucosa and that a further inhibition of the residual autophagy exacerbates the damage caused by this drug, which suggests that the gastrotoxic effect of aspirin is partly due to an impairment of this homeostatic process in epithelial cells.

Disclosure of Interest: None declared

P1775 PREVENTION OF BISPHOSPHONATE-INDUCED GASTRIC MUCOSAL LESIONS BY HYDROGEN SULFIDE (H2S) VIA DOWNREGULATION OF HYPOXIA-INDUCIBLE FACTOR 1ALPHA AND PROINFLAMMATORY CYTOKINES

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Introduction: The use of oral bisphosphonates such as alendronate which is inhibitor of osteoclast mediated bone resorption, has increased dramatically despite its association with adverse gastrointestinal effects, including an increased risk of gastrointestinal bleeding erosions and ulcers. Hydrogen sulfide (H_2S) protects gastric mucosa against gastric injury induced by various ulcerogenes but the role of these gaseous transmitters in pathogenesis of bisphosphonates-induced gastric lesions has not been extensively elucidated.

Aims & Methods: We determined the role of H_2S released from its donor NaHS in gastroprotection against lesions caused by alendronate in the gastric mucosa compromised by mild cold stress. Male Wistar rats were pretreated with NaHS (0.1-20 mg/kg i.g) 30 minutes before alendronate (150 - 700 mg/kg i.g.) (series A). In series B, rats were additionally exposed to 1 h of mild cold stress before NaHS application in rats subsequently treated with alendronate. At day 3 upon alendronate administration, the area of gastric lesions was assessed by planimetry, the gastric blood flow (GBF) was determined by H_2-gas clearance technique, H_2S production as measured by analyzing the key H_2S synthesizing enzymes CSE/CBS/3-MST pathway, and the concentration of myeloperoxidase (MPO) and proinflammatory cytokines IL-1β and TNF-α was determined by ELISA. The expression of proinflammatory markers hypoxia inducible factor 1a (HIF1α), IL-1β and TNF-α, in gastric mucosa were determined by RT-PCR and Western Blot.

Results: Alendronate dose-dependently increased the gastric mucosal damage mainly in antral part of the stomach, and this effect was accompanied by significant fall in the GBF and these effects were exacerbated by cold stress. NaHS (5 mg/kg i.g.) significantly reduced the alendronate-induced gastric lesions in no-stressed and stressed animals and significantly raised GBF and H_2S production assessed by CSE/CBS/3-MST assay while significantly inhibiting the plasma levels of MPO, IL-1β and TNF-α and mRNA and protein expression of HIF-1αa, IL-1β and TNF-α in the gastric mucosa.

Conclusion: H_2S protects gastric mucosa against alendronate-induced gastric damage compromised by stress *via* an increase in gastric microcirculation and a potent anti-inflammatory and anti-oxidative activities as reflected by inhibition of HIF1α, and proinflammatory cytokines IL-1β and TNF-α by this gaseous mediator.

Disclosure of Interest: None declared

P1776 CYP2C19*17 POLYMORPHISM AS A RISK-FACTOR FOR NSAIDS-GASTROPATHY

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Introduction: Single-nucleotide polymorphisms (SNPs) in the *CYP2C* gene cluster have been extensively investigated as predisposing factors for nonsteroidal anti-inflammatory drug (NSAID)-induced gastropathy or upper gastrointestinal bleeding (UGIB). However, results have been inconclusive owing to different study designs, limited genotyping strategies, and small sample sizes.

Aims & Methods: Our aim was to evaluate whether three functional SNPs in the *CYP2C* family of genes—*CYP2C8*3, CYP2C9*3* and *CYP2C19*17*—are associated with *Helicobacter pylori* (*Hp*)-positive or *Hp*-negative NSAID-induced peptic ulcer disease (PUD). This SNPs were selected on the basis of their known functionality from the literature and their common occurrence in Caucasian populations. We investigated 124 patients (76 male, mean age – 64 years) who were categorized into two groups: 1) patients with endoscopically confirmed PUD (64 pts) within 2 weeks of using NSAIDs (including aspirin); 2) patients without endoscopic evidence of PUD (60 pts), whose use (38 pts) or nonuse (22 pts) of NSAIDs prior to endoscopy was determined. Patients were defined as NSAID users if they had taken a drug, as part of a continuous period of treatment lasting for 1 week or more, during the 2 weeks prior to endoscopy. Genomic deoxyribonucleic acid was extracted from ethylenediaminetetraacetic acid whole blood using the Chemagen 5 ml whole-blood deoxyribonucleic acid extraction kit on the Chemagic Magnetic Separation Module I according to the manufacturer's protocol (PerkinElmer chemagen Technologie, Baesweiler, Germany). Genotyping was performed using its proprietary fluorescence-based competitive allele-specific polymerase chain reaction assay.

Results: We found that only one SNP, *CYP2C19*17*, was significantly associated with the presence of PUD (odds ratio 1.45 (95% confidence interval (CI) 1.14 to 1.90); $P = 0.005$). This association with PUD did not differ depending on NSAID use (P value for interaction term = 0.156), NSAID type and *H. pylori* status (positive or negative). A greater proportion of patients with PUD was seen among *CYP2C19*17* variant allele carriers (*1*/17* - 71.9%; *17*/17** - 73.6%) as compared with wild-type homozygotes (*1*/1** - 63.9%, $P = 0.024$ using $\chi 2$ test). No significant association was found between any of the SNPs and UGIB status. Sensitivity analysis including only the *Hp*-negative cases (42 pts, 33.9%) showed no significant association with *CYP2C19*17* when comparing those with or without PUD ($P = 0.072$) or those with or without UGIB ($P = 0.60$).

Conclusion: *CYP2C19*17* polymorphism is associated with NSAID-induced peptic ulcer disease and can be considered as risk-factor for NSAID-gastropathy.

Disclosure of Interest: None declared

P1777 CLINICAL AND DIAGNOSTIC SIGNIFICANCE OF ASCITES FOUND ON PREOPERATIVE COMPUTED TOMOGRAPHY IN GASTRIC CANCER PATIENTS

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Introduction: In gastric cancer, malignant peritoneal carcinomatosis is regarded incurable but routinely performed computed tomography (CT) has questionable accuracy in evaluating the nature of ascites. We tried to evaluate the clinical significance of ascites which was defined by CT in association with the peritoneal seeding.

Aims & Methods: This single-center, retrospective study includes patients with newly diagnosed gastric cancer and ascites on CT and excluded patients with distant metastasis or definite peritoneal carcinomatosis on CT, or no surgical data. Factors associated with malignant seeding were analyzed.

Results: During 10 years, 2207 patients visited our institution on the diagnosis of gastric cancer. Ninety-three patients were eligible and 12 (12.9%) patients were confirmed peritoneal carcinomatosis based on the pathologic examination. Factors indicating peritoneal metastasis identified by univariate analysis include feature of advanced gastric cancer on preoperative endoscopy (odds ratio [OR], 1.14; $p = 0.031$), regional lymph node metastasis (OR, 5.37; $p = 0.013$), and undifferentiated pathology on endoscopic biopsy (OR, 5.60; $p = 0.038$). Regional lymph node metastasis was significant as predictors of carcinomatosis (OR, 0.592; $p = 0.038$) on multivariate analysis.

Conclusion: Regional lymph node metastasis was associated with peritoneal metastasis. Ascites alone defined on CT is rarely relevant to peritoneal carcinomatosis, and so overestimation should be avoided.

Disclosure of Interest: None declared

P1779 IS THERE STILL A REASON TO SCREEN FOR GASTRIC PREMALIGNANT LESIONS?

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Introduction: Gastric cancer (GC) was the second most common cancer until recently. Worldwide the incidence of the gastric cancer has dramatically decreased in the last years, while the incidence of the esophageal cancer (adenocarcinoma) has increased. GC is now the fifth most common cancer in the world, after lung, breast, colorectal and prostate cancer and the third leading cause of cancer death. About 1 million (952 000) persons are diagnosed with GC every year and about 723 000 die every year(1). Still, GC is the third worldwide cause of mortality from malignant diseases. In Romania GC had an incidence of 19/100000 inhabitants before 1990, but it dramatically decreased.

Aims & Methods: This is a retrospective study to follow-up if the incidence of GC continued to decrease in our region in the last 10 years. The trends in the incidence of the esophageal cancer were also followed-up. The study included 12384 patients (53% females, mean age 62.3years) who underwent upper digestive endoscopy in the Clinical Emergency Hospital, between 2005 and 2014. Multiple biopsies were made.

Results: In the last 10 years from 12384 patient who underwent endoscopy, 678 patients were diagnosed with gastric and esophageal cancer. From these 528 had GC (non-cardia gastric cancer) and 150 had esophageal cancer.

In all the 10 years the incidence of GC/year remain stable, between 45 patients/year and 52 patients/year, more frequent in males (67%). Most of the tumors were located in the corpus (54%). The incidence of the GC on this period was 5.47% in our group of patients.

Regarding the incidence of the esophageal adenocarcinoma this increased, but the epidermoid carcinoma remains the prevalent histology in our area with 98(65.33%) cases and 52(34.66%) cases of adenocarcinoma. Epidermoid carcinoma/adenocarcinoma ratio decreased from 3.33/1 in 2005 to 1.2/1 in 2014. Regarding gender distribution, there was a high predominance of males (131 males and 19 females).

Conclusion: Despite the fact that in the last 30 years GC decreased, dramatically, in the last 10 years, its incidence remained stable, 5.47% in our database. The incidence of esophageal adenocarcinoma has doubled in the last 10 years, but is still lower than the epidermoid type in our region. The upper digestive cancer rate is still high, so the screening should be cost-effective (2). The population screening for the premalignant gastric lesions with serological biomarkers should be a priority in the future (3,4).

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P1780 DIAGNOSTIC YIELD OF MUCOSAL INCISION WITH DEEP BIOPSY FOR SMALL GASTRIC SUBEPITHELIAL TUMOR: A COMPARISON WITH ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION

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Introduction: Adequate tissue acquisition is important for the definite diagnosis of subepithelial tumor (SET). Endoscopic ultrasound-guided fine needle aspiration (EUS-guided FNA) has better diagnostic yield than routine endoscopic biopsy for these lesions. However, the amount of acquired specimen is sometimes not sufficient to diagnose.

Aims & Methods: The purpose of this study was to determine the safety and diagnostic yield of mucosal incision with deep biopsy compared to EUS-guided FNA for small gastric SETs. A retrospective review of patients who underwent both EUS-guided FNA and incision by needle-knife with deep biopsy for the SET, which size was from 20 to 30mm under endoscopic examination, from January 2013 to September 2014 was performed. A total of 15 patients (M: F = 6: 9) were enrolled. We analyzed the diagnostic yield of EUS-guided FNA and mucosal incision with deep biopsy.

Results: The median age of patients was 49 years (interquartile range [IQR], 37.6-55.5 years) and the median size of the SETs was 20.7 mm (IQR 18.2-26.1 mm). The locations of tumors were 7 upper third, 2 middle third, and 6 lower third of stomach. The diagnostic yield of mucosal incision with deep biopsy was 86.7% (13/15), whereas that of EUS-guided FNA was 73.3% (11/15) ($P = 0.625$, McNemar test). The histological diagnoses were 8 leiomyomas, 3 gastrointestinal stromal tumors, 2 heterotopic pancreases, 1 schwannoma, and 1 nondiagnostic lesion. There was one delayed bleeding in patient with mucosal incision with deep biopsy site. Other bleedings, which were occurred during procedures, were minor and easily controlled by using hemoclip, coagrasper, and/or fibrin glue injection.

Conclusion: Mucosal incision by needle-knife with deep biopsy could be alternative diagnostic tool to diagnose gastric SETs with size from 20 to 30mm under endoscopic examination by getting sufficient tissue sample with relatively higher diagnostic yield. It could be useful to make therapeutic decision for small size of gastric SETs.

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P1781 IS PROBE-BASED CONFOCAL ENDOMICROSCOPY BETTER THAN WHITE LIGHT ENDOSCOPY FOR THE GENETIC AND HISTOLOGIC STUDY OF GASTRIC CANCER: A PILOT STUDY

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Introduction: Although high yield of biopsy for gastric cancer is mandatory to perform genetic and histologic study using gastric cancer tissues obtained from endoscopic biopsy, proportion of cancer cells in biopsy samples is very low. We aimed to evaluate whether probe-based confocal laser endomicroscopy (pCLE) can increase the yield of endoscopic biopsy for gastric cancer compared to white light endoscopy (WLE).

Aims & Methods: Between April 2014 and March 2015, thirty patients diagnosed with gastric cancer were enrolled in the study. Patients were randomly allocated to either pCLE or WLE group. In the pCLE group, lesions were examined by both WLE and pCLE. Then, five pieces of tissue was acquired by biopsy forcep at the lesion where showing the most distinct feature of gastric cancer on pCLE. In cases of the WLE group, lesions were examined by WLE, and then biopsy samples were obtained at the five lesion just as usual endoscopic procedure. The primary outcome was proportion of cancer cells in biopsy samples according to the differentiation of gastric cancer. The secondary outcome was number of biopsy samples which contain cancer cell and concordance of histology between biopsy and resected tissue.

Results: Of 30 patients enrolled in the study, 12 had early gastric cancer. The remaining 18 patients showed advanced gastric cancer. Number of patients with undifferentiated cancer was 8 (53.3%) and 9 (60.0%) in the pCLE and the WLE group, respectively. The proportion of cancer cells in biopsy samples did not differ between the pCLE and the WLE group (median proportion [interquartile range (IQR)]; pCLE vs. WLE, 60% (40–70%) vs. 40% (20–60%), $P = 0.136$). However, the proportion of cancer cells in biopsy samples of cancers with undifferentiated histology was higher in the pCLE group than the WLE group (median proportion [IQR]; pCLE vs. WLE, 65% (45–77.5%) vs. 30% (15–40%), $P = 0.010$). The median number of biopsy samples which contain cancer cell did not differ between the two groups ($P = 0.288$). In addition, concordance rate of histology between biopsy and resected tissue did not differ between the groups ($P = 0.667$).

Conclusion: Biopsy technique for gastric adenocarcinoma with undifferentiated histology using pCLE provided superior result in terms of proportion of cancer cells in biopsy samples compared to that under WLE. When genetic or histologic analyses are planning to investigate, pCLE should be under active consideration for tissue acquisition of gastric adenocarcinoma with undifferentiated histology.

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superficial gastric neoplasia (with videos). *Gastrointest Endosc* 2013; 77: 899–908.

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P1782 PREDICTIVE FACTORS OF PYLORIC STENOSIS AFTER ENDOSCOPIC MUCOSAL DISSECTION AND ITS PROPER MANAGEMENT

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Introduction: Endoscopic submucosal dissection (ESD) is a curable method for resection of gastric neoplasia. But, it can cause early complications such as bleeding and perforation, and late complication such as pyloric stenosis which would be treated by endoscopic balloon dilation. In this study, we evaluated the predictive factors of pyloric stenosis after ESD and its proper treatment method.
Aims & Methods: A total of 1621 cases of gastric neoplasia was resected by ESD at our institution from June 2005 to December 2012 and 125 cases were located in the pylorus. We reviewed retrospectively the cases of pyloric stenosis and analyzed clinical factors such as size, surface area, circumferential extent, and number of ESD. Also, we reviewed treatments of stricture site.
Results: Pyloric stenosis was occurred in six cases. In analysis, post-ESD stenosis was related to longitudinal diameter of resected specimen (>5cm, $P=0.035$) and circumferential mucosal defect over 75% ($P=0.019$). Also, stricture was higher in more than 2 times of ESD procedure than single ESD ($P=0.024$). Six patients of post ESD pyloric stenosis were managed with endoscopic balloon dilation and 4 patients improved the symptom.
Conclusion: Longitudinal diameter of specimen (>5cm) and circumferential mucosal defect (>75%) are associated with pyloric stenosis after ESD.
Disclosure of Interest: None declared

P1783 LONG-TERM FOLLOW-UP RESULT OF ENDOSCOPIC RESECTION OF GASTRIC GASTROINTESTINAL STROMAL TUMOR

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Introduction: Although endoscopic resection (ER) for various gastric tumors has been widely promoted, the suitability for gastrointestinal stromal tumor (GIST) is not clear. The aim of this study was to evaluate the feasibility, efficacy, safety, and long-term follow-up results of ER for gastric GIST.
Aims & Methods: The medical records of 49 patients who underwent ER for gastric GIST were collected between January 2000 and July 2014. After procedure, the recurrence of tumor was checked by endoscopy and abdominal CT during follow-up. Demographics, clinical data, therapeutic outcomes, complications, pathological characteristics, and follow-up outcomes were analyzed.
Results: ER including endoscopic enucleation, endoscopic snare resection (SR), and endoscopic submucosal dissection (ESD) technique was performed in 49 patients. Procedure-related complications developed in 16 patients: perforation (22.4%, 11/49), intra-procedure bleeding (8.2%, 4/49) and post-procedure bleeding within 7 days which required additional endoscopic hemostasis (6.1%, 3/49). Median follow-up period was 52.0 months (range: 12-116). En-bloc resection was achieved in 91.8% of patients (45/49); 91.9% (34/37) in enucleation, 80.0% (4/5) in EMR, 100.0% (7/7) in ESD. Complete resection rate was 71.4% (35/49); 70.3% (26/37) in enucleation, 80% (4/5) in EMR, 71.4% (5/7) in ESD. Recurrence occurred in 20% of patients (5/25); 15.8% (3/16) in enucleation, 33.3% (1/3) in EMR, 33.3% (1/3) in ESD. The rate of recurrence showed increasing tendency in lesions larger than 3cm, comparing lesion less than 3.0cm [66.7%(2 of 3) vs 13.6%(3 of 22); p = 0.091], and in the group of incomplete resection than the group of complete resection [50.0%(3 of 6) vs 10.5%(2 of 19); p = 0.070]. The median recurrence period was 73.0 months (range: 19-102).
Conclusion: Endoscopic resection (especially, enucleation, ESD technique-used endoscopic muscular dissection) could be alternative option for gastric GIST treatment. Long-term follow-up over 5 years should be considered in cases of incomplete resection and with lesion size larger than 3cm.
Disclosure of Interest: None declared

P1784 COMPARISON OF CLINICAL AND ENDOSCOPIC CHARACTERISTICS AMONG UPGRADE, CONCORDANCE AND DOWNGRADE PATHOLOGY AFTER ESD

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Introduction: Histologic discrepancies between endoscopic forceps biopsy (EFB) and endoscopic resection (ER) specimens, including ESD and endoscopic mucosal resection, have been reported at rates ranging from 2.7–49%. Our aims were to analyze the prevalence of upgraded, concordant, and downgraded pathology results after ESD and to compare their clinical and endoscopic characteristics.
Aims & Methods: We retrospectively reviewed the 1186 consecutive ESD performed at our center from February 2005 and December 2011, and included 837 cases diagnosed as low or high-grade dysplasia on the pre-ESD endoscopic forceps biopsy. The following endoscopic variables were analyzed; tumor size, surface area, sampling ratio (tumor size/number of forceps biopsy, surface area/number of forceps biopsy), predominant gross morphology, and surface configuration such as depression or ulceration.
Results: There was upgrade group in 203 cases (24.3%), concordance group in 552 cases (65.9%), and downgrade group in 82 (9.8%). Our database presented the mean length as follows: upgraded group 20.3 ± 9.7mm, concordant group 18.4 ± 8.6mm, and downgraded group 13.2 ± 7.8mm. The mean surface were represented as these: upgraded group 316.0 ± 302.1mm^2, concordant group 249.6 ± 232.1mm2, and downgraded group 141.2 ± 209.8mm2. Mean sampling ratio in tumor size were calculated as follows: upgraded group (6.9 ± 3.8mm/fragment and 99.2 ± 88.5 mm2/fragment), concordant group (6.6 ± 4.0mm/fragment and 94.8 ± 84.6 mm2/fragment), and downgraded group (4.8 ± 3.5mm/fragment and 51.1 ± 74.8mm2/fragment). Compared with upgraded and concordant group, the downgraded group showed smaller tumor size and lower sampling ratios (all, $P < 0.001$). And then the upgraded group had higher incidence of ulceration (13.5% vs 4.1%) and depression (46.5% vs 32.9%) more than concordant group (all, $P < 0.001$).
Conclusion: The tumor size and sampling ratio were predictable factor for downgraded final pathology after of ESD. And the ulceration and depression were forecasted for upgraded final pathology after ESD.
Disclosure of Interest: None declared

P1785 THE CLINICAL CHARACTERISTICS AND OUTCOMES OF AGENT ORANGE EXPOSED EARLY GASTRIC CANCER PATIENTS AFTER ESD

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Introduction: Currently, endoscopic submucosal dissection (ESD) is accepted as one of the treatment modalities for early gastric cancer and shows excellent treatments outcomes. Agent Orange (AO) is an herbicide used in the Vietnam War to defoliate forest areas. Many Korean veterans who participated in the Vietnam War were exposed to this chemical. But, the influence of the material remained uncertain to the stomach cancer disease course. So, we investigated the clinical characteristic and outcomes of AO exposed early gastric cancer (EGC) patients after ESD.
Aims & Methods: From January 2008 to December 2013, 121 EGC patients, including 61 AO exposure veterans, treated by ESD and followed up more than 12 months were enrolled, retrospectively. All patients were checked by gastrofiberscope and CT scan regularly for recurrence. Synchronous and metachronous lesion were defined as a new lesion found out within 1 year and as a new lesion found out more than 1 year after 1st ESD treatment. We analyzed the clinical characteristics and outcomes such as survival rate, the synchronous and metachronous lesion occurrence between the two groups whether or not exposed to AO.
Results: The median age was lower in AO exposed patients than in those not exposed (66 (57-78) vs. 77.5 (52-85), $p < 0.05$). Otherwise, there was no difference between the two groups in clinical characteristics such as tumor location, type, size, and histology, statistically. On the clinical outcomes, there was no relationship between AO exposure and the occurrence of the synchronous and metachronous lesion, statistically (8.3% vs. 3.3%, p = 0.272, 13.3% vs. 8.2%, p = 0.305). There was no meaningful difference of the two groups about the cumulative survival rate and disease free survival rate, too.
Conclusion: Although the AO exposed EGC patients were younger, the clinical characteristics and the clinical outcomes were not different in compare with those who were not exposed to AO.
Disclosure of Interest: None declared

P1786 GASTRIC POLYPS: WHAT IS THE CLINICAL SIGNIFICANCE?

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Introduction: Gastric polyps are a frequent endoscopic diagnosis, but the evidence supporting approach of this pathologic finding is scarce, which is reflected in the absence of clear recommendations.
Aims & Methods: Characterize a cohort of patients undergoing endoscopy and gastric polypectomy.
240 patients were included in which were made 447 polypectomies. We performed a retrospective review of demographics, phenotype of polyps (number, size and histology), presence of *Helicobacter pylori* and clinical outcome in the period from 01/01/2012 to 31/12/2014.
Results: Mean age 62.3 years; 67.9% were female; Mean age in patients with polyps dysplasia was 66.8 years and in patients with polyps without dysplasia was 61.9 years. Histological type: 64.2% (n = 287) hyperplastic, 17% (n = 76) nonspecific/foveolar polypoid hyperplasia, 10.7% (n = 48) fundic glands, 3.8% (n = 17) inflammatory fibroid, 2.2% (n = 10) adenomas, 0.9% (n = 4) hamartoma, 0.9% (n = 4) neuroendocrine tumor and 0.2% (n = 1) adenocarcinoma. 2.2% of polyps had dysplasia (all adenomas) - low-grade 70%, high grade 30%. Polyps < 5 mm were observed in 42.5% and ≥ 5 mm in 57.5%. 19.6% had previous polypectomy. Size of polyps ≥ 5 mm was significantly associated with risk of dysplasia ($p < 0.05$). *H. pylori* infection present in 50.4%.

Location of polyps in gastric body was associated with female sex ($p < 0.05$). It was also found that location in gastric body associated to polyps < 5mm ($p = 0.01$).
There was no statistically significant difference between dysplasia and presence of *Hp*, histological type or association with familial syndromes.
Conclusion: All polyps with more than 5 mm must be excised by the potential risk of malignancy. In this population the most frequent polyps were hyperplastic. The dysplasia/carcinoma is an uncommon phenomenon in gastric polyps.
Disclosure of Interest: None declared

P1787 HISTOLOGICAL DIFFERENTIATION AND MUCIN PHENOTYPE IN WHITE OPAQUE SUBSTANCE-POSITIVE GASTRIC NEOPLASIAS

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Introduction: White opaque substance (WOS) on magnifying endoscopy with narrow band imaging (M-NBI) was first reported by Yao *et al.* as a substance in the superficial area of gastric neoplasias that obscured the subepithelial microvascular architecture. Yao *et al.* reported that WOS is caused by lipid droplets and used oil-red-O staining to detect the accumulation of lipid droplets in the cells of WOS-positive gastric neoplasms [1]. In a previous study from our group, the accumulation of lipid droplets was confirmed as a cause of WOS in gastric neoplasias by immunohistochemical and immunoelectron microscopic studies of adipophilin, which was recently identified and validated as a marker of lipid droplets [2]. However, the precise clinicopathological significance of WOS-positive gastric neoplasias remains unclear.
Aims & Methods: The aim of the present study was to investigate the characteristics of the histological differentiation and mucin phenotype in WOS-positive gastric epithelial neoplasias.
A total of 130 gastric epithelial neoplasias (46 adenomas and 84 early adenocarcinomas) from 120 consecutive patients were retrospectively evaluated. The presence or absence of WOS was evaluated by M-NBI. Lipids were examined by immunohistochemical staining for adipophilin. Tissue phenotypes were immunohistochemically classified as intestinal (I), gastrointestinal (GI), and gastric (G) using antibodies against CD10, MUC2, MUC5AC and MUC6. The histological differentiation and mucin phenotype of WOS-positive neoplasias were characterized and examined according to adipophilin expression.
Results: The presence of WOS by M-NBI was correlated with histological differences between adenoma or differentiated type adenocarcinoma and mixed type or undifferentiated type adenocarcinoma ($P = 0.0153$, Fisher's exact test). Adipophilin was only expressed in primary adenoma and well to moderately differentiated adenocarcinoma components but not in undifferentiated components. WOS and adipophilin expression were only observed in neoplasias with I or GI phenotypes, but not in those with the G phenotype ($P < 0.0001$, Fisher's exact test).
Conclusion: WOS in gastric epithelial neoplasias indicates differentiation into a mature histological subtype with GI or I mucin phenotype.

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Disclosure of Interest: None declared

P1788 THE USEFULNESS OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC NEOPLASMS IN THE REMNANT STOMACH

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Introduction: Endoscopic submucosal dissection (ESD) appears to be desirable for early gastric neoplasms (EGNs) in the remnant stomach because it is less invasive than surgical resection. However, ESD after gastrectomy is a technically difficult procedure because of the limited working space in the remnant stomach as well as the presence of severe fibrosis and staples left under a suture line.
Aims & Methods: The aim of this study was to evaluate the usefulness of ESD for early gastric neoplasms in the remnant stomach. Between June 2007 and December 2014, ESD was performed for 680 EGNs in 447 consecutive patients at the National Hospital Organization Kure Medical Center/Chugoku Cancer Center. These lesions were divided into two groups: 22 lesions in the remnant stomach of 17 patients (Remnant Group) and 658 lesions in the entire stomach of 430 patients (Entire Group). We compared the treatment results, adverse events and clinical outcomes of ESD between two groups.
Results: Among the 17 patients in Remnant Group, 11 had previously undergone a distal gastrectomy, three a gastric conduit, two a proximal gastrectomy and one a partial gastrectomy. The en block resection rate was 95.5% (21/22) for Remnant Group and 97.1% (639/658) for Entire Group. The en bloc resection rate with tumor-free margins was 91.0% (20/22) for Remnant Group and 94.4% (621/658) for Entire Group (a non-significant difference [n.s.]). In terms of adverse events, the rate of perforation was 0% (0/22) for Remnant Group and 0.5% (3/658) for Entire Group. The rate of delayed bleeding was 0% (0/22) for Remnant Group and 3.2% (21/658) for Entire Group (n.s.). Histopathologically, three lesions in Remnant Group were diagnosed as non-curative resection. One of these patients had undergone piecemeal EMR due to severe fibrosis. In another patient, the lesion invaded the submucosa to a depth into 800μm. These two patients declined additional surgical treatment. Only one patient underwent additional surgery because the lesion invaded the muscularis propria. The curative resection rate was 86.4% (19/22) for Remnant Group and 88.6% (583/658) for Entire Group (n.s.). The local recurrence rate was 0% (0/21) during the median follow-up duration of 25 months for Remnant Group and 0.6% (4/630) during the median follow-up duration of 36 months for Entire Group.
Conclusion: In terms of treatment results, adverse events and clinical outcomes, there were no significant differences between the remnant-stomach and entire-stomach groups. Therefore, ESD for EGNs in the remnant stomach can be a feasible and safe therapeutic method.
Disclosure of Interest: None declared

P1789 ENDOSCOPIC RESECTION OF NON-AMPULLARY DUODENAL EPITHELIAL TUMORS: A SINGLE-CENTER EXPERIENCE

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Introduction: Because non-ampullary duodenal epithelial tumors (NADETs) are rare, the standardized clinical management of NADETs has not been established. Endoscopic resection (ER) is a standard treatment for superficial tumors in the digestive tract, and ER was recently applied to NADETs.
Aims & Methods: The aim of our study was to investigate the clinical outcomes and adverse events of ER of NADETs at the National Hospital Organization Kure Medical Center/Chugoku Cancer Center, Kure, Japan. Twenty-five consecutive patients with 26 NADETs underwent ER by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) between May 2008 and January 2015. We analyzed clinicopathological features of NADETs, clinical outcome and adverse events for ER of NADETs.
Results: The median tumor size was 12mm (range 3–40mm). The lesions were 11 adenomas, 12 mucosal carcinomas and 3 carcinoid tumors. The ERs included 21 EMRs and 5 ESDs. Six lesions underwent additional argon plasma coagulation after ER. Immediate closure following ER was performed in all but one of the 26 lesions by means of prophylactic clipping. The en block resection rate was 88.5% (23/26) and the en bloc resection rate with tumor-free margins was 73.1% (19/26). Regarding adverse events, only one delayed bleeding and one delayed perforation were observed, in the same patient, who required emergency surgery. This was the only case in which prophylactic clipping was not applied. Additional surgery was done in two other cases. One mucosal carcinoma underwent piecemeal EMR, and as that patient had an advanced colon cancer, additional duodenal resection and surgery for the colon cancer was performed at the same time. An other patient underwent ESD for a carcinoid tumor, and since the histopathologically vertical margin was positive, additional surgery was conducted. Among the other 23 patients, no recurrence was observed during the 22-month median follow-up period.
Conclusion: Duodenal ER was feasible as a therapeutic procedure. Prophylactic clipping can probably reduce the risk of adverse events.
Disclosure of Interest: None declared

P1790 DIAGNOSTIC VALUES OF SERUM PEPSINOGENS, GASTRIN 17 AND *HELICOBACTER PYLORI* IGG ANTIBODIES FOR ATROPHIC GASTRITIS OR GASTRIC CANCER PATIENTS SCREENING IN A HIGH-RISK AREA IN CHINA

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Introduction: Gastric cancer (GC) is still highly prevalent in the world and remains the second most common leading cause of cancer death. In recent years, the usefulness of the serum pepsinogens (PG), gastrin-17 (G-17) and *Helicobacter pylori* IgG Antibodies (Hp-IgG) has been used for screening of early diagnose chronic gastric atrophy and gastric cancers.
Aims & Methods: To estimate if serum levels of PG, G-17 and Hp-IgG are valuable as non-invasive methods to diagnose patients with Atrophic gastritis (AG) and those with Gastric cancer (GC) in Gansu province in China. A total of 190 patients who underwent endoscopic examination and biopsy were enrolled in this study. Based on the pathological results of endoscopic biopsies, these studied subjects were classified into the following four groups: normal group (n = 40); AG group (n = 45), including antrum-predominant AG (AAG, n = 30) and corpus-predominant AG (CAG, n = 15); early GC group (EGC, n = 45) and advanced GC group (AGC, n = 60). In AGC and GGC groups there were gastric antral cancer(n = 45), gastric body cancer(n = 42) and cardiac cancer(n = 18) in all. Serum levels of PgI, PgII and G17 were tested by enzyme-linked immunosorbent assay (ELISA) and Hp-IgG was measured with Gastro Panel kit.
Results: Serum PGI and PGR values were decreased significantly in AG, EGC and AGC groups compared with normall group ($P < 0.05$). PGR was decreased

in EGC and AGC compared with AG group (P = 0.02). G17 was significantly increased in EGC and AGC groups compared with normal group (P < 0.05). In AG group G17 was significantly decreased in AAG compared with CAG (P = 0.03). The positive rate of Hp-IgG was most high in advanced GC group (72.58%). The PGI combined with PGR test showed the predicted percentage of correct were 64.6%, 74.8%, 76.0%, 78%, respectively for diagnose patients with AAG, CAG, gastric antral cancer and gastric body cancer. While the percentage increased to 72.3%, 83.5%, 78.7%, 86.0% when combined PGI, PGR with G17 and Hp-IgG. And it showed an estimate sensitivity and specificity of 31.1%, 94.1%; 66.7%, 91.8%; 77.1%, 80%; 50.0%, 95.0% for diagnosing patients with gastric antral cancer, gastric body cancer, AAG and CAG when combined these serum markers.
Conclusion: Our findings suggested the low levels of serum PGI and PGR and high levels of G17 are predictive for patients with GC. Serum Pgs combined with G17 and Hp-IgG could reflect function of gastric mucosa and increase the screening rate for patients with GC and AG in this high risk area in China.

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P1791 ASSESSMENT VALUES OF USING SERUM PEPSINOGEN COMBINED WITH *HELICOBACTER PYLORI* IGG ANTIBODIES– THE "ABC METHOD" FOR GASTRIC CANCER SCREENING IN A HIGH-RISK AREA IN CHINA

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Introduction: Gastric cancer remains one of the most important malignant tumors. Japanese scholars began to recommend the use of serum Hp-IgG antibodies and PG - ''ABC method'' for large-scale screening for early gastric cancer in 2007. While this method has not yet been widely used in China.
Aims & Methods: To evaluate if the ''ABC method'' is useful to screen patients with gastric cancer in China. A total of 1008 participants were diagnosed(by endoscopy examination combined with endoscopic biopsies)as normal group (n = 323), atrophic gastritis (AG) patients (n = 648), early gastric cancer (EGC) patients (n = 8), advanced gastric cancer (AGC) patients (n = 4), gastric and duodenal ulcer patients (n = 25). PGI, PGR levels and Hp-IgG were analyzed by latex immunoassay and colloidal gold method, respectively. The ''ABC method'' was cited to group the studied patients, such as group A[Hp(-)PG(-)], B[Hp(+)PG(-)], C[Hp(+)PG(+)] and D[Hp(-)PG(+)]for analysis.
Results: PGI and PGR values decreased significantly in patients with AG(P = 0.04) and PGR decreased the most in patients with AGC group (P = 0.01). It showed that the incidence of AG in A, B, C and D group was 61.83%, 59.74%, 74.52% and 88.33%, respectively. While the incidence of GC in A, B, C and D group was 1.14%, 0.57%, 2.55% and 3.33%, respectively. The incidence of AG were significantly higher in group C and D than those in group A and group B (P < 0.05, respectively). No significant difference in the incidence of GC was found in four groups (P > 0.05).
Conclusion: The ''ABC'' method is valuable to assess the degree of atrophic gastritis but not the incidence of gastric cancer. Some cohort studies is needed in China.

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P1792 ESD(ENDOSCOPIC SUBMUCOSAL DISSECTION) FOR EARLY GASTRIC CANCER IN ELDERLY PATIENTS

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Introduction: Endoscopic submucosal dissection(ESD) is the effective therapy for early gastric cancer (EGC). Japan has the longest life expectancy in the world, the number of eldely patients in whom ESD performed has also increased. However, there were few reports about outcomes of ESD for EGC.
Aims & Methods: The aim of this study is to evaluate clinical outcomes of ESD for EGC in elderly patients.
131 elderly patients (≧75 years) with early gasric cancer received first ESD at our hospital between February 2002 and July 2012. Clinical outcomes were analyzed. The patients were classified into a curative group and a noncurative group. We compared the characteristics of patients and lesions, and the overall survival rates between the two groups. We also analyzed the predictors for survival using the cox regression modeling.
Results: The subjects comprised 85 males and 46 females with a mean age (SD) of 79.9 (±3.8) years. En bloc, R0 and curative resection were achieved in 90.1%, 92.4% and 85.5%, respectively. 31 patients were died, none of them died due to gastric cancer. As additional treatment in the noncurative group, 5 patients underwent operation, 2 underwent ESD and 1 patient underwent APC. 11 patients was monitored without additional treatment in the noncurative group. There were no significant differences in age, gender, location and depth of the lesions, and lymphovascular invasion between the two groups. The size of tumor in the noncurative group was larger than that in the curative group. The overall 3- and 5-year survival rates in the curative group were 81.6% and 71.1%, respectively, and the rates in the noncurative group were 80.5% and 71.6%, respectively. These differences are no statistically significant. On univariate analysis, cardiovascular disease tended to contribute to survival(p = 0.0549). The cumulative survival rate was significantly lower in patients with cardiovascular disease than in those without cardiovascular disease(p = 0.0483, Log-rank test).
Conclusion: ESD was useful for EGC in elderly patients. However we should carefully consider the indication of ESD for patients with cardiovascular disease.
Disclosure of Interest: None declared

P1793 CLINICOPATHOLOGICAL FEATURES OF MIXED-TYPE EARLY GASTRIC CANCER

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Introduction: En bloc resection of larger lesions and lesions with ulcer scars is now possible by endoscopic submucosal dissection (ESD), allowing for detailed pathological evaluation. We often experience cases with a preoperative diagnosis of differentiated adenocarcinoma and a postoperative diagnosis of mixed differentiated and undifferentiated adenocarcinoma (mixed-type early gastric cancer: MGC). Although MGC has a higher incidence of metastases to lymph nodes than pure differentiated early gastric cancer (PGC), adequate evidence for its clinical management has not been well investigated.
Aims & Methods: This study aimed to evaluate the clinicopathological features of MGC by comparisons between MGC and PGC. Among 330 cases of early gastric cancer who underwent ESD in our hospital between April 2009 and February 2015, we examined age, sex, main histological type, histological type of preoperative biopsy, tumor location, morphological type, tumor size, depth of invasion, depth of submucosal (SM) invasion, resection margins (lateral and vertical margin), lymphatic and venous invasion, and pathological ulcer scars in 284 PGC cases (197 males, 87 females; mean age 71.8 y; 315 lesions), and 31 MGC cases (24 males, 7 females; mean age 71.5 y; 31 lesions). The following cases were excluded: undifferentiated early gastric cancer (6), Barrett's esophagus adenocarcinoma (4), remnant gastric cancer (2), and recurrent cancer after endoscopic resection (3). Histological types were classified according to the Japanese Classification of Gastric Carcinoma: papillary (pap), well-differentiated (tub1), and moderately-differentiated (tub2) as ''differentiated'' and poorly-differentiated (por) and signet-ring cell carcinoma (sig) as ''undifferentiated''.
Results: There were no significant differences in tumor locations (U/M/L = 41/142/132 and 7/10/14 in PGC and MGC, respectively), morphological types (elevated/flat/depressed = 137/7/171 and 8/2/21 in PGC and MGC, respectively), lateral margins (positive/negative = 20/295 and 1/30 in PGC and MGC, respectively), and pathological ulcer scars (positive/negative = 22/293 and 5/26 in PGC and MGC, respectively). Regarding main histological type and histological type in preoperative biopsy, tub2 was observed significantly higher in MGC than PGC (51.6% vs. 3.8%, $P<0.01$ and 45.2% vs. 4.4%, $P<0.01$). Twenty-eight of 31 (90.3%) cases in MGC were diagnosed as ''differentiated'' on preoperative biopsy specimens. Compared to PGC, tumor size in MGC was significantly larger (23.2 ± 11.4 mm vs. 14.9 ± 10.9 mm, $P<0.01$) and there were more SM cancers (51.6% vs. 11.4%, $P<0.01$), deeper SM invasion (683.8 ± 793.0 μm vs. 1468.8 ± 1259.9 μm, $P<0.01$), more positive for vertical margins (12.9% vs. 2.5%, $P<0.05$), more lymphatic invasions (22.6% vs. 1.6%, $P<0.01$), and venous invasions (6.5% vs. 1.3%, $P<0.01$).
Conclusion: In cases in which histological type in preoperative biopsy shows tub2, we should pay particular attention to the possibility of mixed-type early gastric cancer. This study elucidated that the clinicopathological features of mixed-type early gastric cancer possessed higher malignant potential than pure differentiated early gastric cancer.
Disclosure of Interest: None declared

P1794 IS TUMOR AREA MORE HELPFUL TO PREDICT CLINICAL BEHAVIORS THAN TUMOR SIZE IN GASTRIC CANCER?

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Introduction: Tumor burden is important to predict clinical behaviors of cancer such as lymph node metastasis (LNM), recurrence after treatment, or survival rate. Tumor size has been used as an indicator of tumor burden such as indication of endoscopic resection in early gastric cancer (EGC) to predict LNM. Several studies reported the clinical significance of tumor area or volume measured by endoscopic ultrasound in EGC or esophageal cancer.

Aims & Methods: The aim of study was to investigate whether tumor area can be more helpful to predict clinical behaviors than tumor size in gastric cancer. Between January 2000 and December 2005, data for 4,719 patients (2208 EGC; 2511 advanced gastric cancer) who underwent gastrectomy for gastric cancer were reviewed retrospectively. Tumor area was calculated by multiplying long and short diameter of the tumor in surgical specimen. Tumor size means long diameter of the tumor in specimen. Clinical behaviors included LNM, recurrence rate, and survival rate. Clinical behaviors were compared between tumor area and tumor size using area under receiver operating characteristic (AUROC) curves. For survival rate, integrated AUC (iAUC) was used.

Results: The mean tumor size and tumor area was 39.82 mm (1-280) and 1.787 mm^2 (1-56000). Tumor size and tumor area showed a strong correlation (correlation coefficient 0.880, $P<0.01$). The cutoff value for prediction of LNM was 33 mm of tumor size and 858 mm^2 of tumor area. There was no significant difference between tumor size and tumor area for prediction of LNM (AUC 0.874 vs. 0.873, respectively). For prediction of recurrence rate, the cutoff value was 38 mm of tumor size and 1.480 mm^2 of tumor area. However, there was no significant difference between tumor size and tumor area for prediction of recurrence rate (AUC 0.857 vs. 0.857, respectively). For survival rate, the cutoff value was 12 mm of tumor size and 100 mm^2 of tumor area. However, tumor size and area didn't show the significant differences to predict survival rate (iAUC, 0.557 vs. 0.554, respectively). When analyzed among EGC or advanced gastric cancer, prediction power about clinical behaviors between tumor size and tumor area was not significantly different.

Conclusion: Tumor area was not more helpful to predict clinical behaviors than tumor size in gastric cancer. Therefore, tumor size may be sufficient as an indicator of tumor burden.

Disclosure of Interest: None declared

P1795 CLINICAL OUTCOME OF CLUTCH CUTTER ENDOSCOPIC SUBMUCOSAL DISSECTION (CCESD) FOR EARLY GASTRIC CANCER IN ELDERLY PATIENTS

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Introduction: Endoscopic submucosal dissection (ESD) has the advantage of permitting en bloc and histologically complete resection for early gastric cancer. There is currently little information on the clinical outcomes of ESD for gastric cancer in elderly patients.

Aims & Methods: The aim of the present study is to evaluate the clinical outcome of CCESD in elderly patients. We reviewed 232 consecutive patients with early gastric cancer of absolute and expanded indication according to the Japanese Gastric Cancer Association who underwent CCESD between June 2010 and February 2014 at Aso Iizuka hospital. We divided them into two groups according to age: elderly patients(>80 years; $n=64$) and non-elderly patients($\leqq 80$ years; $n=168$). We retrospectively compared the prevalence rates of pre-existing comorbidities, anticoagulant therapy, en-bloc resection rate, mean duration of hospitalization, incidence of CCESD-related complications, change of performance status (PS) before and after ESD, and the financial cost of admission.

Results: The elderly group was comprised of 64 patients and the non-elderly group was comprised 168 patients with mean ages of 84.1 and 69.5, respectively. Elderly patients had significantly more pre-existing comorbidities than nonelderly patients, specifically heart diseases. En-bloc resection rates in the nonelderly group were significantly higher than those in the elderly group (100% v.s. 95.3%, $p=0.02$). There were no significantly differences in anticoagulant therapy, mean duration of hospitalization, incidence of CCESD related complications, change of performance status (PS) before
and after ESD, and financial cost of admission.

Conclusion: CCESD has a good clinical outcome in the treatment of early gastric cancer in elderly patients.

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Disclosure of Interest: None declared

P1796 THERAPEUTIC OUTCOMES OF ENDOSCOPIC RESECTION FOR NON-AMPULLARY DUODENAL NEOPLASMS: A SINGLE-CENTER ANALYSIS

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Introduction: Endoscopic resection (ER) for non-ampullary duodenal neoplasms is still challenging because of the difficulty in scope maneuverability in the duodenum and the high incidence of complications: intraoperative perforation, delayed perforation, and delayed bleeding. Even in Japan, where endoscopic submucosal dissection (ESD) is prevalent nationwide, the feasibility of ER for non-ampullary duodenal neoplasms remains unclear.

Aims & Methods: We aimed to investigate the clinical outcomes of ER for non-ampullary duodenal neoplasms. This is a single-center retrospective analysis. We extracted all duodenal ER cases from our prospectively-pooled database and medical records. The following factors were assessed: patient characteristics, ER methods, pathological findings, complications, and tumor recurrence.

Results: From January 2009 to February 2015, 50 sessions of endoscopic treatment for non-ampullary duodenal neoplasms were performed. After excluding one session of additional coagulation following the previous ER, a total of 49 sessions of ER in 46 patients were included in the present analysis (29 males, 17 females; mean age 62.3 ± 10.7 years). Therapeutic techniques were as follows: 2 polypectomies, 19 ESDs including 7 cases of snaring after circumferential incision and 4 cases of snaring after partially submucosal dissection, and 28 cases of endoscopic mucosal resection (EMR). 1 EMR case was aborted because of massive intraoperative bleeding, and emergency surgery was performed for this case. En block resection was achieved in 32 cases (65.3%; EMR 19/ESD 11/polypectomy 2). The pathological findings were as follows: 23 adenocarcinomas (4 submucosal adenocarcinomas), 9 high-grade adenomas, 11 low-grade adenomas and 6 other histological types. R0 en block resection was achieved in 17 cases (34.7%; EMR 7/ESD 8/polypectomy 2). As for complications, the results were as follows: 6 cases of delayed bleeding (12.2%; EMR 3/ESD 3); 1 case of intraoperative perforation (2.0%; EMR 0/ESD 1); 2 cases of delayed perforation (4.1%; EMR 1/ESD 1). Both of the delayed perforation cases were treated conservatively. Among the 29 patients who could be followed >1 year, 2 patients had tumor recurrence during follow-up, but both the cases were treated endoscopically. There have been no metastasis cases to date.

Conclusion: ER for non-ampullary duodenal neoplasms seems feasible, but a relatively high complication rate implies that en block resection may not always be imperative.

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P1797 ALCOHOLIC LIVER DISEASE IS ASSOCIATED WITH AN INCREASED RISK OF GASTRIC NEOPLASM

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Introduction: The risk factors strongly associated with gastric cancer are *Helicobacter pylori* and smoking. However, an association between alcohol drinking and gastric cancer is still controversial. We performed a retrospective study to evaluate whether alcohol induced liver disease (ALD) is associated with the increased risk of gastric cancer development.

Aims & Methods: We reviewed the medical records of 514 patients who were diagnosed with ALD (alcoholic fatty liver disease, alcoholic hepatitis, or alcoholic liver cirrhosis) at Seoul Metropolitan Government Boramae Hospital between January 2000 and December 2011. For each patient, an age- and gender-matched control was identified from a population of asymptomatic individuals. And the clinical characteristics and risk factors associated with the development of gastric cancer of ALD patients group were compared with those of healthy group. A case-control study was performed to determine whether ALD patients had an increased risk of developing gastric neoplasm. Time to detect gastric adenoma was calculated using Kaplan-Meier cumulative curves and estimated using the log-rank test.

Results: The prevalence of gastric neoplasm were 16 (3.1%) in ALD patients and 8 (1.6%) in healthy control ($P = 0.098$). There was significant difference in the prevalence of gastric cancer (2.7% vs 0.6%, $P = 0.007$) between ALD and healthy group. Odds for detecting a gastric cancer in ALD patients were approximately 4.77 times greater than in healthy control (OR = 4.77 (95% CI:1.36-16.69)). Alcohol liver disease (Hazard ratio (HR) = 5.32; 95% CI: 1.51-18.68; $P = 0.009$) and age (HR = 12.49; 95% CI: 1.65-94.84; $P = 0.015$) was significant risk factors in a multivariate Cox-regression analysis. In addition, a significant difference was found in the cumulative incidence of gastric cancer between ALD and healthy subjects (Log rank test, $P = 0.005$).
Conclusion: The yield of gastric neoplasm was significantly higher in patients with alcoholic liver disease than in healthy subjects. Careful endoscopy surveillance is warranted in patients with ALD who expected long-term survival.
Disclosure of Interest: None declared

P1798 DISCREPANCY BETWEEN ESTIMATED PRE-ESD INDICATION AND POST-TREATMENT CURATIVE RESECTION CRITERIA IN EARLY GASTRIC CANCER

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Introduction: Early gastric cancer (EGC) lesions estimated to be within endoscopic submucosal dissection (ESD) indications before treatment often turns out to be out-of-expanded criteria on the pathological evaluation of resected specimen. We investigated the curative resection rates according to the pre-treatment clinical indications for ESD in EGC patients.
Aims & Methods: We retrospectively reviewed data of EGCs meeting the absolute or expanded indications before ESD between 2004 and 2011 at the National Cancer Center, Korea. The pre-ESD clinical indications were compared with the post-ESD criteria for curative resection. Pre-ESD factors, which are associated with out-of-expanded criteria cases at the final ESD pathologic evaluation, were also analyzed.
Results: Of 756 patients, pre-ESD estimated indications were absolute in 660 patients and expanded in 96 patients. En-bloc resection rates were not different between both pre-ESD indication groups (98.6% in pre-ESD absolute indication and 96.9% in pre-ESD expanded indication, $P = 0.197$). However, curative resection rate was significantly lower in patients with pre-ESD expanded indication than in those with pre-ESD absolute indication (64.6% vs. 81.7%, respectively; $P < 0.001$). In patients with pre-ESD absolute indication, post-ESD pathological criteria were absolute in 407 patients (61.7%), expanded in 162 (24.6%), and out-of-expanded in 91 (13.8%). In patients with pre-ESD expanded indication, post-ESD curative resection critera turned out to be absolute in 26 patients (27.1%), expanded in 41 (40.2%), and out-of-expanded in 29 (30.2%). Rate of non-curative resection due to out-of-expanded criteria were significantly higher in pre-ESD expanded group than in absolute group ($P < 0.001$). Of pre-ESD expanded indications, rates of post-ESD out-of-expanded criteria were 27.4% (17/62 patients) in mucosal EGCs with differentiated histological type of size > 2 cm without ulcer, 21.1% (4/19 patients) in those with differentiated histological type of size ≤ 3 cm with ulcer, and 53.3% (8/15 patients) in those with undifferentiated histological type of ≤ 2 cm without ulcer. A multivariate analysis showed that age > 65 years, tumor size > 2 cm, upper third of tumor location, and undifferentiated histologic type on pre-ESD evaluations were significant risk factors for out-of-expanded criteria after ESD.
Conclusion: Non-curative resection because of out-of-expanded criteria was found in as much as one third for EGC lesions clinically meeting expanded indication before ESD. Possibility of additional surgery should be emphasized to patients before undergoing ESD for EGC lesions meeting expanded indications, especially for tumors with undifferentiated histological type.
Disclosure of Interest: None declared

P1799 THE LONG-TERM OUTCOMES OF ESD FOR UNDIFFERENTIATED-TYPE EARLY GASTRIC CANCER AND INCIDENCE OF MULTIPLE GASTRIC CANCERS (SYNCHRONOUS OR METACHRONOUS)

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Introduction: Endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) in histology of undifferentiated-type (UD-type) adenocarcinoma is gradually prevailing from its minimally-invasive approach, though it is defined as clinical research in expanded indication of ESD according to Japanese Gastric Cancer Association (JGCA). There are still few reports of long-term outcomes and no report of multiple gastric cancers (synchronous or metachronous).
Aims & Methods: The aim is to clarify long term outcomes of ESD for UD type EGC and frequency and histological type of synchronous and metachronous cancer. We treated 248 UD-type EGC in 237 patients by ESD which is preoperatively diagnosed as expanded indication (within 20 mm, intramucosal, without ulceration, UD-type adenocarcinoma) from May 2004 to October 2014, in Cancer Institute Hospital, Tokyo, Japan. Median observation period was 46.5 months.
Results: Noteworthy, 237 patients (Male/Female 132/105, 60.6 years old on average) include 82 of *H.pylori* (Hp) uninfected patients (Male/Female 49/33, 56.9 years old in average). Regarding the mean age and tumor diameter, HP+ patients were significantly older and larger than HP- patients (62.6 vs 57.0 ($p < 0.001$), 13.4mm vs 8.2mm ($p < 0.001$)). Histological type of signet ring cell carcinoma (sig) and poorly differentiated adenocarcinoma (por) were 78.1%/21.9% for Hp + and 90.4%/9.6% for Hp - patients ($p < 0.001$). About macroscopic type, 79% of lesions were depressed type and 21% were flat type. Depressed type was significantly more dominant in HP+ patients than HP- patients ($p < 0.001$). Curative resection rate was 81% (192/237) and in 45 non-curative resection cases, 43 cases were performed additional surgery and 2 cases were followed without surgery. The reasons of non-curative resection were as follows: sm invasion/lymohovascular involvement/ulceration in tumor 24/5/9. About long-term outcomes, 222 cases are alive, 13 cases died of other causes and 2 cases died of gastric cancer, both of which were performed additional surgery, because one case had mp invasion and lymphovascular involvement, and the other case had sm massive invasion. They had recurrence and died of gastric cancer a year and 4 years later. Overall survival rate was 94.0% in 3 years and 90.1% in 5 years. Synchronous and metachronous cancers were detected in 7 cases (8 lesions) and 2 cases (3 lesions), respectively. Histological type was tub1/pap/sig/por 2/1/4/1 for synchronous cancer and tub1/tub2 2/1 for metachronous cancer. In total, 54.5% of the multiple cancers were UD-type. Synchronous cancers were detected in 1.32% (5/155 in Hp +, 2/82 in Hp -). The cumulative incidence rate of metachronous cancer was 0% in 3 years and 2.6% in 6 years. The incidence of synchronous and metachronous cancer were not different between Hp + and Hp - in this study.
Conclusion: Long-term outcomes of ESD for the UD type EGC in expanded criteria is satisfactory. Multiple gastric cancers were not frequent, however, the ratio of UD type was very high after resecting UD type gastric cancers by ESD.
Disclosure of Interest: None declared

P1800 DEVELOPMENT OF THE STRUCTURED ASSESSMENT OF GASTROINTESTINAL SYMPTOMS (SAGIS) INSTRUMENT AS A NOVEL INSTRUMENT TO MEASURE THE SEVERITY OF GASTROINTESTINAL SYMPTOMS IN THE CLINICAL SETTING

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Introduction: The assessment of gastrointestinal symptoms is key for targeted management of patients with a variety of gastrointestinal disorders. On the other hand, symptom assessment in the clinical setting is constrained by the available time and potentially biased by the special areas of interest of the clinician. Thus there is a need for a clinical instrument that supports the standardised assessment of patients.
Aims & Methods: Development of the SAGIS consisted of initial interviews with 8 patients referred for the diagnostic work up of digestive symptoms and relevant complaints identified. The instrument was refined with initially 22 and later 21 items developed and included. In addition, patients were asked to document what was their first and second most important problem. The questionnaire was given to 1384 consecutive patients. The sample was randomly split into derivation (n = 716) and validation datasets (n = 668). In addition, completed forms were handed with the case- notes to the treating physician at the time of the consultation, and after the consultation the clinician provided a working clinical diagnosis.
Results: Exploratory factor analysis conducted on the derivation sample supported a five factor model. This accounted for 68% of the total variance. The five GI symptom clusters were labelled as abdominal pain/discomfort (seven items), diarrhea/incontinence (five items), gastroesophageal reflux disease/regurgitation symptoms (four items), nausea/vomiting (three items) and difficult defecation and constipation (2 items). Confirmatory factor analysis conducted on the validation sample supported the initially developed five-factor measurement model ($c2/df = 4.76$; CFI = 0.92; RMSEA = .075). Further, 19 of 21 items demonstrated consistent factor loadings across gastrointestinal disease groups (e.g. functional gastrointestinal disorders (FGID), inflammatory bowel disease, liver disease, $p < 0.01$). Evidence of discriminant validity comes from observing that epigastric symptoms (F1) was higher in the FGID group than all other ($p < 0.0001$) and all symptom groups demonstrated some differentiation between disease groups.
Conclusion: The SAGIS questionnaire has good psychometric properties to assess type and severity of gastrointestinal symptoms in a standardised manner. The SAGIS shows differentiation across gastrointestinal disease groups and appears to support the clinical assessment of and symptom-based categorisation of patients.
Disclosure of Interest: None declared

P1801 UNITED EUROPEAN GASTROENTEORLOGY (UEG) WEEK – PROVIDING A PLATFORM FOR RESEARCHERS TO ACHIEVE FULL PUBLICATION FOLLOWING ABSTRACT PRESENTATION

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Introduction: The UEG week is the largest and most prestigious meeting about digestive diseases in Europe. Like other scientific meetings it encourages abstract submissions, permitting researchers the opportunity to convey novel research findings rapidly and also acquire informal peer review prior to full publication. The percentage of abstracts that actually achieve full publication is however highly variable, ranging between 11-78% from other medical specialty meetings.
Aims & Methods: Given the paucity of data evaluating gastroenterology meetings, this study aimed to evaluate UEG week abstracts and assesses their conversion rate to full publications in indexed journals. All abstracts presented at UEG week meetings between 2009 and 2011 were assessed in October 2014. PUBMED and EMBASE databases were reviewed using cross-referencing of first author, senior author and at least one key word from the abstract title. Abstracts and possible full publications were then examined in tandem to ensure they represented the same study. Abstracts that were withdrawn were excluded from the study. In addition to publication rates, data was collected on lag time to publication, journal impact factors and factors that may influence subsequent publication. Statistical analyses were performed using contingency tables and c2 statistics for categorical data using SPSS version 20.0.
Results: 6595 abstracts (1212 oral, 5348 poster presentations) were presented at UEG weeks between 2009-2011. Of these, 30.8% (2033/6595) went on to full publication in indexed journals, with a mean impact factor for journals of 3.93. The mean lagtime between abstract and full publication was 16 months. Abstracts selected for oral presentation had a conversion rate of 37.9% (459/1212), which was significantly higher than poster presentations at 29% ($p < 0.0001$). Poster sections with the highest conversion rates to full publications were Therapeutic Endoscopy/Interventional Radiology (39.3%), Oncology (38.3%) and Inflammatory Bowel Disease (34.3%), which were all significantly higher than Pancreas and Surgery sections at 25.9% and 22.9% respectively ($p < 0.001$)
Conclusion: This study demonstrates that almost one in three abstracts presented at UEG week progress to full publication, providing credibility to the process of abstract submission and enhancing the reputation of UEG week as being a premier platform for researchers to present their work. Given recent initiatives to enhance the quality of abstract submission at UEG week including abstract prizes, travel grants and poster champ award, the likelihood is that this conversion rate is only likely to increase.
Disclosure of Interest: None declared

P1802 PEPSINOGEN TEST NEGATIVE AND ANTI-HELICOBACTER PYLORI ANTIBODY NEGATIVE CHRONIC ATROPHIC GASTRITIS: CAN WE SCREEN IT VIA SERUM TEST?

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Introduction: The combination of serum anti-*Helicobacter pylori* IgG antibody (*Hp*Ab) and serum pepsinogen (PG), is known as the ABC method, classifies subjects into four different risk groups (A, B, C, or D) of developing gastric cancer (GC). Individuals in group A (*Hp*Ab(-)PG(-)) have the lowest GC risk but are not cancer free and the esophagogastroduodenoscopy (EGD) identifies chronic atrophic gastritis (CAG) in a certain number of them. The individual with CAG has a high probability of previous exposure to *Helicobacter pylori* (*Hp*) and a material risk of developing GC. Periodic GC screening via EGD is required for such a case. If any noninvasive and simple test could identify the individual with CAG, it would make GC screening more efficient for the selection of candidates who definitely require the periodic EGD.
Aims & Methods: The data of EGD screening program at Ota Memorial Hospital (OMH) between June 2012 and January 2015 was reviewed. *Hp*-er Hx and the false negative result in PG and *Hp*Ab were analyzed as the presumed predictive factor for CAG. The false negative in PG (PG(±)) and *Hp*Ab (*Hp*Ab(±)) were defined as follows: *Hp*Ab(±) is $3U/ml \leq HpAb < 10U/ml$ and PG(±) is $PG1 \leq 40ng/ml$ or $PG1/2 \geq 2.5$. Clinicopathological characteristics of GC cases detected in group A were also analyzed.
Results: The 11346 subjects were enrolled in an EGD screening program of OMH. The ABC method was undertaken by 10404 individuals. Of these, 142 cases were excluded from the analysis due to a past history of gastrectomy, which influences PG. Proportions of group A, B (PG(-)*Hp*Ab(+)), C (PG(+)*Hp*Ab(+)) and D (PG(+)*Hp*Ab(-)) were 72.5% (7442 individuals), 18.3% (1878), 8.2% (841), and 1% (101) respectively. In group A, EGD identified CAG in 1846 individuals (24.8%). 24.2% (1798 individuals) had *Hp*-er Hx. PG(±), *Hp*Ab(±), and "PG(±) or *Hp*Ab(±)" were recognized in 11.4%, 17.4%, and 20.7% of group A, respectively. Sensitivity, specificity, and predictive accuracy of *Hp*-er Hx, PG(±), *Hp*Ab(±), and "PG(±) or *Hp*Ab(±)" to CAG were 76.1, 46.0, 70.3, 83.4% in sensitivity, 92.9, 72.4, 88.6, 64.1% in specificity, and 88.7, 65.9, 84.1, 68.9% in predictive accuracy, respectively. Malignant neoplasms were found in 38 individuals during the term considered. 24 cases were diagnoses as GC (detection rate was 0.21%). 12 cases belonged to group A and EGD found CAG at 10 of these. These 10 cases were identified by the test results as "PG(±) or *Hp*Ab(±)", although they were not always detected via *Hp*-er Hx, PG(±), or *Hp*Ab(±) alone. Other two cases of GC in group A did not have CAG and were negative to *Hp*-er Hx, PG, and *Hp*Ab.
Conclusion: "PG(±) or *Hp*Ab(±)" revealed the highest sensitivity to CAG in group A, while specificity and predictive accuracy were high in *Hp*-er Hx and *Hp*Ab(±) alone. Half of GC cases detected in our screening program were classed as group A. Of these, all 10 cases with CAG could be identified via serum test as the result of "PG(±) or *Hp*Ab(±)". It should be also mentioned that CAG negative GC might increase its prevalence in Japan because the national financial support for *Hp*-er started on February in 2013.
Disclosure of Interest: None declared

P1803 ANALYSIS OF ESOPHAGEAL AND GASTRIC CANCER SCREENING AT MINQIN COUNTY OF WUWEI CITY, CHINA

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Introduction: Gastric cancer remains one of the most important malignant tumors and is considered as the second most common leading cause of cancer deaths worldwide. Gansu Province is the high incidence place in China, especially the Hexi area. gastric cancer is still the first cause of death in Gansu Province. Therefore, the prevention and early diagnosis of gastric cancer has great significance.
Aims & Methods: To explore the effects of gastroscopy combined with pathological biopsy pathologic in screening and follow-up at high-incidence regions of gastric cancer, and the prevalence of *Helicobacter pylori* infection, and the implication of endoscopic treatment for early cancer and precancerous lesions. In this study, 1343 natural populations were enrolled, with aged from 35 to 69 years old, from 5 villages randomly selected from Minqin county, Wuwei city, Gansu province of China. Between July 29th and Aug 24th in 2013, C13-urea breath test was used to diagnose *Helicobacter pylori* infection, endoscopic examination and pathological biopsy were performed for suspicious lesions. lugol chromoendoscopy was performed for screening early esophageal cancer. Follow-up by endoscopic examination and biopsy were accomplished for important cases. The clinically evaluated cases of gastric and esophageal cancer had been assigned to surgical operation or endoscopic treatment accordingly, and then follow-up.
Results: The positive rate *Helicobacter pylori* infection was 61.1% (820/1341), which accounted for 49% in men, 51% in women. A total of 1244 (92.8%) people were successfully accepted endoscopic screening, meanwhile, 41 (3.3%), 87 (7.0%) and 692 (55.6%) cases were diagnosed as gastric polyps, gastric ulcer and different degrees of chronic atrophic gastritis respectively. The overall cancer detection rate was 1.1% (14/1244), including 0.72% (9/1244) and 0.4% (5/1244) of gastric cancer and esophageal cancer respectively. Of 14 screened cancer cases, early stage cancer accounted 66.7% (6/9) and 80% (4/5) for gastric and esophageal cancer respectively. Surgical procedures were performed in all advanced cancers cases and 1 early gastric cancer. The rest of the early stage cancer were underwent endoscopic submucosal dissection successfully. With subsequent follow-up about 1 years, 1 case of early gastric cancer was underwent ESD again for ectopic early gastric cancer after 3 months of ESD, the rest cases without discomfort and recurrence.
Conclusion: Endoscopic and histological biopsies screening and treatment for precancerous and early stage cancer is a positive effect mode on prevention and treatment for gastric neoplasms. It is favorable for detecting early esophageal cancer to use esophageal iodine staining in gastric cancer screening. *Helicobacter pylori* infection rate is higher in Minqin County of Wuwei city.

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P1804 *HELICOBACTER PYLORI*, MGUS AND MYELOMA: A POSSIBLE PHYSIOPATHOLOGICAL LINK?

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Introduction: Multiple myeloma is a haematological cancer of unknown origin, characterized by abnormal accumulation of plasmocytes secreting a pathological monoclonal immunoglobulin (mc Ig), and always preceded by a stage of monoclonal gammopathy of undetermined significance (MGUS). The pathogenic mechanisms leading to the development of MGUS are not understood. Our aim was to test the hypothesis that chronic antigenic stimulation by infectious

pathogens, in particular by *Helicobacter pylori*, may be one of the mechanisms involved in the development of MGUS stage.
Aims & Methods: Patients with MGUS or myeloma presenting a mc Ig at concentration >8 g/L were included. *H. pylori* serology was performed and the mc Ig of these patients was purified. The analysis of the specificity of purified mc Ig was done using a new assay developed by our team, based on "protein chips", the Multiplexed Infectious Antigen Array (MIAA) assay. This assay includes the main antigenic epitopes of *H. pylori* and of 7 other pathogens (HCV, EBV, CMV, HSV-1, HSV-2, VZV, *T. gondii*). Whenever purified mc Ig specifically recognized *H. pylori*, confirmation of *H. pylori* recognition using western blotting was performed.
Results: Out of 242 patients examined at the Nantes University Hospital, 42 (17.4%) presented with *H. pylori*-positive serology. The mc Ig was successfully purified for 31 of these patients. For 5/31 patients (2 with MGUS, 3 with myeloma), the mc Ig was specifically directed against a *H. pylori* antigen: urease B in 3 cases, CagA in 1 case, and HSPB in 1 case.
Conclusion: The data suggest a causal relationship between *H. pylori* infection and the presence of mc Ig for a subset of patients with MGUS and myeloma. Prospective therapeutic studies are necessary to establish whether eradication of the bacterial infection will lead to the decrease or disappearance of mc Ig, particularly for MGUS patients.
Disclosure of Interest: None declared

P1805 *HELICOBACTER PYLORI* INFECTION IN PERIMENOPAUSAL WOMEN

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Introduction: *H. pylori* infection causes symptoms or its course is asymptomatic. The external gastrotoxic factors or deficiency of enteroprotective factors may adversely affect the natural history of chronic gastritis in Hp-infected patients. Protective factors include among others female hormones and melatonin, which secretion decreases with age, especially affecting postmenopausal women. At this period women often complain of gastrointestinal symptoms. It is not clear whether this is due to hormonal disorders or coexisting Hp infection.
Aims & Methods: The study was conducted in a group of 65 women before and after menopause. Group I –women without Hp infection and gastrointestinal tract pathology, Group II–with asymptomatic Hp infection. Diagnostic procedures-endoscopic and histologic appearance of the gastric mucosa, UBT-13C, the levels of 17-β-estradiol, FSH and melatonin. In the second stage the study included only women from group II. In 2006–2014 the overall assessment of their health state was performed every 12 months and examinations included all procedures as at the start of the program 2 years after the last menstruation. Two groups of women were determined in the postmenopausal period: IIa–without gastrointestinal complaints, IIb–with dyspeptic symptoms. In group IIb a 10-day antibacterial treatment was introduced (pantoprazole + amoxicillin + metronidazole or levofloxacin). The follow-up UBT-13C test was performed 8 weeks after the end of the treatment.
Results: No significant differences in the levels of estradiol, FSH and melatonin in both groups of women before menopause draws attention. In postmenopausal period the major changes occurred in the secretion of hormones. Compared to baseline estradiol levels decreased from 54.90 ± 4.91 to 20.00 ± 7.14pg/ml in the group with asymptomatic infection ($p < 0.001$) and to 17.40 ± 6.58pg/ml in the group with dyspeptic symptoms ($p < 0.001$);level of FSH increased to 62.60 ± 15.33mIU/L in group IIa ($p < 0.001$) and to 85.47 ± 17.71mIU/L in group IIb ($p < 0.001$). No significant differences were observed in the levels of 17β-estradiol and FSH between groups IIa and IIb. The level of melatonin decreased in both groups-respectively 9.93 ± 2.96pg/ml ($p < 0.05$) and 6.83 ± 2.32pg/ml ($p < 0.01$). However the level of melatonin was lower in the group with symptomatic infection– 6.83 ± 2.32 pg/ml ($p < 0.05$)-compared to the group with asymptomatic infection – 9.93 ± 2.96 pg/ml ($p < 0.05$). No significant differences found between both groups with regard to endoscopy pictures and UBT-13C test result. After the treatment, eradication of Hp was obtained in 25 women (92.6%). Dyspeptic symptoms resolved in 14 patients (51.8%) and decreased in 9(33.3%). Four patients (14.8%) still complained of mild epigastric pain.
Conclusion: Asymptomatic *H. pylori* infection can progress to symptomatic phase in postmenopausal women due to decreased secretion of female hormones and melatonin which have gastroprotective properties.

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Disclosure of Interest: None declared

P1806 THE IMPACT OF *HELICOBACTER PYLORI* ERADICATION ON SERUM HEPCIDIN-25 AND IRON PARAMETERS IN PATIENTS WITH IRON DEFICIENCY ANEMIA

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Introduction: The aim of this study was to evaluate the efficacy of a bismuth-based quadruple regimen as first-line therapy for *Helicobacter pylori* (HP) eradication in patients with unexplained iron deficiency anemia (IDA). We evaluated serum hepcidin-25, iron, ferritin, total iron binding capacity levels before and after eradication of *H. pylori* in IDA patients to assess whether it plays a role in IDA related to *H. pylori* infection.
Aims & Methods: Eighty consecutive patients with unexplained iron deficiency anemia and *H. pylori* infection were enrolled in this study. All patients received Pantoprazole (40 mg b.i.d.), bismuth citrate (120 mg q.i.d.), tetracycline (500 mg q.i.d.), and metronidazole (500 mg t.i.d.) for 14 days as the eradication regimen. Blood was sampled before treatment to eradicate *H. pylori* and again 1 month later. We used commercial enzyme-linked immunosorbent assay kit to determine serum hepcidin-25 levels in both groups.
Results: Hemoglobin, Fe, TIBC and ferritin levels improved in all the subjects after *H. pylori* eradication. Serum hepcidin-25 levels decreased significantly after with *H. pylori* eradication ($p < 0.001$).
Conclusion: Gastric *H. pylori* infection is a common cause of iron deficiency anemia of previously unknown origin in adult patients. Our result provides evidence that hepcidin level decreases after successful *H. pylori* eradication with the improvement of iron deficiency anemia.

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P1807 ASSOCIATION BETWEEN *HELICOBACTER PYLORI* INFECTION, THE TYPE OF GASTRIC PATHOLOGY AND GHRELIN SERUM CONCENTRATION

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Introduction: *Helicobacter pylori* could play a role in appetite regulation by affecting gastric secretion of ghrelin and leptin.
Aims & Methods: We aimed to evaluate the association of *H. pylori* infection and the type of gastric pathology with serum ghrelin and leptin concentrations and anthropometric nutritional status of dyspeptic patients. Fasted adults referred for an upper gastrointestinal endoscopy were enrolled in this study. A sociodemografic survey was administered to the patients and the ^{13}C-Urea Breath Test was performed. Height and weight were assessed for BMI calculation, and waist circumference to determine central adiposity. Serum total ghrelin and leptin levels were analyzed by ELISA. Four biopsies, two from the antrum and two from the corpus, were obtained during endoscopy for histopathology evaluation and Polimerase Chain Reaction DNA amplification. Statistical analysis was performed using a χ^2 test, Mann–Whitney U test, Kruskal-Wallis test and linear regression.
Results: 163 patients (40.8 ± 14.0y), 98/65 females/males, were included. Prevalence of *H. pylori* infection was 53.4% (CI95%;45.7-65.8%). Presence of *H. pylori* was associated with the type of gastric pathology both in the antrum ($P < 0.0001$) and the corpus ($P < 0.0001$), with a higher prevalence of active chronic gastritis among *H. pylori* positive patients. Overweight/obesity and central adiposity did not differ significantly between *H. pylori* infected and uninfected patients ($P = 0.09$ and $P = 0.87$, respectively). Median ghrelin concentrations were 306.5 pg/mL (IQR; 230.0–385.5) for the *H. pylori* positives and 358.3 pg/mL (IQR; 253.8-547.8) for the *H. pylori* negatives. Statistical analysis demonstrated that the infection was associated with lower serum ghrelin concentrations ($P = 0.016$), remaining associated after adjusting for BMI and gender in a linear regression analysis ($P = 0.019$). Moreover, the type and severity of gastric pathology in the corpus was also associated with lower ghrelin serum levels ($P = 0.03$), independently of the infection. Median leptin values were 1.75 ng/mL (IQR; 0.71–4.70) in the infected group and 1.84 ng/mL (IQR; 0.50-5.09) in the uninfected group, which were not significantly different ($P = 0.76$).
Conclusion: *H. pylori* infection and the type of gastric pathology in the corpus were associated to lower ghrelin serum concentrations in adult dyspeptic patients, supporting the role of *H. pylori* in the regulation of appetite.
Disclosure of Interest: None declared

P1808 ANTI-INFLAMMATORY ACTIVITY OF EGUALEN SODIUM HYDRATE IN A MOUSE MODEL OF *HELICOBACTER PYLORI* INFECTION

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Introduction: Consistent infection by *Helicobacter pylori* and chronic gastritis have been shown to be correlated with the development of gastric cancer. Triple antibiotic therapy is standard treatment for eradication of the bacteria, but the emergence of antibiotic resistance is an increasing concern. Several alternative treatments have been studied, but none have yielded efficacy comparable to that of antibiotic therapy. Egualen sodium hydrate, an azulene derivative, has protective effects on the stomach, ameliorating damage of stomach mucosa, and has been used as an antiulcer medication. In the present study, we investigated the anti-inflammatory activity of egualen sodium hydrate in a mouse model of *H. pylori* infection, including histopathological analysis and investigation of the host immune response.

Aims & Methods: C57BL/6 mice were divided into four groups of 10 animals each, as follows: Group 1, negative control; Group 2, infection control (0.5 mL sham vehicle: carboxymethyl cellulose solution only); Group 3, treatment with low-dose (20 mg/kg) egualen sodium hydrate; and Group 4, treatment with high-dose (60 mg/kg) egualen sodium hydrate. Starting eight weeks after challenge infection with *H. pylori* (5×10^7 CFU/mouse), animals in Groups 2-4 were treated by once-daily oral gavage for 4 weeks with sham vehicle or egualen sodium hydrate. At 4 days after the final dose administration, mice were sacrificed and tissues were harvested for evaluation of drug efficacy. CFU of colonizing bacteria in mouse stomach was calculated, the severity of gastritis was evaluated histologically, and cell proliferation was analyzed by histochemical staining for BrdU. Localized expression (in gastric mucosa) of the genes coding for Cox-2 and selected cytokines (interleukin [IL]-10, TNF-α, Interferon [IFN]-γ) also were measured using real time-PCR. Data were analyzed and compared using Kruskal–Wallis test and Student T-test.

Results: The severity of gastritis was significantly reduced in the egualen sodium hydrate-treated mice. The gastritis score in high-dose egualen-treated mice (1.7 ± 1.45) was significantly lower than that in the infection control mice (3.8 ± 1.45) ($p = 0.014$). The number of BrdU-labelled cells in the stomach of the high-dose egualen sodium hydrate-treated mice (39.2 ± 18.3 cells/20 glands) was significantly reduced compared to that observed in the infection control mice (63.0 ± 22.8 cells/20 glands) ($p = 0.004$). Neither the number of colonizing bacteria nor cytokine expression levels differed significantly among the groups.

Conclusion: Treatment with egualen sodium hydrate brought significant improvement of *H. pylori*-induced gastritis in mouse. This effect did not depend on reduction of bacterial number, suggesting that egualen sodium hydrate might serve as a therapy for preventing the progression of gastritis in patients not amenable to antibiotic therapy.

Disclosure of Interest: None declared

P1809 ROLE OF INFLAMMATORY MONOCYTES IN VACCINE-INDUCED REDUCTION OF HELICOBACTER INFECTION

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Introduction: Despite the proven ability of immunization to reduce *Helicobacter* infection in mouse models, the precise mechanism of protection has remained elusive.

Aims & Methods: In this study, we evaluated the role of inflammatory monocytes in the vaccine-induced reduction of *Helicobacter* infection.

Results: We first showed by using flow cytometry analysis that $CD11b^+CCR2^+Ly6C^{low}$ inflammatory monocytes accumulated in the stomach mucosa during the vaccine-induced reduction of *Helicobacter* infection. To determine whether inflammatory monocytes play a role in the vaccine-induced reduction of *Helicobacter* infection, these cells were depleted with anti-CCR2 depleting antibodies. Remarkably, depletion of inflammatory monocytes is associated with an impaired vaccine-induced reduction of *Helicobacte*r infection on day 5 post infection. Finally to determine whether inflammatory monocytes have a direct or indirect role, we studied their antimicrobial activities. We observed that inflammatory monocytes produced TNF-a and iNOS, two major antimicrobial factors. Lastly, by using a *Helicobacter in vitro* killing assay, we showed that inflammatory monocytes kill *H. pylori.*

Conclusion: Collectively, these data show that inflammatory monocytes play a direct role in the immunization-induced reduction of *Helicobacter* infection from the gastric mucosa.

Disclosure of Interest: None declared

P1810 THE GASTRIC MUCOSA FROM *HELICOBACTER PYLORI*-INFECTED PATIENTS HAS A LOWER LEVEL OF DUAL OXIDASE-2 (DUOX2) EXPRESSION THAN FROM UNINFECTED PATIENTS

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Introduction: *Helicobacter pylori* (*H. pylori)* is a well-recognized gastroduodenal pathogen and class I carcinogen. Dual oxidase-2 (DUOX2) and NOX2, members of NADPH oxidase family, have several critical physiological functions including hormone biosynthesis and host mucosal defense.

Aims & Methods

Aim: To investigate DUOX2 and NOX2 expression in human stomach in the presence and absence of *H. pylori* infection.

Methods: The biopsies were obtained from patients underwent endoscopic diagnosis. The serum of patients was assayed for two virulent factors of *H. pylori,* CagA and VacA. The inflammation in gastric mucosa was analyzed with histology. Quantitative real-time PCR was used to detect the expression of three members of NADPH oxidase, NOX1, NOX2 and DUOX2, as well as lactoperoxidase (LPO) in the gastric mucosa. DUOX2 protein levels were also quantified by Western blots and immunohistochemistry. NOX2 protein level was only observed by immunohistochemistry.

Results: The expression of DUOX2 mRNA and protein was lower in gastric mucosa of patients with *H. pylori* infection compared to those without infection. Among the *H. pylori*-infected patients, those infected with CagA and VacA strains had the lowest DUOX2 expression levels than those infected with at least one virulent factor or both CagA and VacA negative strain. The levels of NOX2 mRNA and protein were higher in patients infected with *H. pylori* than those without infection. NOX1 and LPO mRNA was undetectable in the gastric mucosa.

Conclusion: DUOX2 is expressed in the inflamed human gastric epithelium, with lower expression levels in patients with *H. pylori* infection than those without *H. pylori* colonization. This finding suggests that *H. pylori* infection may suppress DUOX2 expression to promote its own survival.

Disclosure of Interest: None declared

P1811 DIFFERENCE IN CAGA SEROPOSITIVITY AND PEPSINOGEN I AND II STATUS AMONG DIFFERENTIATED AND UNDIFFERENTIATED GASTRIC CANCER AND PEPTIC ULCERS

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Introduction: The CagA protein is a well-known virulent factor of *Helicobacter pylori (H. pylori*), and is related to an increased risk of peptic ulcers or gastric cancer (GC). Meta-analysis has shown a positive association between CagA seropositivity and GC. On the other hand, almost all *H. pylori* strains possess the *cagA* gene in Japan, but patients infected with *cagA*-positive *H. pylori* do not always induce serum CagA antibodies. Therefore, it is difficult to use CagA seropositivity as a marker for GC. A low level of serum pepsinogen (PG) has been used in Japan as a serum biomarker for early GC detection, the combined use of serum *H. pylori* antibody and PG measurement is useful for evaluating the risk of GC. However, few studies have considered serum CagA antibody and PG status when investigating GC classified by histopathological differentiation.

Aims & Methods: We aimed to estimate the seropositivity rates of *H. pylori* antibodies, CagA antibodies, and the abnormal PG status in patients with differentiated-type (i.e. intestinal type by Lauren) or undifferentiated-type (i.e. diffuse type) GC or gastric ulcers (GUs) or duodenal ulcers (DUs). A total of 234 patients, including 138 with differentiated-type GC (diff-GC), 21 with undifferentiated-type GC (undiff-GC), 44 with GUs, and 31 with DUs, were enrolled. The seropositivity of *H. pylori* antibodies and CagA antibodies were judged by the manufacturer's recommendations. The levels of serum gastrin PG I and II were measured and serum PG status was defined as abnormal when the criteria of PG I < 70ng/mL and PGI/II ratio < 3.0 were fulfilled.

Results: There was no significant difference in seropositivity rates of *H. pylori* antibodies between groups (diff-GC, 87.7%; undiff-GC, 85.7%; GU, 97.1%; DU, 96.0%). However, the seropositivity rates of CagA antibodies were significantly lower in the diff-GC group than in the other groups (diff-GC, 75.4%; undiff-GC, 90.5%; GU, 100.0%; DU, 96.8%); furthermore, CagA antibody titer levels were significantly lower in the diff-GC group than in the GU or DU groups (mean levels: diff-GC, 51.7 U/mL; undiff-GC, 68.1 U/mL; GU, 86.7 U/mL; DU, 89.6 U/mL). The rate of abnormal PG status was significantly higher in the diff-GC and undiff-GC groups than in the GU or DU groups. On the other hand, in the diff-GC group, the rate of the *H. pylori* seropositivity and abnormal PG status (Hp(+)/PG(+)) patients, and the CagA seropositivity and abnormal PG status ((CagA(+)/PG(+)) patients was 68.2%, 55.8%, respectively; the rates of Hp(+)/PG(+) patients were significantly higher than those of CagA(+)/PG(+) patients. The rate of the Hp(+)/PG(+) patients, and the CagA(+)/PG(+) patients in the undiff-GC group was 81.0%, 71.2%, respectively.

Conclusion: There is a difference in seropositivity rates and titer levels of CagA antibodies among the *H. pylori* related gastroduodenal diseases. In particular, these values were lower in patients with diff-GC than in those with undiff-GC or peptic ulcers. Therefore, this result suggests that the immune response against CagA is lower in patients with diff-GC. Moreover, the rate of CagA(+)/PG(+) patients did not surpass the rate of Hp(+)/PG(+) patients in the diff-GC and undiff-GC groups; therefore, the combined use of CagA antibodies and PG status would not be useful for detecting GC.

Disclosure of Interest: None declared

P1812 INSUFFICIENCY OF SECRETIN IN PATIENTS WITH PEPTIC ULCER DISEASE

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Introduction: Peptic ulcer disease belongs to classic acid-related disorders. The important factor contributing to duodenal ulcer occurrence is duodenal acidification which is an alkaline in normal case. Dysmotility of gastroduodenal area such as so-called arterio mesenteric duodenal compression and duodenogastric reflux also promotes ulceration. The main acidity regulator in duodenum outside of a digestion phase is gastrointestinal hormone secretin which is secreted by S-cells of duodenal mucosa and stimulates the production of liquid part of pancreatic juice by pancreas.
Long-term *Helicobacter pylori* persistency supports inflammation and ulceration which possibly can change production of APUD (Amine Precursor Uptake and Decarboxylation) system hormones.
Aims & Methods: The aim of our investigation was to study the secretin level in blood serum of patients with *Helicobacter pylori*-associated peptic ulcer disease.
Materials and methods: The study involved 148 patients with duodenal ulcer. The diagnosis of peptic ulcer was confirmed by endoscopy. ^{13}C-urea breath test detected *Helicobacter pylori* infection in all patients. The secretin content was determined by ELISA using of a set "Secretin", Peninsula, USA.
Results: During examining of patients with ulcer a reduction of secretin level in serum to 23.91 ± 0.83 ng/L was detected vs. 41.27 ± 2.66 ng/L ($p < 0.001$) in healthy persons. Thus, significant decrease of this index to 1.73 times was found in all patients with ulcer indicating to secretin insufficiency.
Considering that secretin inhibits gastrin secretion, i.e. naturally decreases gastric secretion, its insufficiency is one of the mechanisms of hypersecretion. Patients with low levels of secretin in the blood turned out to have the lowest pH. Direct strong correlation was detected between these indicators ($r = 0.71$; $p < 0.001$). Credible feedback was also found between the levels of secretin and the labeled $^{13}CO_2$ concentration in exhaled air during the ^{13}C-urea breath test ($r = -0.49$; $p < 0.001$). Furthermore, the higher $^{13}CO_2$ concentration was observed (indicating more intensive affection of mucosa membrane by *Helicobacter pylori*), the lower level of secretin was detected.
Conclusion: Secretin insufficiency was found in patients with duodenal ulcer. It could be considered as a result of continuous inflammation caused by *Helicobacter pylori*.
Disclosure of Interest: None declared

P1813 MIR-155 IS A MUCOSAL BIOMARKER FOR SEVERITY OF GASTRIC INFLAMMATION AND CORRELATES WITH HELICOBACTER PYLORI VIRULENCE FACTORS

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Introduction: *Helicobacter pylori (H.pylori)* infection is the main cause of gastric mucosal inflammation and the recognized trigger of gastric carcinogenesis. Pathogenicity of *H.pylori* is partly dependent on main bacterial virulence factors, such as *cagA* and *vacA*, but also on host genetic, environmental and other factors. We have recently identified a link between microRNA (miRNA) miR-155 and *H. pylori* infection and development of preneoplastic conditions (1).
Aims & Methods: Here we perform in depth analyses on miR-155 expression in large cohort of gastric mucosa samples and correlate the results with *H.pylori* infection specifically histological phenotype of gastritis, *H.pylori* virulence factors/genotype. In the prospective study (HELDIVPAT, ERA-NET), 192 patients (with normal mucosa (N), chronic gastritis (CNAG), atrophic gastritis ± intestinal (AG) underwent upper GI endoscopy. Gastric biopsies were histologically characterized according to Sydney classification. *H.pylori* genotyping (*cagA*, *vacA*) was performed following bacterial cultivation. Quantitative TaqMan assay has been used to evaluate the miR-155 expression.
Results: MiRNA-155 expression was higher in antrum mucosa of CNAG and AG compared to N ($p < 0.001$). Already presence of CNAG/AG without *H. pylori* was associated with increased miR-155 expression in antrum mucosa, while the highest expression was observed in *H. pylori*-related CNAG/AG in antrum ($p < 0.001$). Active *H. pylori*-infection (defined by direct microbiological cultivation and/or histological visibility), was associated with greater miR-155 expression compared to patients without detectable *H. pylori* despite *H. pylori*-positive serology ($p = 0.015$). In subgroup analyses regarding the bacterial virulence factors, expression of miR-155 was dependent on *H. pylori cagA* and *vacA* with highest expression in *cagA*+and *vacA s1i1m1* genotype strains ($p < 0.001$). Histological analyses showed the strong correlation of miR-155 expression with chronic lymphatic inflammation score in a *H. pylori*-dependent manner; however, the correlation to PNMs infiltration, atrophy or intestinal metaplasia was rather modest or missing.
Conclusion: Here, we suggest the link between *H. pylori* infection and mucosal miR-155 expression. According to our results miR-155 is a biomarker of chronic *H. pylori*-triggered inflammation in gastric mucosa. The extent of miR-155 expression is dependent on *H. pylori* genotype and may be predictive for progression of gastric mucosa inflammation. Further studies are needed to evaluate the biomarker potential in clinical settings.

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P1814 DIFFERENCES IN HEPCIDIN EXPRESSION IN THE GASTRIC MUCOSA BETWEEN PATIENTS WITH H. PYLORI-RELATED NODULAR GASTRITIS AND CHRONIC GASTRITIS

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Introduction: *Helicobacter pylori* (*H. pylori*) infection is a cause of unexplained iron-deficiency anemia (IDA). The mechanism through which *H. pylori* contributes to IDA is unclear, but may involve hepcidin, an antimicrobial peptide and a key hormone in iron homeostasis. We have found that serum levels of prohepcidin, the precursor of hepcidin, in patients with *H. pylori*-related disease (nodular gastritis (NG), duodenal ulcer (DU), gastric ulcer (GU), or gastric hyperplastic polyp (GHP)) are higher than those in uninfected adults, and are higher in *H. pylori*-infected patients with NG compared to those with DU, GU or GHP (*Helicobacter* 20(1):11-8. 2015). These data suggest that iron depletion in patients with H. pylori infection is due to hepcidin overproduction induced by *H. pylori*, and that the iron-deficient state in NG patients is strongly related to hepcidin. However, it is unclear why overproduction of hepcidin occurs in patients with NG in comparison with other *H. pylori*-infected patients. We have also shown that hepcidin is located in gastric parietal cells and lymphocytes in the deep layer of the lamina propria in the gastric mucosa (UEGW 2014). In the current study, we compared mucosal hepcidin expression and distribution immunohistologically between *H. pylori*-infected patients with NG and those with chronic gastritis.
Aims & Methods: The subjects were 15 patients with NG (M:F = 1:14) and 20 patients with chronic gastritis (M:F = 8:12). All patients were *H. pylori*-positive and all underwent esophagogastroduodenoscopy (EGD). During EGD, biopsy specimens were obtained from the greater curvature of the gastric antrum and corpus. These specimens were fixed in 10% formalin and embedded in paraffin. Immunohistochemical staining of sections from the specimens was performed using a monoclonal antibody against hepcidin (Abnova, Taiwan). The study was approved by the ethics committee of our institution. Written informed consent was obtained from all patients.
Results: Hepcidin was expressed in the cytoplasm and intracellular canaliculi of gastric parietal cells in both groups, with no differences in expression levels and patterns of distribution in the gastric mucosa. However, hepcidin was strongly expressed in the germinal center of lymph follicles in patients with NG. Lymph follicles were observed in the gastric antrum and corpus, and there was no difference in hepcidin expression between these lymph follicles.
Conclusion: Our results show that hepcidin is produced in lymph follicles in the gastric mucosa of patients with *H. pylori*-related NG. Histological findings of lymph follicles in the gastric mucosa are characteristics of NG. This suggests that overproduction of hepcidin in lymph follicles is a cause of the difference in iron-deficiency between patients with NG and other *H. pylori*-infected patients.
Disclosure of Interest: None declared

P1815 MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION IN TIMES OF INCREASING CLARITHROMYCIN RESISTANCE – A NATIONWIDE SURVEY AMONG GERMAN GASTROENTEROLOGISTS

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Introduction: Recommendations for diagnosis and treatment of *H. pylori* infection have been prosposed by national and European guidelines, with special attention to antimicrobial resistance. The aim of this study was to explore the current management strategies among gastroenterologists in Germany.
Aims & Methods: Between 12/2014 and 02/2015, a standardized questionaire including 19 multiple choice questions was sent to 1507 gastroenterologists in private practice. Data were captured and analyzed using the SurveyMonkey software.
Results: 540 questionaires (36%) were completely returned and analyzed. The following regimens were used for 1-line therapy in patients without penicillin intolerance: PPI + CLA + AMX 84%, PPI + CLA + MET 12%, bismuth quadruple therapy (BQT) 3%; in patients with penicillin intolerance: PPI + CLA + MET 81%, BQT 19%. The prevalence of CLA resistance in Germany was correctly estimated by 58% of responders. Country of origin and previous macrolide exposure were always assessed prior to 1-line therapy by 22% and 17% of responders (sometimes assessed by 40% and 34%). In 2-line therapy, BQT (42%) and levofloxacin triple therapy (24%) were the preferred regimens, however 29% of responders have used another clarithromycin-contaning triple therapy. After failure of 2-line therapy, 70% of responders

always performed antibiotic susceptibility testing, and 26% did so depending of the planned 3-line regimen.
Conclusion: Awareness of clarithromycin resistance as important risk factor for treatment failure appears to increase among gastroenterologists in Germany. Bismuth quadruple therapy is already the most commonly used 2-line regimen, and is increasingly being used in 1-line therapy of *H.pylori* infection. However, 30% of responders still do not adhere to current recommendations for 2-line therapy
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P1816 TREND IN *HELICOBACTER PYLORI* ERADICATION RATES BY SECOND-LINE BISMUTH-BASED QUADRUPLE THERAPY AND RELATED FACTORS IN ERADICATION THERAPY

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Introduction: Trends in eradication rates of *Helicobacter pylori* by second-line bismuth-based quadruple therapy, comprised of a proton pump inhibitor, metronidazole, bismuth and tetracycline, have been understudied.
Aims & Methods: The aims of this study were to identify *H. pylori* eradication rates using second-line eradication therapy during the last ten years and identify risk factors related to eradication failure. This study included 362 patients who were failed to first-line triple therapy and received 7 days of bismuth-based quadruple therapy between January 2005 and December 2014. We retrospectively demonstrated *H. pylori* eradication rates with respect to the year of therapy as well as demographic and clinical factors. *H. pylori* eradication was confirmed by a ^{13}C-urea breath test or a rapid urease test at least 4 weeks after the completion of bismuth-based quadruple therapy.
Results: The overall *H. pylori* eradication rate was 95.3%. Annual eradication rates from 2005 to 2014 were 100.0%, 92.9%, 100.0%, 100.0%, 100.0%, 97.4%, 100.0%, 93.8%, 84.4%, and 98.9% respectively, by per-protocol analysis. The eradication rate in second-line bismuth-based quadruple therapy decreased during the last ten years ($P = 0.003$). Multivariate analysis showed that diabetes mellitus (OR 5.84; 95% CI 1.78-19.20) was associated with the failure of *H. pylori* eradication therapy.
Conclusion: The efficacy of second-line bismuth-based quadruple therapy for *H. pylori* infection has decreased during the last ten years, however, the overall *H. pylori* eradication rate was still high. Therefore, bismuth-based quadruple therapy is worth considering as second-line therapies for *H. pylori* eradication in Korea.
Disclosure of Interest: None declared

P1817 COMPARATIVE EFFICACY OF FIRST LINE HELICOBACTER ERADICATION THERAPIES – A BAYESIAN NETWORK META-ANALYSIS

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Introduction: With the declined *Helicobacter pylori* (*H. pylori*) eradication rate, many new regimens have been developed. However, there is no systematic comparison to evaluate their efficacy.
Aims & Methods: We conducted a network meta-analysis in Bayesian framework to investigate the efficacy of different *H. pylori* eradication regimens. We searched Pubmed and Cochrane Central Register of Controlled Trials for randomized controlled trials that evaluated *H. pylori* eradication rate in treatment-naïve adults. Using a random effect model, we performed traditional pairwise meta-analyses and network meta-analysis by R software and WINBUGS, respectively.
Results: We identified totally 66 trials with 18,923 treatment naive patients. Network meta-analysis suggested that, when compared with clarithromycin-based triple therapy for 7 days, sequential therapy for 14 days (OR 4.18, 95% CI: 2.54-6.95) and concomitant therapy for more than 10 days (OR = 3.44, 95CI: 2.18-5.50) presented highest efficacy. Increasing age was inversely correlated with eradication rate.
Conclusion: From network analysis, we found the 14 days sequential therapy, and more than 10 days concomitant therapy had significantly higher eradication rate compared with the standard *H. pylori* eradication therapy.
Disclosure of Interest: None declared

P1818 OUR STRATEGY TO ERADICATION OF *H. PYLORI* IN PATIENTS WITH FREQUENT FAILURES OF ERADICATION

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Introduction: For the patients who had failed in eradication of *H. pylori* by the first and second-line regimens, the triple therapy with sitafloxacin, amoxicillin and PPI has been performed as the rescue therapy, which has yielded with relatively high eradication rates. However, some patients cannot clear their infection with this regimen. Strategy for patients allergic to penicillin has not been well established. In our institution, personalized therapy has been performed. Here, we report results of our strategies for patients who had failed in eradication more than three times and those who are allergic to penicillin.
Aims & Methods: DNA samples were extracted from gastric juice or tissue samples collected during endoscopy. CYP2C19 genotypes of patients and 23S rRNA mutations of *H. pylori* were measured by automated SNP analyzer. Culture test was performed to check the susceptibility of H. pylori to variety of antimicrobial agents. Based on CYP2C19 genotypes and susceptibility test results, we designed the personalized regimen.
Results: Incidences of clarithromycin and levofloxacin resistant strains were 80.0% and 60.0%, respectively, while that of sitafloxacin was 9.5%. The incidence of extensive metabolizer of CYP2C19 was 88/9%. The eradication rate with the triple PPI (high dose)/metronidazole/sitafloxacin was 83.9% (73/87), that with the triple PPI (high dose)/amoxicillin/ecabet sodium was 83.8% (31/37), that with the triple PPI (high dose)/amoxicillin/metronidazole was 100.0% (18/18). In patients allergic to penicillin, the eradication rate with the triple PPI/sitafloxacin/metronidazole therapy was 97.7% (43/44).
Conclusion: Personalized strategy based on CYP2C19 genotypes and susceptibility test results could yield with sufficient eradication rates in patients with frequent failures with the previous regimens.
Disclosure of Interest: None declared

P1819 NEW STRATEGY FOR THE QUICK ACHIEVEMENT OF POTENT GASTRIC ACID INHIBITION IN RAPID METABOLIZERS OF CYP2C19 WITH ONE-DAY PRETREATMENT WITH FOUR TIMES DOSING OF RABEPRAZOLE

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Introduction: Since proton pump inhibitors are metabolized by CYP2C19, it is difficult for the subjects with rapid metabolizer genotype of CYP2C19 (RMs) to attain sufficient acid inhibition with a PPI at the standard dose within a short term. Therefore, the eradication rates of *H. pylori* with the standard triple therapy in RMs are lower in comparison with those in intermediate (IM) or poor metabolizers (PM) of CYP2C19. Recent studies have indicated that rabeprazole (RPZ) 10 mg 4 times a day (qds) attains sufficient acid inhibition even in RMs. However, to dose rabeprazole 10 mg 4 times daily is costly and difficult to keep the good adherence, while it would be possible to keep the good adherence if the dosing period of 4 times daily is one day.
Aims & Methods: Then, we investigated the effect of one-day pretreatment with RPZ 10 mg qds on the following treatment with RPZ 10 mg twice daily (bd). The results were compared with the acid inhibitions attained with RPZ 10 mg qds in RMs and RPZ 10 mg bd in IMs and PMs.
Fourteen *H. pylori*-negative healthy volunteers, consisting of CYP2C19 RMs (n = 5), intermediate metabolizers (IMs) (n = 5), and poor metabolizers (PMs) (n = 4), were enrolled in the study. RMs received three different 1-week regimens in a crossover manner, as follows: (1) RPZ 10 mg bd from day 1 to 7, (2) RPZ 10 mg qds for 1 day (day 0) followed by RPZ 10 mg bd from day 1 to 7, and (3) RPZ 10 mg qds from day 1 to 7. IMs and PMs received RPZ 10 mg bd from day 1 to 7. For each regimen, 24-hour intragastric pH-monitoring tests were performed three times on days 1, 4 and 7.
Results: The median pH values with RPZ 10 mg bd, the pretreatment regimen and the RPZ qds in RMs were 3.18, 5.09, 4.42, respectively. Those on day 4 were 5.0, 4.87, 5.44, respectively. Those on day 7 were 4.72, 5.14, 5.59, respectively. The median pH values of IMs and PMs on day 1, 4, and 7 were 4.05 and 5.02 on day 1, 5.7 and 6.15 on day 4, and 5.96 and 6.29 on day 7, respectively. The pretreatment regimen in RMs attained the intragastric pH profile that was almost the same as those of RPZ qds and RPZ 10 mg bd in PMs and higher than that of RPZ bd in RMs on day 1. The similar results were observed on days 4 and 7.
Conclusion: We could demonstrate that the one-day pretreatment with RPZ 10 mg qds made it possible for RPZ 10 mg bd to attain sufficient acid inhibition in RMs of CYP2C19. Level of acid inhibition with this strategy was almost the same as those in IMs and PMs of CYP2C19. We are sure that this new strategy overcomes the insufficient eradication rates of *H. pylori* in RMs with low cost and is applicable for the treatments of other acid related disorders.
Disclosure of Interest: None declared

P1821 THE EFFICACY OF 10-DAY HIGH-DOSE METRONIDAZOLE CONTAINING SEQUENTIAL THERAPY FOR SECOND LINE *HELICOBACTER PYLORI* ERADICATION AFTER FAILURE OF STANDARD TRIPLE THERAPY

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Introduction: The global eradication rate of the standard first line triple therapy has fallen below 80% in many countries(1). It has been reported that the combination of levofloxacin and metronidazole shows a synergistic effect against anaerobic bacteria and high-dose metronidaozole can overcome metronidazole resistancy(2, 3). We hypothesized that the addition of high-dose metronidazole might also lead to a higher eradication rate for levofloxacin-based therapy in the treatment of *H. pylori* infection.
Aims & Methods: This pilot study aimed to assess the efficacy of 10-day high dose metronidazole containing sequential therapy treating patients after failure of standard triple therapy and to determine what clinical factors influenced the efficacy of salvage regimens.
Ninety-eight patients who failed *H pylori* eradication using the standard triple therapy (proton pump inhibitor bid, clarithromycin 500 mg bid., amoxicillin 1g bid.x 7 days) are randomly assigned to either 10-day levofloxacin containing triple therapy(esomeprazole 40 mg bid., amoxicillin 1 g bid., and levofloxacin 500 mg qd) or 10-day high-dose metronidazole containing sequential therapy (EALM-10, esomeprazole 40 mg bid., amoxicillin 1 g bid. for 5 days and followed by levofloxacin 500 mg qd and metronidazole 500 mg tid for 5 days). Repeated endoscopy with rapid urease test, histological examination and culture is performed at four weeks after the end of anti-*H pylori* therapy. If patients refused follow-up endoscopy, urea breath tests are conducted to assess *H. pylori* status. The rates of eradication, adverse events and compliance will be compared between groups by chi-square test, and the clinical and bacterial factors influencing the efficacy of salvage regimens are assessed by multivariate analysis.
Results: Eradication rates attained by EAL-10 and EALM-10 were 79.1%; 95% CI = 68.1-90.1% and 86.0%; 95% CI = 73.8-98.2%, $p = 0.372$ in the intention-to-treat analysis; 88.4%; 95% CI = 76.7-100% and 95.6%; 95% CI = 82.7-108.5%, $p = 0.213$ in the per protocol analysis. The adverse events were 18.6% vs. 22.2%, $p = 0.674$; The compliance was 100% in both groups. Univariate analysis showed that the clinical factors influencing the efficacy of *H. pylori* eradication therapy were antibiotics resistances to levofloxacin alone ($p = 0.011$) and dual resistances to both levofloxacin and metronidazole.($p < 0.001$).
Conclusion: This study suggests that 10-day high-dose metronidazole containing sequential could be a good treatment option as second line *H. pylori* eradication after failure of standard triple therapy as it achieved a grade "A" success rate.

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Disclosure of Interest: None declared

P1822 FIVE-YEAR SEQUENTIAL CHANGES IN ANTIBIOTIC RESISTANCES OF *HELICOBACTER PYLORI* AMONG PATIENTS WHO FAILED FIRST-LINE THERAPY

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Introduction: Antibiotics resistance of *Helicobacter pylori (H. pylori)* is the major cause of eradication therapy failure. Levofloxacin-based treatment, has been recommended after failure of first line standard triple therapy. Since the rapid development of quinolone resistance worldwide, especially in Asia, empiric second line quinolone-based therapy should be carefully monitored.
Aims & Methods
Aim: This study was designed to access the 5-year sequential changes in antibiotic resistances of *H. pylori* in Southern Taiwan after failure of first line standard triple therapy.
Methods: We analyzed 137 *H. pylori*-infected isolates from patients who failed eradication after standard first line triple therapies from January 2010 to December 2014. The *H. pylori* strains were tested for amoxicillin, clarithromycin, levofloxacin, metronidazole and tetracycline susceptibility using the E-test. The minimal inhibitory concentration (MIC) was determined by the agar dilution test. *H. pylori* strains with MIC values ≥ 0.5, ≥ 1, ≥ 1, ≥ 4 and ≥ 8 mg/L were considered to be the resistant breakpoints for amoxicillin, clarithromycin, levofloxacin, tetracycline and metronidazole respectively.
Results: High resistance rate was found in Clarithromycin (65-75%) and metronidazole (30-40%) among patients who failed first line standard therapy. The resistances of amoxicillin and tetracycline remained very low, but levofloxacin resistance was as high from 25% to 37.5%.

Table: Trend of antibiotics resistance rate annually in treatment of *H. pylori*

		Proportion (95% C.I.) (%)	P value Chi-square test for linear trend
Amoxicillin	2010	0 (-)	-
	2011	0 (-)	
	2012	0 (-)	
	2013	0 (-)	
	2014	0 (-)	
Clarithromycin	2010	70.8 (51.2-90.4)	P = 0.736
	2011	65.6 (48.2-83.0)	
	2012	65.0 (42.1-87.9)	
	2013	75.0 (54.2-95.8)	
	2014	70.7 (57.9-83.5)	
Levofloxacin	2010	37.5 (16.6-58.4)	P = 0.391
	2011	34.4 (17.0-51.8)	
	2012	30.0 (8.0-52.0)	
	2013	35.0 (12.1-57.9)	
	2014	26.8 (7.9-41.0)	
Metronidazole	2010	37.5 (16.6-58.4)	P = 0.312
	2011	25.0 (9.1-40.9)	
	2012	30.0 (8.0-52.0)	
	2013	30.0 (8.0-52.0)	
	2014	43.9 (23.3-59.8)	
Tetracycline	2010	0 (-)	P = 0.556
	2011	0 (-)	
	2012	10.0 (0-24.4)	
	2013	0 (-)	
	2014	2.4 (0-7.4)	

Conclusion: Increase in antibiotics resistance of *H. pylori* in southern Taiwan is becoming a problem for effective eradication in Taiwan. Clarythromycin should not be prescribed in second line *H.pylori* eradication. Levofloxacin-based second-line therapy should be used cautiously under careful monitoring the status of resistances in the area.
Disclosure of Interest: None declared

P1823 THE EFFECT OF *HELICOBACTER PYLORI* ERADICATION ON THE GASTROINTESTINAL FLORA IN PEPTIC ULCER

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Introduction: Recent reports indicated that *Helicobacter pylori* (*H. pylori*) might have an effect on the gastrointestinal flora, moreover, gastric commensal bacteria are observed in the development of peptic ulcer (PU), including gastric ulcer (GU) and duodenal ulcer (DU).
Aims & Methods: In our study, we aimed to observe the effect of *H. pylori* eradication on gastrointestinal flora in PU with completely cure. A case-control study in China was performed at Jiangsu Shengze Hospital between December, 2013 and April, 2014. Gastric mucus and feces specimens were used to extract bacteria DNA to quantify by real-time polymerase chain reaction.
Results: Following institutional ethical approval, 40 DU cases, 9 GU cases and 30 chronic gastritis cases served as controls were enrolled. Twenty-three DU patients and 3 GU patients completed the study. In *H. pylori*-related DU cases, after the eradication of *H. pylori*, an increase of Lactobacillus group, Clostridium leptum subgroup, Enterobacteria and a decrease of Clostridium coccoides subgroup were seen in the antrum. In the corpus, the number of Lactobacillus group was increased and the expression of Clostridium coccoides subgroup was significantly down-regulated. In feces samples, only the number of Lactobacillus group was increased. Moreover, the distribution was different between the female and the male patients with DU.
Conclusion: The existence of *H. pylori* in stomach suppressed the colonization of Lactobacillus group, Clostridium leptum subgroup and Enterobacteria. And Lactobacillus group could promote the healing of duodenal ulcer. Gender is a confounding factor in distribution and/or recolonization in DU patients.

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Disclosure of Interest: None declared

P1824 EFFICACY OF FIRST-LINE BISMUTH-CONTAINING QUADRUPLE THERAPIES WITH LEVOFLOXACIN OR CLARITHROMYCIN FOR THE ERADICATION OF *HELICOBACTER PYLORI* INFECTION: A ONE-WEEK, OPEN-LABEL, RANDOMIZED TRIAL

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Introduction: The aim of the present open-label, randomized control trial was to determine the clinical efficacy and safety of two one-week bismuth-containing quadruple regimens and one levofloxacin-based triple regimen for the eradication of *H. pylori* infection in treatment- naïve patients. The influence of susceptibility and host CYP2C19 polymorphisms on the efficacy was also evaluated.
Aims & Methods: Eligible patients were randomly to receive esomeprazole and colloidal bismuth pectin along with clarithromycin and amoxicillin (EBCA), esomeprazole and colloidal bismuth pectin along with levofloxacin and amoxicillin (EBLA), or esomeprazole along levofloxacin and amoxicillin (ELA) for one week. The primary outcome was the eradication rate in the intention-to-treat (ITT) and per-protocol (PP) analyses. This trial was registered with Chinese Clinical Trial Registry, Number: TRC13003256.
Results: Overall, 270 patients were randomized. The eradication rates in the above three groups were 80.25%, 89.66% and 81.93% in PP analysis and 72.22%, 86.66% and 75.56% in ITT analysis, respectively. The eradication rate of EBLA was significantly higher than that of EBCA ($P = 0.016$) in ITT analysis. No significant differences were found among these groups in terms of adverse effects and compliance. The efficacy was significantly affected by levofloxacin resistance for EBLA ($P = 0.01$) and ELA ($P = 0.04$), but not by polymorphisms of CYP2C19 gene for any of the three groups.
Conclusion: One-week bismuth-containing quadruple therapies and levofloxacin-based triple therapy can all obtain an acceptable eradication rate and levofloxacin-based quadruple regimen exhibits the highest eradication rate. The antibiotic resistant rate of levofloxacin was associated with the eradication rate.

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Disclosure of Interest: None declared

P1825 BROCCOLI SPROUT EXTRACT CONTAINING SULFORAPHANE (BSES) CAN PREVENT LIPID PEROXIDATION IN THE GASTRIC MUCOSA WITH *HELICOBACTER PYLORI* INFECTION

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Introduction: The standard triple therapy for *Helicobacter pylori* (*H. pylori*) eradication has become less effective, requiring the development of new treatment strategies that increase the eradication rate and reduce adverse effects. A broccoli sprout extract containing sulforaphane (BSES) exhibits anti-oxidative and bactericidal activity against *H. pylori*.
Aims & Methods: The aims of this study were to investigate whether BSES inhibits *H. pylori* infection density, and exerts an anti-oxidative effect on gastric mucosal damage. The enrolled subjects were randomized double blindly into three groups. Finally, 33 *H. pylori* (+) BSES treatment subjects (group A), 28 *H. pylori* (+) placebo subjects (group B), and 28 *H. pylori* (-) BSES treatment subjects (group C) were studied. *H. pylori* infection density was quantified indirectly by a C^{13}-urea breath test (UBT) and measurement of the ammonia concentration in gastric juice aspirate through the gastroscopic examination. Malondialdehyde (MDA), as an oxidative damage biomarker, and reduced glutathione (GSH), as an anti-oxidant biomarker, were measured in gastric mucosa by ELISA.
Results: BSES treatment did not significantly affect UBT values or ammonia concentration in Group A ($p = 0.634$, $p = 0.505$, respectively). BSES treatment did significantly reduce mucosal MDA concentrations in Group A ($p < 0.05$) and Group C ($p < 0.001$), while gastric mucosal GSH concentrations were not different before and after treatment in all three groups.
Conclusion: BSES did not inhibit *H. pylori* infection density. However, BSES prevented lipid peroxidation in the gastric mucosa and may play a cytoprotective role in *H. pylori*-induced gastritis.

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Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 09:00–14:00
SMALL INTESTINAL III – HALL 7

P1826 MAGNIVIEW ZOOM ENDOSCOPY FOR THE DETECTION OF MARKERS OF COELIAC DISEASE: A FEASIBILITY STUDY

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Introduction: Coeliac disease (CD) remains underdiagnosed. Previous studies have shown that 5-13% of patients with CD have undergone a previous gastroscopy where the opportunity to take duodenal biopsies and make a diagnosis had been missed. Clinicians may rely on the presence of endoscopic markers of CD to guide biopsy however these have been shown to lack the required sensitivity. A routine duodenal biopsy approach may solve this problem but this is time consuming and expensive. Methods to improve the macroscopic detection of CD at endoscopy to guide biopsy would seem advantageous. Magniview endoscopes are capable of 136x optical zoom without loss of definition. At this level of magnification it should be possible to identify blunting and absence of villi. We aimed to assess the feasibility of magniview in patients with suspected CD.
Aims & Methods: Patients with attending for a duodenal biopsy to diagnose CD were invited to take part. Appearances were graded on a 3-point scale: normal, partial villous atrophy or marked villous atrophy. All patients received 4 biopsies from the second part of the duodenum and at least 1 biopsy from the bulb. Concurrently serum for endomysial (EMA) and tissue transglutaminase (tTG) antibodies were taken at the time of endoscopy. Macroscopic markers of CD are compared VA on histology as the gold standard. Sensitivity of endoscopic markers was compared to a control group CD who had standard endoscopy using the Fisher exact test.
Results: 27 patients (52% female, mean age 49.6) have been recruited to date. 14 (51.9%) patients tested had positive serology. In total 13 (48%) patients were diagnosed with CD. All 13 patients diagnosed with CD were correctly identified on Magniview giving a sensitivity, specificity, PPV and NPV of 100% (72 - 100), 71% (42 - 90), 76% (50 - 92) and 100% (66 - 100) respectively. 4 patients had a false positive Magniview assessment. Of these 3 (75%) were felt to have partial villous atrophy. A single patient with false positive Magniview had a positive EMA and tTG and was felt to have marked villous atrophy in the bulb but normal D2. However biopsies were normal from both sites. Sensitivity of standard endoscopy for detecting VA in 89 patients with coeliac disease was inferior to Magniview (41.6% vs. 100%, $p < 0.0001$).
Conclusion: The addition of Magniview to standard endoscopy to aid the diagnosis of CD is feasible and currently has 100% sensitivity and negative predictive value. However a larger study in a lower prevalence population is required to fully elucidate the utility of Magniview in clinical practice.
Disclosure of Interest: None declared

P1827 PRE-ENDOSCOPY POINT OF CARE TESTING FOR COELIAC DISEASE IN ANAEMIA: A COST SAVING ECONOMIC MODEL

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Introduction: Current British iron deficiency anaemia guidelines recommend pre-endoscopy serological testing for coeliac disease (CD) and duodenal biopsy only for patients with a positive test. However many patients who attend endoscopy for investigation of anaemia do not have serology available. Thus the clinician is then committed to perform a duodenal biopsy. This gap in clinical practice could

be bridged by a rapid point of care test (POCT). We aimed, to assess the role of a novel POCT (Simtomax which detects IgA and IgG de-amidated gliadin peptide antibodies) in anaemic patients in a pre-endoscopy setting.
Aims & Methods: Group 1, a multicentre retrospective analysis of patients attending endoscopy for duodenal biopsy was undertaken in 4 UK hospitals (Whipps Cross, Hull, Bradford, Addenbrookes). The presenting characteristics and availability of serology prior to endoscopy was recorded. Group 2, patients presenting to endoscopy for investigation of anaemia were prospectively recruited. All patients received the POCT prior to their OGD and duodenal biopsy. Results were compared to the gold standard of villous atrophy.
Results: Group 1, 2339 patients (58% female, mean age 75.3) underwent duodenal biopsy. Serology was available prior to endoscopy in 912 patients (39%). Anaemia was the most common indication (934 patients, 39.9%). In anaemia, serology was available prior to OGD in 32%. On multivariate analysis of presenting characteristics patients with anaemia were less likely to have serology available than other groups (AOR 0.55 (0.44 - 0.70) $p < 0.0001$). CD was more likely if patients had serology done prior to their OGD (8.1% vs. 1.1%, $p < 0.0001$).
Group 2, 129 patients (64% female; mean age 56.6) being investigated for anaemia underwent POCT and duodenal biopsy. 23 patients (17.8%) were diagnosed with CD. Sensitivity, specificity, positive and negative predictive values of the POCT were 100% (82 - 100), 76% (67 - 84), 48% (34 - 63) and 100% (94 -100). In this cohort 81 (63%) duodenal biopsies could have been avoided. Based on a cost of £86 for duodenal biopsy this could result in a saving of £5,399 per 100 endoscopies. In a recent 3 month audit in Sheffield 479/2719 (18%) OGDs were performed for anaemia. Using the POCT in Sheffield could save £103,445 per year.
Conclusion: Availability of coeliac serology prior to endoscopy is poor. Diagnostic yield of duodenal biopsy is significantly higher in patients who have had serology prior to their endoscopy ($p < 0.0001$). An accurate POCT prior to endoscopy could significantly reduce the numbers of unnecessary duodenal biopsies resulting in significant cost savings. In this pilot cohort, Simtomax had 100% sensitivity. Further large studies are required.
Disclosure of Interest: None declared

P1828 COMPARISON OF THREE COMMERCIALLY AVAILABLE POINT OF CARE TESTS FOR COELIAC DISEASE

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Introduction: Coeliac disease (CD) remains an underdiagnosed condition. A rapid finger prick based point of care test (POCT) may increase uptake of serological testing in appropriate patient groups. There are 3 commercially available POCTs on the UK market and in continental European pharmacy outlets: Biocard an IgA tissue tranglutaminase (tTG) test (BHR pharmaceuticals); Celiac Quick Test (Biohit Healthcare) detecting IgA, IgG and IgM tTG and Simtomax (Tillotts Pharma) which detects IgA and IgG antibodies against deamidated gliadin peptides (DGP). A fourth POCT has also been developed but not marketed (Xeliac Test Pro, Personal Diagnostics), with availability being solely from the manufacturer and no published data existing supporting its validity. Of the 3 commercially available POCTs, there is a limited evidence base with significant ascertainment bias. For this reason we decided to compare 3 commercially available tests in an endoscopic setting.
Aims & Methods: Patients referred with a positive endomysial antibody (EMA) for duodenal biopsy to confirm CD were invited to take part. All patients had whole blood taken for repeat serum EMA, tTG and immunoglobulins. All patients were tested simultaneously with the 3 POCTs as per the manufacturers' instructions. All patients had quadrantic duodenal biopsies from the sec ond part of the duodenum as well as a duodenal bulb biopsy. Demonstration of villous atrophy (VA) on duodenal biopsy was required to diagnose CD.
Results: 82 patients (51.2% female, mean age 41.0) have been recruited. In 10 patients the EMA had normalised on repeat testing. None of these patients had VA on duodenal biopsy. 9 of these patients were referred with a weak EMA and had a negative tTG. One patient had a tTG of 10 times the upper limit of normal, and subsequent gluten challenge revealed a positive EMA and VA. Of the remaining 72 patients 59 new cases of CD were confirmed with the presence of villous atrophy, of the 13 EMA positive patients without VA 8 had Marsh 1 or 2 changes present with the remaining 5 patients having normal histology. Full sensitivity, specificity PPV and NPV for all of the tests compared to VA on duodenal biopsy are shown in table 1.

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Serum tTG	98.3 (89.7- 99.9)	34.8 (17.2 – 57.2)	79.5 (68.1 – 87.7)	88.9 (50.7 – 99.4)
Biocard	72.9 (59.5 – 83.3)	65.2 (42.8 – 82.8)	84.3 (70.9 – 92.5)	48.4 (30.6 – 66.6)
Celiac Quick Test	71.2 (57.7 – 81.9)	52.2 (31.1 – 72.6)	79.2 (65.5 – 88.7)	41.4 (24.1 – 60.9)
Simtomax	96.6 (87.3 – 99.4)	30.4 (14.1 – 53.0)	78.1 (66.6 – 86.6)	77.8 (40.2 – 96.1)

Conclusion: In this pilot data set Simtomax appears to be the most sensitive of the POCTs when compared to histology with similar results to serum tTG as screening test. Further work is required in larger cohorts and lower prevalence populations to confirm the utility of these tests in adult CD.
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P1829 FRAX SCORE CAN BE USED TO AVOID SUPERFLUOUS DXA SCANS FOR DETECTING OSTEOPOROSIS IN COELIAC DISEASE

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Introduction: The W.H.O. developed the FRAX tool to estimate the patient's 10-years probability of fracture, and this tool is widely used to decide which patients should undergo Dual energy X-ray Absorptiometry (DXA) scan and appropriate therapy; on the other hand, most guidelines recommend DXA for all patients at higher risk of osteoporosis (OP).
Aims & Methods
Aim: To evaluate if the FRAX tool can replace and/or optimize the DXA scan in coeliac disease (CD), a well known cause of secondary OP.
Methods: We prospectively enrolled all CD patients aged over 40 years diagnosed at our third level University Centre. At time of diagnosis all CD patients underwent FRAX score calculation for risk of major osteoporotic fracture and DXA scan (used as gold standard) in order to assess the accuracy of FRAX score in diagnosing/predicting OP. FRAX score was constituted by 10 variables (Table 1). The FRAX score was dichotomized as normal or pathological in accordance with the National Osteoporosis Guideline Group (NOGG). About DXA scan the diagnosis of osteoporosis was made in presence of a T-score $\leq$ -2.5 SD. Statistical analysis included use of X^2 and Mann-Whitney U test when indicated. To test the concordance between FRAX score and DXA scan the Cohen's k measure was applied. Diagnostic accuracy (sensitivity, specificity, positive and negative predictive values) of FRAX score versus DXA scan was evaluated by MedCalcSoftware. All differences were considered significant with a $p < 0.05$. The remain statistical analysis was performed using SPSS software.
Results: Finally, 60 CD patients were enrolled (M/F = 7/53; mean age 44.8 years). A pathological FRAX score was evident in 5 out of 60 patients (8.3%) while final diagnosis of OP based on DXA scan was made in 3 patients (5%) ($k = 0.6$); only 1 patient with OP (1.6%) showed a 10-year risk of major fracture > 10% according to NOGG criteria. About diagnostic accuracy, FRAX score showed: 0 true positive, 52 true negative, 5 false positive and 3 false negative cases (sensitivity of 0%, specificity 91%, positive predictive value 0%, negative predictive value 94%).
Table 1

1	Age		Between 40 and 90 years
2	Sex		Male/female
3	BMI	Weight	Kg
Height	cm		
4	Previous fractures		Yes/not
5	Parent Fractured Hip		Yes/not
6	Current Smoking		Yes/not
7	Glucocorticoids		Yes/not
8	Rheumatoid arthritis		Yes/not
9	Secondary osteoporosis		Yes/not
10	Alcohol 3 or more units/day		Yes/not

Conclusion: The prevalence of OP in CD patients at diagnosis appears to be quite low and only a small proportion of patients would require a DXA. The FRAX score could be an effective tool to avoid useless DXA scans in CD patients in view of its high negative predictive value. These results could contribute to improving the diagnosis of CD comorbidities by allowing for a significant reduction in diagnosis-related time and costs.
Disclosure of Interest: None declared

P1830 INVESTIGATION OF IRON DEFICIENCY ANAEMIA. DUODENAL BIOPSIES – ARE THEY WORTH IT?

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Introduction: The prevalence of iron deficiency anaemia (IDA) in adult men and postmenopausal women in the developed world is 2-5%[1]. British Society of Gastroenterology (BSG) IDA Guidelines recommend tissue transglutaminase (tTG) antibody as a screening test for coeliac disease. Indications for duodenal biopsies include patients with diarrhoea, weight loss and positive tTG serology. Where coeliac serology is positive, duodenal bulb and D2 biopsies should be taken[2]. BSG IDA Guidelines do not recommend duodenal biopsy for tTG negative, asymptomatic patients[3]. However a separate BSG guideline for

diagnosis of coeliac disease recommends duodenal biopsies in IDA patients irrespective of Coeliac serology due to the finding of seronegative coeliac disease[2].
Aims & Methods: This audit was carried out to assess adherence to BSG IDA Guidelines for duodenal biopsies in patients referred for IDA investigation with negative tTG antibodies. The study also set out to establish the positive diagnostic yield where biopsies were taken in the same cohort. Patients referred to Newcastle upon Tyne NHSFT adult IDA service between 2011 and 2014 identified as ttG negative and who underwent endoscopy were included.
Results: Two hundred patients were identified, median age 66 (range 19-91); 126 (63%) female and 74 (37%) Male. 114 (57%) patients had duodenal biopsies taken despite tTG being negative and asymptomatic. 28 (19.7%) patients were symptomatic and duodenal biopsies taken, though only 8 (28%) of these patients had 4 biopsy samples and none were from duodenal bulb. Where biopsies were taken, none confirmed coeliac disease. 5/142 (3.5%) patients biopsied had lymphocytic duodenitis but none of them were subsequently diagnosed or treated as coeliac disease.
Conclusion: Duodenal sampling in tTG negative patients did not yield any additional positive diagnosis of coeliac disease. This confirms the recommendations of BSG IDA guidelines. The results of this audit do not appear to support the recommendations made within the BSG coeliac disease guideline for duodenal biopsy being performed regardless of coeliac serology. However, the fact that only 4.9% of patients who had duodenal biopsies taken had duodenal bulb sampled, may limit this conclusion. More efficient use of local endsoscopy and pathology resources can occur by appropriate selection of patients on whom to perform duodenal biopsies.

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Disclosure of Interest: None declared

P1831 EXOCRINE PANCREATIC INSUFFICIENCY IN UNTREATED COELIAC DISEASE PATIENTS

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Introduction: Low faecal Elastase 1 (FE-1) is found in some coeliac disease (CD) patients before starting treatment with a gluten-free diet. This indicates that exocrine pancreatic insufficiency (EPI) is a contributing factor of malabsorption in this group.
Aims & Methods: We aimed to evaluate if EPI is a common finding in untreated CD patients. In patients with suspicion of coeliac disease, endoscopic secretin stimulation test (EST) was performed. During the same upper endoscopy procedure diagnostic duodenal biopsies were collected.
Duodenal bicarbonate and enzyme activity and FE-1 in patients was compared with results from healthy controls. The cut-off for EPI was FE-1 $<200\mu g/g$ or duodenal bicarbonate <80mmol/L.
Results: 16 CD patients were included and compared with 25 controls. 15 patients were classified as MARSH 3 (a-c) and one as MARSH 1. Our results are displayed in Table 1 (median (IQ range)). In all patients FE-1 was within normal range. Two patients had a bicarbonate concentration below cut-off. Duodenal chymotrypsin ($p = 0.003$) and elastase activity ($p = 0.039$) in patients were lower than in controls.
Conclusion: We did not find reduced faecal elastase or reduced secretin stimulated duodenal bicarbonate in this **small** group of untreated CD patients. However, we did find evidence of lower enzyme activity for duodenal chymotrypsin and elastase. This can be indicative of reduced enzyme output in untreated coeliac disease.

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Disclosure of Interest: None declared

P1832 SUBSTANTIAL PROPORTION OF CELIAC DISEASE PATIENTS IS MISLEADINGLY DIAGNOSED BASED ON SEROLOGY ONLY – DIAGNOSTIC AND THERAPEUTIC EXPERIENCE FROM A REAL-LIFE SETTING IN SWITZERLAND

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Introduction: This study investigates patient-reported symptoms, diagnostics and diet adherence in celiac disease (CD) patients in a real-life setting in Switzerland from a patient's perspective.
Aims & Methods: We performed a large systematic, nation-wide patient survey study among unselected CD patients in Switzerland. Results were analyzed in total and among selected subgroups by means of descriptive statistics.
Results: A total of 1689 patients (76.0% female; mean age 41.3y, range 0-92y, mean age at diagnosis 31.1y, range 0-83y) were analyzed. Only 15.3% initially presented with isolated gastrointestinal (GI) symptoms. The majority complained of both GI and non-specific symptoms (71.5%). 1.8% reported asymptomatic disease. Most of the patients presented to a non-gastroenterologist first (75.1%). However, physician's diagnostic delay was shorter – although not significantly – if patients presented to a gastroenterologist first (31.6 vs. 41.3 months, $p = 0.093$). Irritable bowel syndrome was considered significantly more often in those patients evaluated by a gastroenterologist (21.3% vs. 15.2%, $p = 0.01$). In summary, 35.8% of all CD diagnoses were done by a non-gastroenterologist. 16.4% were diagnosed based on serology and/or genetics, while in the majority diagnosis was established by a combination of serology and duodenal biopsy (46.9%) or biopsy alone (31.9%). Under the diagnostic lead of non-gastroenterologists ordered diagnostic tests differed significantly compared to gastroenterologists, with the latter using more often duodenal biopsy alone or in combination with serology (95.0% vs. 61.1%), while diagnosis without endoscopy was more frequently established by non-gastroenterologists (35.6% vs. 5.2%) ($p < 0.001$). 97.7% of all patients reported to adhere always (77.0%) or only with minor mistakes (20.7%) to a gluten-free diet. More than three out of four patients (79.8%) received expert nutrition counseling. This counseling was more often prescribed, if CD diagnosis was established by a gastroenterologist (83.5% vs. 76.0%, $p = 0.001$). Follow-up serology after 6 months was done in half of all patients (49.4%), while 69.9% had at least one follow-up serology within the first year after diet initiation. 39.7% had a follow-up endoscopy (median duration after diet initiation 12 months, range 1-600 months). 43.7% showed complete clinical remission (CR) 6 months after diet initiation. After 24 months proportion of CR was 61.7%.
Conclusion: According to patient's respective, more than 1 out of 3 CD patients are diagnosed by a non-gastroenterologist. Under the diagnostic lead of the latter, more than a third of patients receive their diagnosis by positive serology and/or genetics only, in evident violation of current diagnostic guidelines. Accordingly, there is a substantial risk of over-diagnoses and therefore unnecessary, potentially life long dietary restrictions as well as follow-up evaluations in these "sham-CD" patients. On the other hand, our data reveals a relevant discrepancy between treatment adherence and rate of CR, which suggests frequent misinterpretation of diet adherence despite a relatively high proportion of patients receiving specialized nutrition counseling.
Disclosure of Interest: None declared

P1833 PREVALENCE OF TREHALOSE MALABSORPTION AND INTOLERANCE IN PATIENTS WITH BLOATING AND ABDOMINAL PAIN

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Introduction: Symptoms suggestive of carbohydrate malabsorption (bloating, abdominal cramps, diarrhea) are a common clinical problem. The disaccharide trehalose (1-α-Glucopyranosyl-1-α-Glucopyranosid), which is present in mushrooms and invertebrates like crab or lobster, requires digestion by intestinal trehalase before its monosaccharide components can be absorbed. In 2001, regulatory approval as a novel food was granted in Europe. Due to its physical features, trehalose is increasingly used as a food-ingredient. In patients with a reduced activity of trehalase, trehalose passes into the colon, possibly resulting in symptoms of carbohydrate malabsorption. There are no data on the prevalence of trehalose malabsorption in symptomatic patients and only few data on the incidence of isolated trehalase deficiency, the highest prevalence of 8% having been found in Greenland.
Aims & Methods: 36 patients (10 male; median age: 35 yrs; range: 20-72yrs) who were referred for a lactose or fructose hydrogen breath test for the evaluation of symptoms suggestive of carbohydrate malabsorption were offered to be additionally tested for the presence of trehalose malabsorption and intolerance on a separate day. Following an established clinical protocol, simultaneous breath hydrogen (H_2) measurements and symptom assessments (bloating and pain on a scale from 0 to 5) were performed for up to 4 hours after ingestion of 50 g trehalose. Malabsorption (TM) was defined as an increase over baseline of breath H_2 concentration of ≥ 20 ppm ($\Delta H_2 \geq 20$ppm); intolerance (TIT) was defined as an increase over baseline in symptom score of ≥ 2 ($\Delta S \geq 2$). Occurrence of TM was compared with lactose (LM) and fructose malabsorption (FM), and of TIT was compared with intolerance of lactose (LIT) and fructose (FIT). Prevalence of hydrogen nonexcretors in our patient population is 17%.
Results: The table shows the number of patients with TM and TIT, and the relations between TM and LM or FM respectively, and between TIT or LIT and FIT, respectively.

		TIT		LM		FM	
		yes	no	yes	no	yes	no
TM	yes	*5*	*5*	*6*	*5*	*1*	*9*
	no	*4*	*22*	*13*	*12*	*2*	*24*
LIT	yes	*6*	*11*	–	–	–	–
	no	*4*	*15*	–	–	–	–
FIT	yes	*2*	*3*	–	–	–	–
	no	*7*	*24*	–	–	–	–

Conclusion: In patients with bloating, abdominal pain and diarrhoea, in whom carbohydrate malabsorption is considered, the prevalence of trehalose malabsorption is ***27.8%*** and of trehalose intolerance is ***25%***. There is a poor concordance between TM and TIT, and there is no relation between malabsorption or intolerance of trehalose with fructose or lactose malabsorption and/or intolerance. The use of trehalose in the food industry has to be declared more thoroughly.

Disclosure of Interest: None declared

P1834 H2 BREATH TEST WITHOUT SIMULTANEOUS SYMPTOM ASSESSMENT HAS NO CLINICAL RELEVANCE

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Introduction: Bloating, abdominal pain and diarrhoea are commonly evaluated by lactose or fructose hydrogen breath test (HBT) and a positive result is usually followed by dietary advice. New guidelines suggest that, in order to improve clinical relevance, HBT should be accompanied by symptom assessment.

Aims & Methods: Retrospective analysis of consecutive patients who were referred between 4/2009 and 8/2014 for lactose or fructose HBT with simultaneous symptom assessment. Following an established clinical protocol, simultaneous breath hydrogen (H2) measurements and symptom assessments (bloating and pain on a scale from 0 to 5) were performed for up to 4 hours after ingestion of 30 g fructose or 50 g lactose. Malabsorption (lactose: LM, fructose: FM) was defined as an increase over baseline of breath H2 concentration of ≥ 20 ppm ($\Delta H_2 \geq 20$ppm); intolerance (lactose: LIT, fructose: FIT) was defined as an increase over baseline in symptom score of ≥ 2 ($\Delta S \geq 2$). Prevalence of hydrogen nonexcretors in our patient population is 17% and prevalence of lactose malabsorption in the general population is 20%.

Results: Lactose HBT was performed in 497 patients (age 37 ± 15 yrs., 358 female, 139 male), and fructose HBT in 344 patients (age: 39 ± 14 yrs, 257 female, 87 male). The table shows the results of HBT($\Delta H_2 \geq 20$ppm) and symptom measurement ($\Delta S \geq 2$) after lactose and fructose, respectively. 28% of patients with LM had no LIT, and 43% with LIT had no LM; 47% of patients with FM had no FIT and 62% of patients with FIT had no FM.

Conclusion: In symptomatic patients referred for HBT, about the same proportion of patients have intolerance of fructose or lactose, or malabsorption of fructose or lactose. However, intolerance is more frequent than malabsorption of the respective carbohydrate and there is a poor concordance between malabsorption and intolerance, which cannot be accounted for by the prevalence of hydrogen nonexcretion. Our data suggest that in order to reliably detect those patients, who will most likely have an improvement on lactose or fructose reduced diet more emphasis has to be put on symptom assessment than on hydrogen breath test.

Disclosure of Interest: None declared

P1835 THE EFFICACY OF CHOLESTYRAMINE TREATMENT IN PATIENTS INVESTIGATED FOR BILE ACID DIARRHOEA

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Introduction: The enterohepatic circulation of bile acids is usually very efficient, with only 1-5% leaking into the large bowel with each cycle. When this homeostasis is affected, excess loss of bile acids into the large intestine can cause bile acid diarrhoea (BAD), which can be associated with ileal disease (type 1) or other predisposing GI conditions (type 3), or can be idiopathic (type 2), and diagnosed with the ^{75}SeHCAT test. The first-line treatment is cholestyramine, a luminal bile acid sequestrant.

Aims & Methods: We aimed to study the efficacy of cholestyramine treatment in a large cohort of patients referred for a ^{75}SeHCAT test as part of the investigation of chronic diarrhoea, and its relationship to gender and BAD subtype/presence or absence of predisposing conditions.

We reviewed 2112 consecutive ^{75}SeHCAT tests performed at the Sahlgrenska University Hospital between 1985 and 2005. Medical records from the referring clinic were also investigated. Patients were included if referred for the investigation of chronic diarrhoea and excluded if no information regarding the effect of cholestyramine treatment was available. Two definitions of an abnormal ^{75}SeHCAT test were used: ^{75}SeHCAT retention on day 7 of either $< 10\%$ or 15%.

Results: 409 cases (276 female, 133 male) were included, of whom 301 (74%, F:M gender = 200:101) had ^{75}SeHCAT retention $< 10\%$. Of these, 224 (74%) experienced symptomatic improvement on cholestyramine, without difference in efficacy between males and females ($p = 0.53$). Of the 107 patients with retention $> 10\%$ (range 10-67%), 68 (64%) also noted symptomatic improvement on cholestyramine ($p < 0.05$ compared to those with retention $< 10\%$), again with no gender difference. As seen in the table, median ^{75}SeHCAT retention was lower in patients with ileal disease, and cholestyramine showed less efficacy in patients with other predisposing GI conditions than ileal disease/resection. The results were similar when a cut-off of ^{75}SeHCAT retention on day 7 of 15% instead of 10% was used.

Conclusion: This retrospective study shows a high degree of efficacy in treating patients with chronic diarrhoea and a positive ^{75}SeHCAT test with cholestyramine. However, also patients with chronic diarrhoea and a normal ^{75}SeHCAT test seem to respond favourably to cholestyramine treatment. Future prospective studies are needed to elucidate underlying mechanisms behind these findings.

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Disclosure of Interest: None declared

P1836 LONG-TERM SAFETY OF TEDUGLUTIDE TREATMENT FOR PATIENTS WITH INTESTINAL FAILURE ASSOCIATED WITH SHORT BOWEL SYNDROME: POOLED DATA FROM 4 CLINICAL TRIALS

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Introduction: Teduglutide (TED) is indicated for the treatment of adult patients (pts) with intestinal failure associated with short bowel syndrome (SBS-IF) who are dependent on parenteral support (PS). In phase III randomised placebo-controlled trials, TED significantly reduced PS volume requirements and number of PS infusion days per week in pts with SBS-IF. Here, we present combined safety data from TED-treated pts in these trials and their respective open-label extension studies.

Aims & Methods: Safety data were pooled from 4 TED clinical studies conducted in adult pts with SBS–IF: two 24-week, double-blind, placebo-controlled trials with 2 respective open-label extensions of 28 weeks' and 2 years' duration.

Results: A total of 173 pts received subcutaneous TED (134 treated with 0.05 mg/kg/d and 39 treated with 0.10 mg/kg/d) across the 4 studies. Of these, 140 (81%) were treated with TED for ≥ 6 months and 111 (64%) were treated for ≥ 12 months; mean duration of TED exposure in all pts was 67 weeks. Most pts (97%) experienced ≥ 1 treatment-emergent adverse event (TEAE); the majority were mild (53%) or moderate (38%) in severity. TEAEs reported by $\geq 10\%$ of pts were 42% abdominal pain; 29% upper respiratory tract infection; 27% catheter sepsis or nausea; 20% headaches or asthenic conditions; 19% injection-site reactions; 18.5% abdominal distension or urinary tract infections; 18% gastrointestinal (GI) stoma complications; 17% catheter site–related reactions or febrile disorders; and $\leq 15\%$ vomiting, musculoskeletal pain, diarrhoea, fluid overload, hypersensitivity, or flatulence. The incidence rates of the most commonly reported GI adverse events (AEs) and fluid overload decreased over time during the treatment period **(Table)**. TEAEs that led to premature discontinuation occurred in 20% of pts (n = 34); the most common was abdominal pain (5%; n = 8). Serious AEs (SAEs) were reported by 58% of pts (n = 101). The only SAE that occurred in $\geq 5\%$ of TED-treated pts was catheter

Abstract number: P1831 Table 1

	FE-1(μg/g)	D-bicarbonate (meq/L)	D-chymotrypsin (U/mL)	D-elastase (U/mL)	D-amylase (U/mL)	D-lipase (10^3 U/mL)
CD patients (n = 16)median (interquartile range)	573 (464-670)	109.5 (96.3-116.0)	0.76 (0.63-1.77)*	0.044 (0.018-0.162)*	277 (209-498)	43.6 (25.9-90.5)
Controls (n = 25)median (interquartile range)	553 (425-587)	114 (101-122)	2,85 (1.88-3.83)	0.137 (0.087-0.192)	296 (196-517)	33.7 (28.7-43.1)

sepsis (25%; n = 43). As previously reported, 3 cases of malignant neoplasms occurred (metastatic adenocarcinoma, non–small-cell lung cancer, and squamous cell carcinoma). Only the metastatic adenocarcinoma was considered treatment related; this pt also had a history of Hodgkin disease treated with chemotherapy and radiation.
Conclusion: TED was generally well tolerated in pts with SBS-IF. No new safety signals were identified in the pooled analysis. The most frequently reported AEs were consistent with the underlying disease condition and the known mechanism of action of TED and tended to occur early in the treatment period. Data from phase III trials demonstrate the safety of long-term TED treatment.
Disclosure of Interest: U.-F. Pape Financial support for research: NPS Pharmaceuticals, Inc., Conflict with: advisory board member for NPS Pharmaceuticals, Inc., E. Delmaestro Conflict with: Employee of NPS Pharmaceuticals, Inc., B. Li Conflict with: Employee of NPS Pharmaceuticals, Inc., N. Youssef Conflict with: Employee of NPS Pharmaceuticals, Inc., D. Seidner Financial support for research: NPS Pharmaceuticals, Inc., Conflict with: advisory board member for NPS Pharmaceuticals, Inc.

P1837 TREATMENT OF INTESTINAL FOLLICULAR LYMPHOMA: PROSPECTIVE STUDY OF COMPARISON BETWEEN "WATCH AND WAIT" AND "RITUXIMAB-CONTAINING CHEMOTHERAPY"

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Introduction: The treatment modality of intestinal follicular lymphoma (FL) without mass formation causing bowel obstruction remains unstandardized.
Aims & Methods: In this study we compared "watch and wait" and "rituximab-containing chemotherapy (R-Chemo)" in the treatment of intestinal FL in a prospective way. Fifty eight patients met the GELF criteria for low-tumour-burden (LTB) and had no mass formation that could cause bowel obstruction. Informed consent of the treatment were obtained from these patients. Thirty-five cases [M/F = 17/18, age 62.5+/-9.6 (mean +/- S.D.), clinical stage (CS) (Lugano classification) I: 17, II1: 0, II2: 8, IV: 10, WHO grade 1: 34, 2: 1, 3: 0, follicular lymphoma international prognostic index (FLIPI) Low: 23, Intermediate: 11, High: 1] were followed by "watch and wait", median time period of 52 months (14-117 months). Twenty-three cases [M/F = 12/11, age 59.1+/-7.1 (mean +/- S.D.), CS I: 15, II1: 0, II2: 1, IV: 7, WHO grade 1: 23, 2: 0, FLIPI Low: 16, Int.: 6, High: 1] were treated by R-Chemo and followed for the median time period of 63.5 months (20-149 months). The CS was confirmed at diagnosis [1]. In "watch and wait" group, esophagogastroduodenoscopy (EGD) and blood test were performed every four months and positron emission tomography (PET) or CT scan [contrast-enhanced (CE+), from neck to pelvis], colonoscopy and capsule endoscopy (CE) were performed every year. In "R-Chemo" group, blood test, EGD and CE were performed every year and colonoscopy and CT scan were performed every two years after confirming CR of the lesions by BM aspiration, PET-CT or CT scan and double-balloon enteroscopy (DBE) at the end of treatment.
Results: There was no difference in age, sex, CS, WHO grade, FLIPI and BM involvement and clinical data between "watch and wait" and "R-Chemo". In "R-Chemo", both overall survival (OS) and event-free survival (EFS) of this group were 100%. In 2 patients under "watch and wait" the lesions enlarged and the macroscopic findings worsened. Another patient had CS progression and enlargement of the area of the lesions. Three patients had CS progression but they met the indication for "watch and wait" because they remained within the criteria for LTB and had no passage disturbance. In two patients, the gastrointestinal lesions transformed into diffuse large B-cell lymphoma and they received rituximab chemotherapy at 37 months and 49 months, which led to CR with no recurrence. OS of this group was 100%.
Conclusion: Comparing "watch and wait" and "R-Chemo", "watch and wait" is appropriate for the treatment of LTB intestinal FL even in the era of rituximab. However, transformation of intestinal FL to an aggressive lymphoma can occur. During "watch and wait" treatment, periodic observation of the clinical course is necessary.

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Disclosure of Interest: None declared

P1838 HIGHER OCCURRENCE OF DUODENAL LESION IN LYNCH SYNDROME RELATED TO MSH2

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Introduction: Lynch syndrom (LS) is the most common cause of inherited Colorectal Cancer (CRC) with autosomal dominant inheritance. LS patients have an increased risk for small bowel adenocarcinoma but routine screening of the small intestine is not recommended in both US and European recommandations (1,2). Esophagogastroduodenoscopy (EGD) is recommended at age 30–35 years for gastric cancer screening but there is no recommendation for systematic subsequent surveillance (1,2). The aim of the present study is to determine the prevalence of duodenal lesion (adenoma or adenocarcinoma) in a cohort of LS patients.
Aims & Methods: Patients identified with LS and registered in a tertiary center were identified. Patients with an upper endoscopy were included in the present study.
Results: 135 LS patients were identified. Six out of 135 (4.4%) had a duodenal lesion. Ratio male/female was 5/1. No patients had a known familial history of duodenal adenoma. The mean age at diagnosis was 59.7 years (range 51-71). Lesions were located in the descending duodenum (n = 2), the genu inferius (n = 2), the duodenal bulb (n = 1) or in the ampulla (n = 1). At the time of diagnosis lesions were adenomas with low-grade dysplasia (n = 1), high-grade dysplasia (n = 2), intra-muquous adenocarcinoma (n = 1) and invasive adenocarcinoma (n = 2). The incidence rate of LS patients with a MSH2 or MLH1 mutation was 6.8% (5 out of 74) and 2.9% (1 out of 35), respectively. No patients with MSH6 or EPCAM mutation experienced a duodenal lesion.
Conclusion: The prevalence of duodenal neoplasm was 4.4% in LS patients and was higher in MSH2 mutations carriers (6.8%) than in MLH1 patients (2.9%). Those data stressed the usefulness of an upper endoscopy survey in LS' patients, in particular in MSH2 mutations carriers.

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Disclosure of Interest: None declared

P1839 THE STRATEGY FOR THE EVALUATION OF JEJUNOILEAL INVOLVEMENT OF MALIGNANT LYMPHOMA PERFORMED BY COMBINATION OF DOUBLE BALLOON ENDOSCOPE (DBE), CAPSULE ENDOSCOPE (CE), AND FDG-PET

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Introduction: The examination of the jejunoileum is important to determine the most appropriate treatment. Here, we investigated the strategy for the evaluation by using double-balloon endoscope (DBE), capsule endoscope (CE), and FDG-PET to detect small intestinal (jejunoileum) involvement of malignant lymphoma.
Aims & Methods: A total of 89 cases of malignant lymphoma examined by DBE (84 cases), CE (5 cases), or both examination (1 case) between March 2004 and June 2014 were analyzed. Among them, FDG-PET was performed in 67 cases. As histopathological classification, 41 cases were with diffuse large B-cell lymphoma (DLBCL), 26 with follicular lymphoma (FL), 8 with MALT, 4 with mantle cell lymphoma (MCL), 3 with peripheral T-cell lymphoma (PTCL), 2 with enteropathy associated T-cell lymphoma (ETL), and 1 with T-lymphoblastic lymphoma (T-LBL), T-cell prolymphocytic leukemia (T-PLL), small lymphocystic lymphoma (SLL), anaplastic large cell lymphoma (ALCL), and Hodgkin disease (HD).
Results: Jejunoileal involvement of malignant lymphoma was observed in 51 cases (57.3%) by DBE or CE. As endoscopic findings by DBE, 19 cases had ulcerative type (17 DLBCL cases, 1 T-LBL case, 1 MALT case), 13 had elevated type (11 FL cases, 1 MALT case, 1 PTCL case), 11 had multiple lymphomatous polyposis (MLP) type (9 FL cases, 2 MCL cases), 2 had stenosis type (FL cases), 1 had diffuse-infiltrating type (1 TPL case), 4 had diffuse-infiltrating plus

Abstract number: P1834

		Lactose $\Delta H2 \geq 20ppm$			Fructose $\Delta H2 \geq 20ppm$		
		Yes	**No**	**Total**	**Yes**	**No**	**Total**
Intolerance ($\Delta S \geq 2$)	**Yes**	108	83	191(38,4%)	49	79	128(37,2%)
	No	42	264	306(61,6%)	43	173	216(62,8%)
Total		150(28.2%)	347(71,8%)	497	92(26,7%)	252(73,3%)	344

Abstract number: P1835

Predisposing clinical feature	F:M gender	Median 75SeHCAT (10th, 90th percentile)*	75SeHCAT < 15%*	75SeHCAT < 10%*	Cholestyra-mine effect*	Cholestyramine effect in patients with 75SeHCAT < 10%*
Ileal disease or resection (n = 31)	68% (F = 21)	2.0% (0.01, 6.24)	97% (n = 30)	97% (n = 30)	81% (n = 25)	83% (n = 24)
Other predisposing GI conditions (n = 184)	61% (F = 113)	7.9% (1.0, 23.6)	75% (n = 138)	61% (n = 113)	61% (n = 113)	65% (n = 73)
No predisposing conditions (n = 185)	50% (F = 93)	4.5% (0.7, 15.8)	90% (n = 167)	83% (n = 154)	79% (n = 147)	81% (n = 124)

*$p < 0.001$ when comparing the three groups. 7 day ^{75}SeHCAT retention not available in one case, pre-investigation diagnosis not available in 9 cases.

ulcerative type (2 ETL cases, 1 PTCL case, 1 MALT case), 2 had ulcerative plus elevated MLP type (1 FL case, 1 MCL case), 1 had elevated MLP type (MCL), and 1 had diffuse-infiltrating plus elevated type (DLBCL). As endoscopic findings by CE, 2 had elevated type (FL), 1 had ulcerative type (DLBCL), and 1 had MLP type (FL). Among 14 cases of FL having other gastrointestinal (GI) lesions, 13 cases (92.9%) showed jejunoileal involvement. However, compared to this rate, frequency of jejunoileal involvement in FL cases (58.3%, 7/12 cases) that did not have lesions in other GI tract was significantly low (P = 0.014). In the cases except FL, no relationship was seen between jejunoileal involvement and other GI lesions. The sensitivity, specificity, positive predictive value, and negative predictive value of FDG-PET in 23 FL cases were 27.8%, 80.0%, 83.3%, and 23.5%. In the 44 cases except FL, the values were 80.0%, 87.5%, 84.2%, and 83.1%, respectively. Three cases were perforated during chemotherapy. All cases complicated with perforation were ulcerative type of DLBCL.

Conclusion: FDG-PET is insufficient to detect jejunoileal involvement in FL cases. Therefore, DBE or CE should be performed when other gastrointestinal lesions are observed. In the cases except FL, FDG-PET is feasible for detection of jejunoileal involvement. Since DLBCL ulcerative type has a high risk of intestinal perforation during chemotherapy, the evaluation for jejunoileal involvement should be done by DBE for FDG-PET positive cases.

Disclosure of Interest: None declared

P1840 A SMALL BOWEL ADENOCARCINOMAS PROSPECTIVE COHORT: FINAL ANALYSIS OF DEMOGRAPHIC DATA FROM NADEGE STUDY

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Introduction: Small bowel adenocarcinoma (SBA) is a rare tumour poorly studied. Data are coming from register study or monocentric retrospective studies. The purpose of the NADEGE cohort (*Cohorte Nationale d' ADEnocarcinomes du GrêlE*) is to describe characteristics, prognosis and chemotherapy regimens of SBA in unselected patients (pts) at a nationwide level.

Aims & Methods: All the pts with a SBA diagnosed from January 2009 to December 2012 were enrolled in the NADEGE cohort. The study involved 72 centres in France that enrolled 330 eligible pts. This work presents the final demographic data.

Results: Pts were predominantly male (59%) and median age was 63 years [23-90]. WHO performance status was 0-1 in 52%, 2 in 30%, 3-4 in 17% and not determined (ND) in 21% of the pts. Primary locations were duodenum (60.9%), jejunum (21.2%), ileum (17%) and ND (0.9%). The tumour was poorly differentiated (18.8%), moderately (34.8%), well differentiated (38.2%) and ND (8.2%). A predisposing disease was reported in 72 (21.8%) cases: Crohn disease 28 (8.5%), Lynch syndrome 20 (6.1%), familial adenomatous polyposis (FAP) 7 (2.1%), celiac disease 6 (1.85%) and Peutz-Jeghers syndrome 2 (0.6%). The tumour was metastatic at diagnostic in 99 (30%) pts. Among 194 resected localized tumours the stage was 0 (3%), I (7.7%), II (31.4%), III (47.4%), and ND (10.8%). Adjuvant chemotherapy was performed in 10/61 (16%) stage II and 36/92 (39%) stage III. FOLFOX regimen was used in 36/46 (78%) pts. A palliative chemotherapy was performed in 73/99 (74%) of pts with metastatic disease. Oxaliplatin regimen was decided for 59% of the metastatic patient. According to the location of primary tumours duodenum/jejunum/ileum the tumours were: metastatic in 62/201 (31%), 20/70 (28%) and 17/56 (31%); poorly differentiated in 33/201 (16%), 11/70 (16%) and 18/56 (32%) of cases. Among the resected tumours, according to primary tumours duodenum/jejunum/ileum there were: T4 in 27/107 (25%), 21/50 (42%) and 10/34 (29%), stage III in 54/107 (50%), 19/50 (38%) and 19/34 (56%). Primary tumours were duodenum/jejunum/ileum: 7%/14%/78% (p = 0.0001%) in case of Crohn disease and 60%/35%/5% (p = 0.01%) in case of Lynch syndrome. Multivariate analysis revealed that Crohn disease was significantly associated with ileum primary ($p < 0.0001$) and Lynch syndrome with early tumour stage (p = 0.02).

Conclusion: NADEGE cohort is a large prospective SBA study. Predisposing disease is more frequent than in colorectal cancer. Several tumours characteristics differs according to predisposing disease. FOLFOX chemotherapy is the main regimen used in adjuvant and metastatic setting. Follow-up is ongoing until 2017 to determine predictive factor for survival.

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P1841 CLINICAL USEFULNESS OF VIRTUAL ENTEROSCOPY FOR SMALL INTESTINAL NEOPLASMS

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Introduction: We established a new imaging technique, virtual enteroscopy (VE) (or 3D-CT enteroclysis), to explore the small bowel (1). The examination is performed routinely to detect gross lesions in the small intestine in our hospital. The clinical performance of VE was analyzed to evaluate its safety, feasibility, and usefulness for small intestinal neoplasms.

Aims & Methods: Data on VE performed in our hospital from May 2011 to March 2015 were reviewed. In VE, the small bowel was inflated with air using a nasojejunal tube or nasoduodenal tube, CT images were taken, and then 3D overviews, virtual endoscopy views, and virtual dissection views were generated using a virtual colonoscopy system. Total volume of injected air, intra-intestinal pressure, and length of the depicted small bowel were recorded. Patients' data were analyzed and images of small intestinal neoplasms were collected.

Results: Seventy-three VEs were performed for 47 males and 26 females. Mean age was 45.9 +/- 18.2 y at the examination. Examinations were indicated for definite/suspected Crohn's disease in 33, intestinal obstruction in 28, suspected small intestinal neoplasms in 5, definite small intestinal neoplasms in 3, suspected Meckel's diverticulum in 1, NSAID enteropathy in 1, obscure gastrointestinal bleeding in 1, and enterovesicular fistula in 1. Vomiting/belching and abdominal pain (requiring pain medication) were noted in 9 and 2 patients, respectively, but no additional treatments were necessary. The volume of air and intraintestinal pressure were recorded in 59 examinations for patients without previous resection of the small bowel. Mean total volume of injected air was 1774 +/- 662 ml, mean maximum intraintestinal pressure was 2.66 +/- 0.88 kPa, mean length of the depicted small bowel was 496 +/- 103 cm, and whole small bowel tracing was achieved in 73% of these 59 examinations. Eight small intestinal neoplasms were depicted in 3 cases of intestinal obstruction, in 3 cases of suspected small intestinal neoplasms, and in 2 out of 3 cases of definite small intestinal neoplasms. There was no abnormal finding in one case of Peutz-Jeghers syndrome, in which all major lesions already had been removed by surgery. Surgery was performed for 6 cases, and diagnoses of gastrointestinal stromal tumor (GIST) in 3 cases and in 1 case respectively, of lipoma, Peutz-Jeghers type polyp, and adenocarcinoma. Clinical diagnosis of malignant lymphoma was made and chemotherapy was performed in 1 case. A submucosal tumor was confirmed by video capsule enteroscopy in 1 case, which has been followed up.

Abstract number: P1836 Table: Most Common GI AEs and Fluid Overload by Time to Onset From Start of Teduglutide Treatment

	Time Period, week						
AE, %	<4(n = 173)	4 to <12(n = 163)	12 to <24(n = 156)	24 to <36(n = 148)	36 to <48(n = 123)	48 to <72(n = 117)	≥72(n = 69)
Abdominal pain	23	12	9	10	2	0	10
Nausea	15	6	2	1	2	3	1
Abdominal distension	8	7	1	2	0	2	0
GI stoma complication	12	2	1	1	0	2	3
Fluid overload	5	4	3	3	1	3	0

Conclusion: VE can be performed safely and examination of the whole small bowel was possible in the majority of cases. VE can depict elevated lesions more than 1 cm, detect stenosis of small intestinal neoplasms, locate the position of the lesions, and present objective information for surgery and follow up. VE is a powerful new tool for diagnosis, pre-surgical evaluation, and follow-up for small intestinal neoplasms.

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Disclosure of Interest: None declared

P1842 ETIOLOGY OF SMALL BOWEL STRICTURES WITHOUT MASS LESION OR ASSOCIATED LYMPHADENOPATHY

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Introduction: The etiology of small bowel strictures without any mass lesion or associated lymphadenopathy has not been described. In tuberculosis endemic countries, these patients are routinely treated with empirical anti tubercular drugs whereas in western countries these patients are treated as Crohn's disease. However, no data is available which has provided the common etiologies of small bowel strictures and thus can justify such an approach.

Aims & Methods: This is a retrospective study which analyzed surgical case records from Jan 2000 to October 2014 at a tertiary referral centre in North India. The study included all adult patients with small bowel strictures without mass lesions or lymphadenopathy who remained undiagnosed after imaging and endoscopic studies and required surgical resection. Demographic parameters, symptoms, biochemical tests, imaging and endoscopic findings and histologic diagnosis were noted. Statistical analyses were performed using STRATA software version 12.1.

Results: 89 patients fulfilled the inclusion criteria and were included. The most common symptoms were colicky abdominal pain (90%), weight loss (67.4%), acute obstruction (43.8%), fever (33.7%), diarrhea (18%) and gastrointestinal bleeding (7.8%). Most common site of strictures was proximal small intestine (41.5%) and the etiologies were: tuberculosis (27%), Crohn's disease (23.5%), non-specific (20%), ischemic (10%), adenocarcinoma (9%), lymphoma (4.4%) and others (5.5%). Of 38 patients who had been started on presumptive anti tubercular therapy, only 11(28.9%) were confirmed as having intestinal TB.

Conclusion: Tuberculosis and Crohn's disease account for only 50% of the etiologies of small bowel strictures without mass lesion or lymphadenopathy. 13% may have a mitotic etiology We suggest the option of early surgical resection in this group of patients as it will provide both a definitive diagnosis and cure.

Disclosure of Interest: None declared

P1843 FOLLOW-UP IN PATIENTS WITH OGIB AND A NORMAL CAPSULE ENDOSCOPY: NO REASSURANCE IN THE LONG TERM

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Introduction: Obscure Gastrointestinal Bleeding (OGIB) accounts for approximately 5% of all digestive bleeding causes. Capsule Endoscopy (CE) is a useful tool to identify an underlying etiology located in the small bowel (SB). However, data on further long-term follow-up after a negative CE are scarce.

Aims & Methods: The aim of this study was to investigate the outcome of patients who presented with OGIB and had a normal CE of the SB. Standardized application forms of all patients that underwent CE for OGIB between 2002 and 2013 were reviewed and the subgroup of patients with a negative CE result was identified. Follow-up information of these patients was retrieved by contacting the referring physician and/or general practitioner.

Results: Between 2002 and 2013, 458 patients underwent CE for the indication of OGIB, from which 263 (57.4%) had a normal CE. Follow-up (FU) was available for 222 patients (Male, n = 114; Female, n = 108) of whom 81 presented with overt and 141 with occult bleeding. Median FU time was 52.8 months (range 1.4-139.6 months). Ninety-six patients underwent further diagnostics showing a cause for OGIB in 57 (diagnostic yield 59.4%). Further endoscopy was associated with a higher overall diagnosis rate, while further imaging and surgical exploration led to more SB diagnoses ($p < 0.05$). In 45 patients a previous origin for OGIB was suspected and CE was used to exclude a SB etiology. The final cause of anemia was identified in 102 patients: 33 in the upper GI tract, 26 in the lower GI tract, 24 outside the GI tract (i.e. gynaecological, renal, urological or hematological etiology) and 19 in the SB. Final outcome for the complete cohort of negative CEs was: 145 (65.3%) true negative (i.e. non SB cause of bleeding/resolved anemia), 19 (8.6%) false negative (i.e. SB cause of OGIB) and 58 (26.1%) ongoing bleeding without cause. Missed SB lesions were: angiodysplasia (n = 11), Meckel's diverticulum (n = 3), SB malignancy (n = 3), jejunal erosions (n = 1) and NSAID-induced SB ulcerations (n = 1). False negative CEs could not be predicted by age, gender, overt/occult bleeding, hemoglobin value or relevant comorbidities at the moment of CE. Bleeding resolved in 142/220 patients (64.5%) of which 83 underwent non-specific and 59 specific therapy for a GI cause of bleeding, leading to therapy success rates of 68.6% and 67.8% respectively. Worse prognosis was observed in patients with a higher age, comorbidities, using anticoagulants or needing transfusions before CE, following multivariate analysis ($p < 0.05$).

Conclusion: Further diagnostics can initially be deferred after negative CE. However, if anemia persists, diagnostics are warranted: repeat upper and lower GI endoscopy, followed by re-examining the SB. In 59.4% of these patients a cause for anemia was identified during FU, mostly outside the SB. Relevant SB lesions on the other hand account for 8.6% of all negative CEs. OGIB did not resolve in 35.5% of cases and, therefore, negative CEs do not reassure.

Disclosure of Interest: None declared

P1844 ASSESSMENT OF SERUM ANGIOPOIETIN LEVELS IN SMALL BOWEL DISORDERS; ARE THEY PREDICTIVE OF ANGIODYSPLASIA?

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Introduction: We previously presented our data identifying an association between serum abnormalities in the angiopoietin (Ang) pathway in patients with small bowel angiodysplasia (SBA) compared to healthy controls. Other studies have reported varied serum Ang levels in association with other conditions including Chronic Kidney Disease (CKD) and Inflammatory Bowel Disease (IBD). It is not yet known whether there is a differential expression profile of serum Ang1 and Ang2 levels in patients with SBA versus other small bowel conditions.

Aims & Methods: To measure serum levels of Ang1 and Ang2 in a cohort of patients undergoing Small Bowel Capsule Endoscopy (SBCE) for a variety of conditions.

After obtaining ethical approval we prospectively recruited patients undergoing SBCE for any indication in Tallaght Hospital over a 12 month time period. Phlebotomy was performed on participants the day of their SBCE and Haemoglobin and renal function was measured. Serum was collected, centrifuged and stored for batch analysis at -80^{0}C. Commercially available ELISA kits (R&D sytems) were used to measure Ang1 and Ang2 levels according to the manufacturer's guidelines. Patient demographics, indication for and result of SBCE were collected. Results of Ang1 and Ang2 were expressed as a mean and the mean ratio of Ang1/Ang2 in each group was calculated. Results were compared between groups depending on SBCE result using a student's t test with a p value of <0.05 considered statistically significant.

Results: To date, serum from 80 patients has been analysed. Patient's mean age was 52.6 years (16-80), and 48% (n = 38) were Male. The indications for SBCE were: iron deficiency anaemia 50% (n = 40), Suspected Crohn's disease 26% (n = 21), obscure gastrointestinal bleeding 20% (n = 16), and other 4% (n = 3). Of these, 56% (n = 45) had normal findings on SBCE, with positive findings in 44% including; SBA 16% (n = 13), small bowel inflammation 16% (n = 13, including Crohn's = 1)), other bleeding source (GAVE, Dieulafoy's lesion) 5% (n = 4), and other (malabsorption, lymphangiectasias) 7% (n = 5). There were significantly higher mean Ang2 levels in patients with SBA (5112pg/ml, range 2481-18184) compared to both normal findings [3320pg/ml (range 1188-9688), $p = 0.026$ 95% CI -3353.5649 to -231.7855] and inflammation [2629pg/ml (1465-3570), $p = 0.049$ 95% CI 0.7358 to 4966.6489]. There was no difference in Ang2 levels between patients with normal findings and small bowel inflammation, and Ang1 levels were similar in all 3 groups (49295pg/ml vs 49723pg/ml vs 43227pg/ml). There was a trend towards a lower median ratio of Ang1/Ang2 in the SBA patients (11) compared to both the normal (18) and inflammation (18) groups however this did not reach statistical significance. In the group overall there were 7 participants with CKD and 19 patients with anaemia, however, neither factor was associated with a higher mean Ang2 level with means of 4105pg/ml vs 3423pg/ml ($p = 0.36$) and 4106pg/ml vs 3128pg/ml ($p = 0.079$) respectively.

Conclusion: In keeping with our previous findings, elevated Ang2 levels appear selective for SBA in both a cohort referred for SBCE with a variety of conditions and in healthy controls. Ongoing assessment with larger numbers in each group, particularly in small bowel Crohn's disease are necessary to determine whether Ang expression could be a useful clinical selection tool for SBCE.

Disclosure of Interest: None declared

P1845 CONCORDANCE BETWEEN SINGLE-BALOON ENTEROSCOPY, CAPSULE ENTEROSCOPY AND IMAGING IN THE ASSESSMENT OF SMALL BOWEL LESIONS

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Introduction: Baloon-enteroscopy, capsule enteroscopy (VCE), CT-scan and MRI are useful procedures for the diagnosis of small bowel lesions.

Aims & Methods: The aim was to evaluate the agreement and find predictors of non-agreement between baloon-enteroscopy and other diagnostic methods. Retrospective analysis of patients undergoing single-baloon enteroscopy between 2010 and 2014 and comparative analysis with VCE, CT-scan and MRI.

Results: From 165 procedures (101 anterograde and 64 retrograde), 56% were performed in men; mean age was 53 ± 18 years. Gastrointestinal bleeding of obscure origin was the main indication for performing baloon-enteroscopy (n = 54, 33%), followed by Crohn's disease (n = 39, 23%) and polyp/polyposis syndromes (n = 27, 16%). The procedure was normal in 52 (32%), and the main findings were angiodysplasia (n = 23, 14%), ileitis (n = 18, 11%), polyps (n = 14, 9%), stenosis (n = 14, 9%), inflammatory anastomotic changes (n = 12, 7%) and

jejunitis (n = 8, 5%). More than half (n = 102, 62%) had prior VCE and 51 (30%) had CT or MRI within the previous 3 months. The agreement between single-baloon enteroscopy and VCE was good (kappa = 0.60, $p < 0.001$) and was moderate/poor (kappa = 0.39, $p < 0.001$) relative to imaging procedures. No differences were found between the procedures regarding enteroscopy indications nor between anterograde and retrograde enteroscopy.
The agreement between enteroscopy and VCE was good in patients without previous small bowel surgery (kappa = 0.617, $p < 0.001$) and only moderate (kappa = 0.538, $p = 0.021$) in patients with surgical history. The agreement was also higher in jejunal lesions (good: kappa = 0.546, $p < 0.001$) than in ileal lesions (moderate: kappa = 0487, $p < 0.001$).
Conclusion: The agreement between single-baloon enteroscopy and VCE was good, being moderate/poor between enteroscopy and imaging. The absence of previous small bowel surgery and lesions with jejunal location were predictors of greater agreement. The agreement was similar in concerning the different indications for ballon-enteroscopy.
Disclosure of Interest: None declared

WEDNESDAY, OCTOBER 28, 2015 09:00–14:00
NUTRITION III – HALL 7

P1846 ASSESSMENT OF OBESITY AND HEART FIBROSIS DEGREE IN PATIENTS WITH METABOLIC SYNDROME

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Introduction: Assessment of obesity and heart fibrosis degree in patients with metabolic syndrome.
Aims & Methods: To investigate level of obesity and heart fibrosis in patients with metabolic syndrome (MetS).
The research has included 76 patients, from them 43 patients were with MetS (basic group), 33 patients without MetS (control group). Epicardial fat thickness was evaluated by transthoracic echocardiogram. Besides the above we conducted noninvasive evaluation of the fraction of fibrosis of the myocardium we used echocardiography, then we obtained the resulting images in "jpeg" format and analyzed them using software "Image J v.1.4(NIH,2009)". The level of leptin and galectin-3 was investigated.
Results: Patients in the basic group had significantly higher epicardial fat thickness than control (4.67 ± 1.7 vs 2.66 ± 1.15 mm, $p < 0.001$). An average volume fraction of fibrosis in the interventricular septum had significant difference in the groups studied ($22.6 \pm 4.45\%$ in basic and $16.5 \pm 3.95\%$ in control groups, $p < 0.001$). An average level of leptin in the group with MetS was significantly higher in comparison with control - 41.89 ± 33.28 and 17.64 ± 16.87 ng/ml, $p < 0.001$. Correlation was revealed between the level of leptin and weight (r = 0.55), the body mass index (r = 0.70), the degree of obesity (r = 0.33), abdominal obesity (r = 0.47), waist circumference (r = 0.62), level of glucose (r = 0.33) and the high-density lipoprotein (r = -0.30), epicardial fat thickness (r = 0.60), degree left ventricular hypertrophy (r = 0.26), systolic (r = 0.39) and diastolic (r = 0.35) blood pressure, hepatic (r = 0.42) and pancreatic (r = 0.37) steatosis, $p < 0.05$.
An average level of galectin-3 in the group with MetS was reliably higher (1.89 ± 1.71 ng/ml), compared with the control group (1.03 ± 0.22 ng/ml), $p = 0.006$. Positive correlation was revealed between the level of galectin-3 and left ventricular hypertrophy (LVH) (r = 0.29), coronary heart disease (r = 0.35), chronic heart failure (r = 0.34), fraction of fibrosis of the myocardium (r = 0.24), hepatic (r = 0.43) and pancreatic (r = 0.24) steatosis, NAFLD fibrosis score (r = 0.23), $p < 0.05$.
Conclusion: 1) Patients with MetS have epicardial fat thickness significantly more often than control group, leptin level has been correlated with obesity as for the whole body so for the heart, which can be a powerful predictor of cardiovascular disease.
2) All patients with MetS had significantly higher rates of galectin-3. More strongly pronounced septal fibrosis was found in patients with MetS.
3) Relationship has been found between the level of leptin, galectin-3 and diseases related to MetS. The basis of the progress of these diseases is depending on inflammation and fibrosis, and thus it could indicate that these molecules are playing role in development of these pathological processes. That can serve as a prognostic marker of development of cardiovascular and hepatobiliary diseases.
Disclosure of Interest: None declared

P1847 THE CLINICAL SIGNIFICANCE OF MARKERS OF FIBROSIS AND APOPTOSIS IN PATIENTS WITH METABOLIC SYNDROME

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Introduction: The clinical significance of markers of fibrosis and apoptosis in patients with metabolic syndrome.
Aims & Methods: To investigate the level of serum markers of obesity (leptin), apoptosis (caspase-8) and fibrosis (galectin-3) in patients with metabolic syndrome (MetS).
The research has included 76 patients, from them 43 patients were with MetS (basic group), 33 patients without MetS (control group). The average age of 61 ± 12 years. There was held comprehensive survey, including the determination of the level of leptin, caspase-8, galectin-3.
Results: An average level of leptin in the group with MetS was significantly higher in comparison with control - 41.89 ± 33.28 and 17.64 ± 16.87 ng/ml, $p < 0.001$. Correlation was revealed between the level of leptin and weight (r = 0.55), the body mass index (r = 0.70), the degree of obesity (r = 0.33), abdominal obesity (r = 0.47), waist circumference (r = 0.62), level of glucose (r = 0.33) and the high-density lipoprotein (r = -0.30), epicardial fat thickness (r = 0.60), degree left ventricular hypertrophy (r = 0.26), systolic (r = 0.39) and diastolic (r = 0.35) blood pressure, hepatic (r = 0.42) and pancreatic (r = 0.37) steatosis, $p < 0.05$.
An average level of galectin-3 in the group with MetS was reliably higher (1.89 ± 1.71 ng/ml), compared with the control group (1.03 ± 0.22 ng/ml), $p = 0.006$. Positive correlation was revealed between the level of galectin-3 and left ventricular hypertrophy (LVH) (r = 0.29), coronary heart disease (r = 0.35), chronic heart failure (r = 0.34), fraction of fibrosis of the myocardium (r = 0.24), hepatic (r = 0.43) and pancreatic (r = 0.24) steatosis, NAFLD fibrosis score (r = 0.23), $p < 0.05$.
An average level of caspase-8 in a group with MetS was significantly higher than in control (0.28 ± 0.19ng/ml and 0.2 ± 0ng/ml, $p < 0.05$). Positive correlation was revealed between the level of caspase-8 and obesity (r = 0.23), BMI (r = 0.47), atherosclerosis of aorta (r = 0.31), hepatic (r = 0.46) and pancreatic (r = 0.35) steatosis, non-alcoholic steatohepatitis (r = 0.31), gastroesophageal reflux disease (r = 0.25), $p < 0.05$.
Conclusion: In the patients' group with MetS, compared with the control group, were identified the following higher levels of: 1) Leptin, at the level correlated with parameters of obesity, as for the whole organism, as well as for the heart' obesity, which can be a powerful predictor of cardiovascular disease; 2) Caspase-8, as one of the markers of apoptosis 3) Galectin-3, as one of the promising markers of the heart' and liver' fibrosis. Relationship has been found between the level of leptin, caspase-8, galectin-3 and diseases related to MetS, that can serve as a prognostic marker of adverse development of cardiovascular and hepatobiliary diseases.
Disclosure of Interest: None declared

P1848 THE EFFECT OF INTRAGASTRIC BALLOON TREATMENT ON ADIPONECTIN AND ENDOTHELIN-1 LEVELS IN MORBID OBESE PATIENTS

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Introduction: The prevalence of morbid obesity is gradually increasing throughout the world. Morbid obesity is associated with hypoadiponectinemia and endothelial dysfunction. Intragastric balloon treatment (IBT) is an effective therapeutic modality for obesity.
Aims & Methods: The aim of this study was to evaluate short-term outcome of IBT on endothelin-1, adiponectin levels along with metabolic profile and body fat. This single-center study was conducted on 34 consecutive morbid obese patients, 6 man and 28 women, aged 37.1 ± 9.2 years who inserted intragastric balloon (IB) with body mass index (BMI) of 47.6 ± 8.2 kg/m^2. Patients were evaluated by taking a detailed account of their medical, social, psychological, dietary, family and medical history. All subjects' BMI and homeostasis model assessment of insulin resistance (HOMA-IR) were determined. Metabolic variables were obtained after an overnight fasting. The main determined variables included waist circumference, weight loss, insulin sensitivity, lipid profile, alanin transaminase (ALT), aspartat transaminase (AST), and gamma glutamil transferase (GGT), and body fat percentage. All variables including endothelin-1 and adiponectin were studied before inserting and just after removing of IB. Body fat percentage was measured using a body composition analyzer (TANITA TBF300). All endoscopic examinations were performed under conscious sedation with midazolam in the Endoscopy Unit of Diskapi Yildirim Beyazit Education and Research Hospital, Gastroenterology Clinic. Intragastric balloon were removed after 6 months of inserting in all patients. All metabolic variables including adiponectin and endothelin-1 levels were compared with 20 healthy volunteers as a control group.
Results: Anthropometric variables, ALT, triglyceride, waist circumference, fasting glucose, HOMA-IR, adiponectin, and endothelin-1 levels were significantly different between groups ($p < 0.05$). Anthropometric variables, Endothelin-1, ALT, GGT, and body fat percentage decreased significantly in all patients with IBT ($p < 0.05$) but Adiponectin levels increased significantly after this treatment. However, no significant changes were found in AST, fasting glucose, insulin, and HOMA-IR levels. When the lipid profile was assessed, a significant decrease was found only in triglyceride levels. We found a significant positive correlation between endothelin-1 levels and BMI, and GGT (r = 0.366, p = 0.01 and r = 0.453, p = 0.01, respectively).
Conclusion: In morbid obese patients, weight loss achieved by IBT is associated with a decrease in serum endothelin-1 levels and anthropometric variables, and an increase in adiponectin levels.

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Disclosure of Interest: None declared

P1849 THE EVALUATION OF THE EFFECT OF INTRAGASTRIC BALLOON THERAPY ON NASH PREDICTING BIOMARKERS IN MORBID OBESE PATIENTS

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Introduction: Nonalcoholic fatty liver disease is a common morbidity of obesity, and it may be complicated with non-alcoholic steato-hepatitis (NASH) which proceeds to end stage liver disease. In the recent years, M30, an apoptotic cell death serum marker, has promising results leading to determine underlying NASH in obese patients. However, it is still confused whether M30 values in serum declines with improving in body mass index (BMI) values.

Aims & Methods: We aimed to investigate the rate of abnormal NASH biomarkers in morbid obese patients undergoing intra-gastric balloon placement and the effect of intra-gastric balloon placement on the same biomarkers after a six months of therapy.

We analyzed 30 morbid obese (BMI > 40 kg/m^2) patients. In all patients, we placed an intra-gastric balloon, Bioenterics Intragastric Balloon, after a detailed evaluation. None of our patients had a history of heavy alcohol drinks (greater than 20gr/day for man, 10gr/day for woman). Laboratory tests for investigation of other hepatic diseases including viral hepatitis, Wilson disease, hemochromatosis and auto-immune hepatitis were performed and all of them were excluded. In addition to routine laboratory investigations, serum M30 levels (M30 Apoptosese Elisa, Peviva, Sweden) were measured for this intervention. Serum samples obtained before insertion of intra-gastric balloon and after removing of intra-gastric balloon via peripheral venous blood, and stored at -80© were used for M30 level determination. Routine labaoratory parameters, BMI, HOMA-IR index, and mean platelet volume (MPV) values were measured at the baseline and at the end of the treatment.

Results: A total of 30 morbidly obese patients undergoing intra-gastric balloon placement and 40 lean controls, were included into the study. As expected, BMI level, HOMA-IR index and triglyceride levels were higher in patient group than controls. AST and GGT levels were similar in each group, but ALT was higher in patients. Both MPV, a possible indicator to predict underlying hepatic inflammatory process, and APRI index, a score able to predict underlying significant hepatic fibrosis, did not differ in controls from the patient group. The serum apoptotic index, M30 level, was found to be significantly higher in obese patients compared with lean controls. After the six months period of intra-gastric balloon placement therapy, mean BMI values decreased from 47.6 to 41.7 kg/m^2, accompanied with ALT and GGT levels. However, surprisingly, serum M30 levels, APRI index, MPV values and triglyceride levels did not decrease during the treatment period in patient group.

Conclusion: The current study revealed that intra-gastric balloon placement did not improve underlying NASH biomarkers, even though the therapy achieved in success with decreasing the BMI values significantly. Not only M30, but also some other indexes, predicting underlying NASH, did not revealed improving by the intra-gastric balloon placement therapy.

Disclosure of Interest: None declared

P1850 VISCERAL OBESITY AND SERUM GAMMA-GLUTAMYL TRANSFERASE LEVELS: IS THERE A RELATIONSHIP?

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Introduction: Visceral obesity has been associated with increased oxidative stress. Serum gamma-glutamyl transferase (GGT) activity changes in response to oxidative stress and some studies have shown that an increase in serum GGT levels is associated with an increased risk of cardiovascular events.

Aims & Methods: The aim of this study was to assess serum GGT levels in patients with visceral obesity and its relationship with metabolic abnormalities found in visceral obesity. Methods: We evaluated waist circumference (WC), blood pressure (BP) and serum levels of GGT, highty sensitive C-reactive protetin (hsCRP), fasting glucose, total cholesterol, LDL, HDL, triglycerides, ApoA1, ApoB, ApoCIII, Lp(a) and oxLDL in 100 asymptomatic non-smoking patients (56 men/44 women) aged 50–60 years, without cardiovascular disease. Subjects were grouped as it follows: i) WC < 102 cm in men and WC < 88 cm in women; ii) WC ≥ 102 cm in men and WC ≥ 88 cm in women (Adult Treatment Panel III).

Results: The group with visceral obesity had higher levels of GGT (women: 31.8+/−14.7 vs 47.8+/−14.8 U/L, $P<0.05$; men: 37.3+/−21.1 vs 49.0+/−19.5 U/L, $P<0.05$), hsCRP (women: 3.44+/−2.23 vs 2.04+/−1.9mg/L, $P<0.05$; men: 3.51+/−2.90 vs 2.13+/−1.87 mg/L, $P<0.05$), systolic BP (women: 135+/−24 vs 146+/−27 mmHg, $P<0.05$; men: 134+/−22 vs 145+/−25 mmHg, $P<0.05$), triglycerides (women: 129.5+/−54.0 vs 172.9+/−13.0 mg/dl, $P<0.05$; men: 132.2+/−18.0 vs 183.6+/−76.0 mg/dl, $P<0.01$), oxLDL (women: 59.8+/−14.7 vs 67.8+/−14.8 mg/dl, $P<0.05$; men: 61.3+/−21.1 vs 69.0+/−19.5 mg/dl, $P<0.05$) and ApoCIII (women: 8.8+/−4.3 vs 12.3+/−9.9 mmHg, $P<0.01$; men: 9.4+/−5.3 vs 14.4+/−7.4 mmHg, $P<0.01$), and lower levels of HDL (women: 56.8+/−11.8 vs 47.3+/−13.4 mg/dl, $P<0.05$; men: 44.5+/−11.1 vs 36.8+/−10.4 mg/dl, $P<0.05$) and ApoA1 (women: 170.0+/−22.6 vs 152.6+/−27.6 mg/dl, $P<0.05$; men: 144.6+/−22.3 vs 133.2+/−24.2 mg/dl, $P<0.05$). There was no significant difference ($P>0.05$) between the groups in fasting glucose, LDL, ApoB and Lp(a) levels. Serum GGT levels was positively correlated with WC ($r=0.86$, $P<0.01$), systolic BP ($r=0.27$, $P<0.05$), plasma triglyceride ($r=0.29$, $P<0.05$), ApoCIII ($r=0.38$, $P<0.05$), LDL ($r=0.51$, $P<0.01$) and ApoB ($r=0.54$, $P<0.01$); and negatively correlated with HDL ($r=-0.26$, $P<0.01$) and ApoA1 ($r=-0.20$, $P<0.01$).

Conclusion: The study showed that high WC was strongly associated with high levels of GGT and other serum markers of oxidative stress. These results suggested that weight loss or other approaches aimed to reducing visceral obesity may have a significant impact on the prevention of subclinical inflammation and thus reducing cardiovascular risk.

Disclosure of Interest: None declared

P1851 ANTARCTIC MICROORGANISMS AS PRODUCERS OF A NEW ANTIOBESITY DRUG

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Introduction: Today the prevalence of obesity continues to increase that provides challenge to scientists. Obesity is strongly associated with systemic inflammation and with oxidative stress. A recent study showed the presence of melanin in visceral adipose tissue (VAT). This pigment as known has antioxidant and anti-inflammatory properties. In this connection we were interested in study of antiobesity properties of exogenous polyphenolic complex melanin obtained from the antarctic black yeast *Nadsoniella nigra*.

Aims & Methods: So, the aim of our work was to study the influence of melanin on the development of obesity in rats induced by monosodium glutamate (MSG). The study was carried out on 60 white rats, that were divided into 3 groups: intact, MSG- and MSG + melanin groups (10 male and 10 female rats in each group). Newborn rats of MSG- and MSG + melanin groups were administered with MSG (4 mg/g, 8 µl/g, subcutaneously) at 2nd -10th days of life. Since the age of 1 month, rats of MSG-group were treated with water (0.25 ml/100 g), rats of MSG + melanin groups – with melanin (1 mg/kg) dissolved in water (0.25 ml/100 g). Polyphenolic complex melanin was extracted from the antarctic black yeast *Nadsoniella nigra* harvested from Galindez Island and cultivated. Introduction had been performed intermittently (two-week courses alternated with two-week breaks) for 3 months. In 4-month rats anthropometrical parameters and VAT mass were estimated, and adiponectin in serum and leptin in VAT were measured by ELISA.

Results: In 4-month rats we diagnosed the changes of the anthropometrical parameters and significant increase of VAT mass that suggest development of visceral obesity. In male rats, there were more pronounced changes. It was also established the decrease of serum adiponectin by 60% ($p < 0.01$) in males and by 42% ($p < 0.05$) in females and increase of VAT leptin level adiponectin by 61% ($p < 0.01$) in males and by 46% ($p < 0.05$) in females compared with intact rats. The introduction of melanin prevented the visceral obesity that was confirmed by reduction of index Lee and body mass index. Melanin decreased the VAT by 44.5% ($p < 0.01$) in males and by 41.2% ($p < 0.01$) in females compared with MSG-group. Melanin also restored the adipose tissue endocrine function under the conditions of obesity: in MSG + melanin group the level of adiponectin and leptin didn't differ from the intact group.

Conclusion: Thus, the introduction of melanin prevents MSG-induced obesity in rats and recovers the endocrine function of adipose tissue. The antarctic black yeast *Nadsoniella nigra* can be proposed as a producer of the antiobesity drug.

Disclosure of Interest: None declared

P1852 SELECTED ASPECTS OF "BONE – FAT AXIS" FUNCTION IN HEALTHY INDIVIDUALS AND PATIENTS WITH PANCREATIC CANCER

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Introduction: Recently much attention has been paid to a potential biochemical "cross-talk" between metabolisms of the adipose tissue (AT) and bone (marrow), termed "bone-fat axis". We hypothesized that selected substances participating in this molecular "dialog" are associated with body mass and peripheral trafficking of bone marrow-derived stem cells (BMSCs) in both - generally healthy individuals and patients with obesity-associated malignancy, such as pancreatic adenocarcinoma.

Aims & Methods: We performed an analysis of systemic levels of selected substances involved in the regulation of bone (marrow) homeostasis (parathormone, calcitonine, osteopontin, osteonectin, stem cell factor [SCF] and fibroblast growth factor-23) in 35 generally healthy volunteers and 35 patients with pancreatic cancer. Results were correlated with i) absolute numbers of circulating BMSCs enumerated using flow cytometry and ii) body mass values. Additionally, subcutaneous and visceral/omental AT levels of the aforementioned molecules were analyzed in lean and overweight/obese individuals.

Results: Intensified steady-state trafficking of only Lin-CD45 + CD133 + hematopoietic stem/progenitor cells was observed in overweight/obese individuals, and this was associated with BMI values. Also elevated levels of both osteonectin and SCF were detected in overweight/obese patients, and these concentrations were also correlating with BMI values. In comparison to healthy individuals, cancer patients had significantly higher osteopontin levels, and lower values of both osteonectin and osteonectin/osteopontin ratio. While in cancer patients no significant correlation was observed between BMI values

Abstract number: P1856

Nutrients\Groups	Normal production of H2/CH4,n = 24	H_2 - producersn = 154	CH4 - producersn = 33	H_2 + CH4- producers n = 60
Protein, g	81.7 ± 36.0	87.6 ± 45.4	95.9 ± 40.2	84.9 ± 35.4
Fat, g	81.6 ± 42.4	94.6 ± 52.7	76.3 ± 30.9	96.3 ± 48.8
Mono/disaccharides, g	115.3 ± 66.4	113.3 ± 73.1	104.2 ± 52.2	104.3 ± 46.7
Carbohydrates, g	257.3 ± 91.7	254.9 ± 136.7	228.7 ± 104.6	242.6 ± 112.3
Fiber, g	19.9 ± 10.4	16.7 ± 10.8	19.2 ± 10.3	15.8 ± 10.8
Energy, kkal/day	2107.4.1 ± 803.9	2245.0 ± 1079.2	1998.1 ± 738.2	2201.1 ± 842.8
Protein kkal/Total kkal	0.155 ± 0.025*(vs CH4)	0.158 ± 0.040**	0.196 ± 0.065**	0.159 ± 0.051**
Fat kkal/Total kkal	0.339 ± 0.074	0.375 ± 0.083	0.342 ± 0.065	0.386 ± 0.114
Carbohydrates kkal/Total kkal	0.498 ± 0.092	0.457 ± 0.097	0.456 ± 0.114	0.444 ± 0.117
Fat/protein, g/g	0.98 ± 0.24	1.12 ± 0.39***	0.82 ± 0.21***	1.21 ± 0.63***
Carbohydrates/protein, g/g	3.32 ± 0.93	3.13 ± 1.26*	2.73 ± 1.54*	3.0 ± 1.1
MDS/carbohydrates, g/g	0.43 ± 0.18	0.44 ± 0.17	0.47 ± 0.15	0.45 ± 0.15

and numbers of circulating BMSCs, peripheral trafficking of CD34 + KDR + CD31 + CD45-endothelial progenitor cells and CD105 + STRO-1 + CD45-mesenchymal stem cells was associated with values of osteonectin/osteopontin ratio, which were also correlating with BMI ($r = 0.52$; $p < 0.05$). AT levels of examined substances were similar to those measured in plasma, with an exception to osteonectin values, which were around 10-times lower.

Conclusion: Our study highlights that osteonectin, osteopontin and SCF may serve as probable communicating signals between bone (marrow) and AT in both generally healthy individuals and patients with pancreatic cancer. We postulate that these molecules may be overlooked biochemical players linking body mass and BMSCs with obesity-associated cancer development and/or progression in humans.

Disclosure of Interest: None declared

P1854 RANDOMISED CLINICAL TRIAL: CASEIN GLYCOMACROPEPTIDE FOR ACTIVE DISTAL ULCERATIVE COLITIS – A PILOT STUDY

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Introduction: In ulcerative colitis (UC), dietary supplements and nutritional strategies may have anti-inflammatory properties and improve the disease course. We investigated the effects of casein glycomacropeptide (CGMP), a fraction of bovine whey protein, in active UC.

Aims & Methods

Aim: To compare clinical, endoscopic, and mucosal disease activity markers before and after 4 weeks treatment with either CGMP plus usual oral mesalazine dose or increase to maximum oral mesalazine dose in patients with active distal UC.

Methods: In a randomised open label intervention study, 24 adult patients with active UC involving 10-40 cm of the distal colon, were randomised in a 2:1 ratio to their usual treatment plus a daily nutritional supplement of CGMP 30 grams or dose escalation to 4.800 mg oral mesalazine daily (standard treatment) for 4 weeks. Acceptance and adherence to CGMP up to 8 weeks were documented.

Results: After 4 weeks treatment, 10/16 (63%) who received CGMP had unchanged or decreased Simple Clinical Colitis Activity Index (SCCAI) which was similar to those on standard treatment, 4 of 8 (50%) ($p = 0.67$). The number of patients where SCCAI fell 3 or more did not differ between the two groups, 9/16 (56%) versus 4/8 (50%) ($p = 0.77$). Changes in disease extend and severity were similar between the two groups. CGMP was well tolerated and accepted by the patients.

Conclusion: The addition of CGMP as nutritional therapy to standard treatment was safe and well accepted by patients with active distal UC. The disease-modifying effect of CGMP was similar to that of mesalazine dose escalation.

Disclosure of Interest: None declared

P1855 PLASMA AND TISSUE PHOSPHOLIPIDS FATTY ACID PROFILE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Fatty acids (FAs) are involved in the development of inflammatory processess. Their role in the ethiopathogenesis od inflammatory bowel diseases (IBD) is not fully understood. It is known that w-3 FAs and their derivates have an anti-inflammatory effects. In contrast, w-6 FAs are mainly pro-inflammatory compounds. There are some indications that patients with inflammatory bowel diseases are at risk of essentials fatty acid insufficiency (EFAI) and, in severe cases, of essentials fatty acid deficiency (EFAD).

The aim of the study was to assess the relationship between the FAs content in mucosa phospholipids of non-involved/involved colon tissue and clinical activity of the disease in patients with inflammatory bowel diseases.

Aims & Methods: The aim of the study was to assess the relationship between the FAs content in mucosa phospholipids of non-involved/involved colon tissue and clinical activity of the disease in patients with inflammatory bowel diseases. The study included 18 patients with IBD (16 pts with ulcerative colitis, 2 pts with Crohn's disease), M/F 9/9, mean age 60.2 ± 15.5 years. Ten patients without abnormality under colonoscopic examination (M/F 4/6, mean age 47.2 ± 18.7 years) served as controls. Non-involved and involved colon tissues as well as one blood sample were taken from each patient. The clinical activity of the disease was assessed using the Mayo and the Geboes activity index. Total lipids were extracted from tissues homogenate with chloroform-methanol. Next, lipid fractions were isolated from the mixture using aminopropyl columns. After solid phase extraction, serum and tissue FAs of phospholipids fraction were measured by GC-FID. The results of individual FAs were expressed as percentage of total FAs.

Results: Significantly higher the mean percentage of C16 and C18 as well as the sum of saturated FAs in colon tissue of IBD patients as compared to control has been found ($p < 0.03$-0.0005). In contrast the mean percentage of C18:1cis, C18:2(w-6), C18:3(w-3), C20:5(w-3) as well as monounsaturated FAs were significantly lower in IBD patients as compared to control ($p < 0.02$-0.001). Significant negative correlation between clinical activity of the disease and w-3 FAs, w-6 FAs and the PUFA/noPUFA ratio were observed ($r = -0.364$, $p < 0.04$; $r = -0.413$, $p < 0.02$; $r = -0.434$, $p < 0.01$, respectively). In contrast, significant positive correlation between clinical activity of the disease and the ratio of C16:1/C18:2 and the sum of saturated FAs were found ($r = 0.624$, $p < 0.0001$; $r = 0.3689$, $p < 0.01$). The significantly higher the mean percentage of C20:5(w-3) and the sum of polyunsaturated FAs (PUFA) ($p < 0.05$ in both cases) in IBD patients as compared to control were the only differences found in serum.

Conclusion: The fatty acids profile in mucosa of colon tissue phospholipids in patients with inflammatory bowel diseases is characteristic for Essential Fatty Acids Insufficiency.

Disclosure of Interest: None declared

P1856 NUTRITIONAL PATTERNS IN IBS PATIENTS WITH H2/CH4 HYPERPRODUCTION

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Introduction: Bacterial overgrowth is highly prevalent among IBS-patients. Overproducing H_2 or CH_4 was found to correlate with the spectrum of IBS symptoms. However, the influence of diet in IBS patients to H_2/CH_4 production was still not assessed.

Aims & Methods: 271 patients were classified according to Rome III criteria (124 IBS-D and 147 IBS-C) were evaluated by lactulose breath test (LBT, Gastrocheck, Bedfont Scientific Ltd, UK). LBT was performed using 10 g of lactulose mixed in 150 mL of water in fasting condition, and breath samples collected every 15 min for a 180-min period. "H_2-producers" and "CH_4-producers" were defined as the patients produced $H_2 > 20$ ppm more than the basal sample and patients with mean CH_4 excretion of 12 ppm or more, respectively. Dietary pattern of patients was assessed using 24/48/72h recall or validated food diary.

Results: Among patients tested by LBT, 24 patients demonstrated normal production of H_2/CH_4; 33 were CH_4-producers, 154 were H_2-producers and 60 demonstrated excess production of both gases. No differences were found in consumption of energy or protein, fat and carbohydrates between groups of patients with different production of H_2/CH_4 (Table 1). Differences in nutrient delivery and nutritional groups were unreliable because of marked variability in variables due to differences in food intake (men and women, skinny and fat, etc.). However, after recalculation of energy quota of nutrients (kcal from nutrient/total kcal) CH_4-producers demonstrated significantly higher quota of protein in the diet in compare to H_2-producers and to CH_4/H_2-producers ($p = 0.01$ both). Protein quota in patients with normal production of H_2/CH_4 was also significantly lower than in CH_4-producers ($p = 0.03$). In the diet of H_2-producers and H_2+CH_4 producers fat/protein ratio was significantly higher than in the diet of CH_4-producers ($p < 0.001$ and $p = 0.001$, respectively). Analysis of the ratio carbohydrate/protein also showed a significantly lower content of carbohydrates in the diet CH4-producers than in the other groups

(CH_4/H_2-producers, $p = 0.006$, H_2-producers $p = 0.018$, normal production of H_2/CH_4 $p = 0.035$).
Conclusion: Excessive CH4 production is associated with high protein and low carbohydrate quota in the diet. The diet of H2-producers or H2 + CH4 producers, is characterized by increased fat quota. Therefore, treatment options of the bacterial overgrowth should include specific dietary modifications.
Disclosure of Interest: None declared

P1857 USING A FUNCTIONAL FOOD PRODUCT CONTAINING INULIN AND CURCUMIN IN IBS PATIENTS WITH CONSTIPATION (IBS-C): A COMPARATIVE CONTROLLED STUDY

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Introduction: Irritable bowel syndrome (IBS) is the world's most common gastrointestinal functional disorder and is associated with several social and economic costs. Health-related quality of life is often impaired in patients with IBS. The therapeutic approach to patients with IBS is based on symptoms, and fibers may play an important role in treatment.
Aims & Methods: Functional food product (jelly) containing 2g inulin, 5mg curcumin and 2mg of pyridoxine was developed and evaluated. Fifty patients (5 males and 45 females, mean age 47.3 ± 16.3 yrs) fulfilling the Rome III criteria for IBS-C were randomly assigned into two groups: one received standard diet plus two jellies a day for 2 weeks and control group received standard diet. Response to therapy was recorded on a daily basis using Likert scale of abdominal pain, bloating and feeling of incomplete bowel emptying. Stool was evaluated by frequency of bowel movement and Bristol stool scale. Quality of life assessed by IBSQoL questionnaire before and after the treatment.
Results: Using functional food jelly was associated with positive effect on the stool parameters (0.6 ± 0.25 vs 1.15 ± 0.65 t/d in stool frequency, $p = 0.001$, 2.62 ± 1.22 vs 3.99 ± 1.27, index Bristol scale, $p = 0.001$), reduces the severity of abdominal pain (1.69 ± 0.44 vs 1.36 ± 0.44 Likert scale points, $p = 0.001$), bloating (2.03 ± 0.90 vs 1.55 ± 0.83 points of Likert scale, $p = 0.02$) and a sense of incomplete bowel emptying (2.25 ± 0.98 vs 1.68 ± 0.92 points of Likert scale, $p = 0.001$), as well as an increase in quality of life (64.5 ± 13.5% vs 81.2 ± 9.1%, $p = 0.05$). Patients in control group have improvement in abdominal pain (2.16 ± 0.98 vs 1.8 ± 0.55 Likert scale points, $p = 0.05$) and bloating (2.42 ± 0.94 vs 2.16 ± 0.81 Likert scale points, $p = 0.05$) only. No adverse events were observed in both groups.
Conclusion: In conclusion, functional food jelly jelly containing inulin, curcumin and pyridoxine is well tolerated and associated with improve in stool parameters, abdominal pain, Bristol stool scale index and increase in quality of life in patients with IBS-C.
Disclosure of Interest: None declared

P1858 XYLOGLUCAN AND GELATIN FOR THE TREATMENT OF ACUTE GASTROENTERITIS IN CHILDREN: RESULTS OF A RANDOMIZED, CONTROLLED, OPEN-LABEL, PARALLEL GROUP, MULTICENTRE, NATIONAL CLINICAL TRIAL

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Introduction: Gelatin or xyloglucan are currently used for gastroenteric disorders, although data from randomized studies are needed to completely assess the efficacy of these products in acute diarrhea or acute gastroenteritis in different types of patients.
Aims & Methods: To assess the efficacy, safety and time of onset of the antidiarrheal effect of xyloglucan and gelatin (Tasectan Plus®, containing xyloglucan and gelatin of animal origin) in children with acute gastroenteritis receiving oral rehydration solution (ORS).
This randomized, controlled, open-label, parallel group, multicentre, clinical trial included children (from 3 months to 12 years old) with acute gastroenteritis of infectious origin.
Children were randomized to receive a 5-day treatment. Both control and active groups received ORS and active group also received Tasectan Plus® (one sachets/8 hours in children younger than 3 years and 2 sachets/8 hours in children between 3 and 12 years). Diarrheal symptoms and safety were assessed in 3 visits (baseline, at 2 and 5 days) and by phone call at 10 days, and by fulfillment of a diary card by the parents or legal representatives.
The number and characteristics of stools (type 6 and 7 on Bristol Scale) and the evoluation of other diarrheal symptoms (nausea, vomiting, abdominal pain, flatulence, fever and dehydration) were assessed during the 72 hours previous to baseline and, after inclusion, at 24-hour intervals (during the first day of treatment assessments were performed at 1, 3, 6, 12 and 24 hours). Occurrence of adverse events was recorded during the whole study period.
Results: A total of 36 patients (58.3% girls; age: 13.9% ≤ 1 year, 47.2% 1-5 years, 25.0% 5-10 years, 13.9% > 10 years) were included (n = 18 in each group). The group treated with xyloglucan/gelatin and ORS had a better evolution in almost all parameters than the group receiving ORS alone. A faster onset of action was observed in the xyloglucan/gelatine group compared with the control group, since at 6 hours, xyloglucan/gelatin produced a statistically significant higher decrease in the number of type 7 stools (0.11 vs 0.44; $p = 0.027$). At days 3 and 5, xyloglucan/gelatin was also able to produce a statistically significant higher reduction of type 6 and 7 stools in comparison with ORS alone ($p = 0.026$ and 0.034, respectively). A better evolution for nausea, vomiting and abdominal pain was also recorded for the xyloglucan/gelatin group, although the differences vs the control group were not statistically significant. Xyloglucan/gelatin plus ORS was safe and well tolerated, without the occurrence of adverse events throughout the study.
Conclusion: Xyloglucan/gelatin is a fast, efficacious and safe option for the treatment of acute gastroenteritis in children, with a rapid onset of action in reducing diarrheal symptoms.
Disclosure of Interest: None declared

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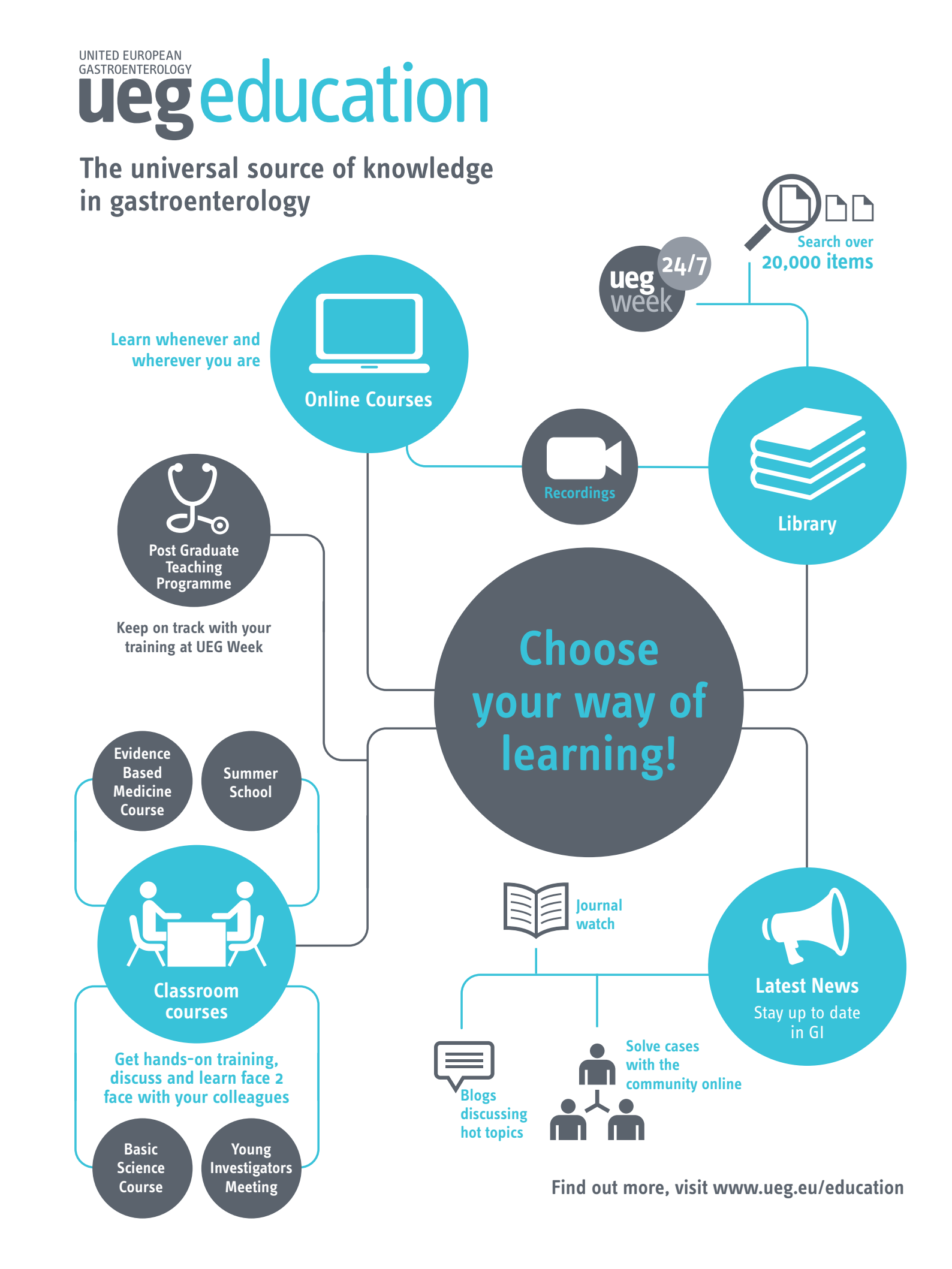
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